



Clinical trial results:

A Phase 3 Study to Evaluate the Efficacy, Safety, and Effect of Withdrawal and Retreatment With Brodalumab in Subjects With Moderate to Severe Plaque Psoriasis: AMAGINE-1

Summary

EudraCT number	2012-000651-13
Trial protocol	PL DE
Global end of trial date	02 October 2015

Results information

Result version number	v1 (current)
This version publication date	16 October 2016
First version publication date	16 October 2016

Trial information

Trial identification

Sponsor protocol code	20120102
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01708590
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Amgen, Inc.
Sponsor organisation address	One Amgen Center Drive, Thousand Oaks, CA, United States, 91320
Public contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com
Scientific contact	IHQ Medical Info-Clinical Trials, Amgen (EUROPE) GmbH, MedInfoInternational@amgen.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	02 October 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary and secondary objectives of this study were to evaluate the efficacy of brodalumab compared to placebo on measures of psoriasis at weeks 12 and 52.

Protection of trial subjects:

This study was conducted in accordance with applicable country, Food and Drug Administration, and International Council for Harmonisation (ICH) Good Clinical Practice (GCP) regulations/guidelines. All subjects provided written informed consent before undergoing any study-related procedures, including screening procedures.

The study protocol, amendments, and the informed consent form (ICF) were reviewed by the Institutional Review Boards (IRBs) and Independent Ethics Committees (IECs). No subjects were recruited into the study and no investigational product (IP) was shipped until the IRB/IEC gave written approval of the protocol and ICF and Amgen received copies of these approvals.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 August 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Canada: 144
Country: Number of subjects enrolled	Germany: 61
Country: Number of subjects enrolled	Poland: 135
Country: Number of subjects enrolled	Switzerland: 24
Country: Number of subjects enrolled	United States: 261
Worldwide total number of subjects	661
EEA total number of subjects	232

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	607
From 65 to 84 years	53
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 73 centers in Europe, Canada, and the United States. Participants were enrolled from 29 August 2012 until 8 March 2013.

Pre-assignment

Screening details:

Eligible subjects were men and women from 18 to 75 years of age with stable moderate to severe plaque psoriasis diagnosed at least 6 months before the first dose of investigational product (eg, no morphology changes or significant flares of disease activity in the opinion of the investigator).

Period 1

Period 1 title	Induction Phase (Weeks 1-12)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

Subjects were randomized at baseline via an interactive voice response system (IVRS) to receive 210 mg brodalumab, 140 mg brodalumab, or placebo in a 1:1:1 ratio stratified by baseline total body weight (≤ 100 kg; > 100 kg), by prior biologic use (subjects with prior biologic use were capped at 50% of the study population), and by geographic region (defined by country for non-US countries and by geographic region in the US [US-West, US-Midwest, US-Northeast, US-South]).

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Participants received placebo matching brodalumab administered via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Arm title	Brodalumab 140 mg
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Arm description:

Participants received 140 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Arm title	Brodalumab 210 mg
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Arm description:

Participants received 210 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Number of subjects in period 1	Placebo	Brodalumab 140 mg	Brodalumab 210 mg
Started	220	219	222
Completed	208	208	212
Not completed	12	11	10
Consent withdrawn by subject	3	3	4
Administrative decision	-	-	1
Other	-	2	-
Adverse event	3	3	2
Ineligibility determined	2	-	-
Lost to follow-up	1	1	1
Protocol deviation	2	1	2
Requirement for alternative therapy	1	-	-
Noncompliance	-	1	-

Period 2

Period 2 title	Withdrawal Phase (Weeks 12 - 52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

Subjects originally randomized to either of the brodalumab arms and who had an sPGA = 0 or 1 at week 12 were re-randomized at week 12 to receive brodalumab at their originally randomized dose or placebo in a 1:1 ratio, stratified by week 12 total body weight (≤ 100 kg vs > 100 kg) and the subject's week 12 response (sPGA = 0 vs sPGA = 1). Subjects originally randomized to the placebo arm and any subjects who did not meet the criteria for re-randomization received 210 mg Q2W brodalumab.

Arms

Are arms mutually exclusive?	Yes
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Arm title	Non-rerandomized Subjects
Arm description:	
Participants who received placebo in the Induction Phase or who did not have an sPGA = 0 or 1 at the week 12 visit received 210 mg brodalumab every 2 weeks (Q2W) from week 12 in the Withdrawal Phase.	
Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered by subcutaneous injection Q2W.	
Arm title	Brodalumab 140 mg / Placebo
Arm description:	
Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal phase.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered by subcutaneous injection every 2 weeks.	
Arm title	Brodalumab 140 mg / Brodalumab 140 mg
Arm description:	
Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive 140 mg brodalumab from week 12 in the Withdrawal phase.	
Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered by subcutaneous injection Q2W.	
Arm title	Brodalumab 210 mg / Placebo
Arm description:	
Participants who received 210 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal Phase.	
Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use
Dosage and administration details:	
Administered by subcutaneous injection every 2 weeks.	
Arm title	Brodalumab 210 mg / Brodalumab 210 mg
Arm description:	
Participants who received 210 mg Q2W brodalumab in the Induction Phase who were re-randomized to	

receive 210 mg brodalumab Q2W from week 12 in the Withdrawal Phase.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection Q2W.

Number of subjects in period 2	Non-rerandomized Subjects	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg
Started	345	59	57
Received Study Drug	344	59	57
Completed	290	6	45
Not completed	55	53	12
Consent withdrawn by subject	11	-	-
Administrative decision	5	-	-
entered retreatment phase	-	53	12
Other	10	-	-
Death	2	-	-
Adverse event	7	-	-
Ineligibility determined	1	-	-
Lost to follow-up	3	-	-
Requirement for alternative therapy	16	-	-

Number of subjects in period 2	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Started	84	83
Received Study Drug	84	83
Completed	2	74
Not completed	82	9
Consent withdrawn by subject	1	-
Administrative decision	1	-
entered retreatment phase	79	5
Other	-	-
Death	-	1
Adverse event	-	2
Ineligibility determined	-	-
Lost to follow-up	1	1
Requirement for alternative therapy	-	-

Period 3

Period 3 title	Retreatment Phase (week 16-52)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst

Blinding implementation details:

Participants who re-randomized at week 12 qualified for retreatment upon return of disease (defined as an sPGA $\geq$ 3) at or after week 16 and through week 52.

Arms

Are arms mutually exclusive?	Yes
Arm title	Brodalumab 140 mg / Placebo / Brodalumab 140 mg

Arm description:

Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal Phase and then received 140 mg brodalumab in the Retreatment Phase.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection Q2W.

Arm title	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg
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Arm description:

Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive 140 mg brodalumab from week 12 in the Withdrawal phase and continued to receive 140 mg brodalumab in the Retreatment Phase.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection Q2W.

Arm title	Brodalumab 210 mg / Placebo / Brodalumab 210 mg
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Arm description:

Participants who received 210 mg brodalumab Q2W in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal Phase and then received 210 mg brodalumab Q2W in

the Retreatment Phase.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection Q2W.

Arm title	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
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Arm description:

Participants who received 210 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive 210 mg brodalumab Q2W from week 12 in the Withdrawal Phase.

Arm type	Experimental
Investigational medicinal product name	Brodalumab
Investigational medicinal product code	AMG 827
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

Administered by subcutaneous injection Q2W.

Number of subjects in period 3 ^[1]	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg
Started	53	12	79
Completed	35	4	66
Not completed	18	8	13
Consent withdrawn by subject	-	1	1
Entered rescue phase prior to week 52	17	7	10
Death	-	-	1
Adverse event	-	-	1
Lost to follow-up	1	-	-

Number of subjects in period 3 ^[1]	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Started	5
Completed	2
Not completed	3
Consent withdrawn by subject	1
Entered rescue phase prior to week 52	2
Death	-
Adverse event	-

Lost to follow-up	-
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Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only participants who qualified for retreatment upon return of disease (defined as an sPGA ≥ 3) at or after week 16 and through week 52 entered the Retreatment Phase.

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description: Participants received placebo matching brodalumab administered via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.	
Reporting group title	Brodalumab 140 mg
Reporting group description: Participants received 140 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.	
Reporting group title	Brodalumab 210 mg
Reporting group description: Participants received 210 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.	

Reporting group values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg
Number of subjects	220	219	222
Age Categorical Units: Subjects			
< 65 years	202	199	206
≥ 65 years	18	20	16
Age Continuous Units: years arithmetic mean standard deviation	46.9 ± 13.2	45.8 ± 13.4	46.3 ± 12.2
Gender Categorical Units: Subjects			
Female	59	57	61
Male	161	162	161
Race Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	8	10	10
Black (or African American)	6	8	3
Native Hawaiian/Other Pacific Islander	2	1	2
White	202	196	203
Other	2	3	3
Weight Units: Subjects			
≤ 100 kg	159	156	156
> 100 kg	61	63	66
Prior Biologic Use Units: Subjects			
Yes	101	99	105
No	119	120	117
Region Units: Subjects			
Canada	47	49	48

France	12	10	14
Germany	20	20	21
Poland	45	45	45
Switzerland	8	9	7
United States-Midwest	10	9	10
United States-Northeast	10	10	12
United States-South	20	19	17
United States-West	48	48	48
Static Physician Global Assessment of Psoriasis (sPGA)			
The sPGA is a 6-point scale ranging from 0 (clear) to 5 (very severe) used to measure the severity of disease (induration, scaling, and erythema).			
Units: Subjects			
Clear	0	0	0
Almost Clear	0	0	0
Mild	0	0	0
Moderate	114	129	121
Severe	91	80	87
Very Severe	15	10	14
Duration of Psoriasis			
Units: years			
arithmetic mean	20.7	19.4	20.4
standard deviation	± 12.1	± 12.5	± 13.2
Psoriasis Area and Severity Index (PASI) Score			
The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease.			
Units: units on a scale			
arithmetic mean	19.72	19.95	19.41
standard deviation	± 7.71	± 7.41	± 6.61
Psoriasis Body Surface Area (BSA) Involvement			
Units: percent			
arithmetic mean	26.9	27.42	25.06
standard deviation	± 17.11	± 17.1	± 15.25
Psoriasis Scalp Severity Index (PSSI)			
The Psoriasis Scalp Severity Index (PSSI) measures the extent of psoriasis involvement and the severity of erythema, infiltration, and desquamation of the scalp. Involvement and severity of psoriasis for the PSSI is scored by physicians using a scale from 0 to 72, where 0 = no psoriasis, and higher scores indicating more severe disease. The PSSI calculation does not include the face or neck area. Data were available for 219, 219 and 222 subjects in each group respectively.			
Units: units on a scale			
arithmetic mean	19.97	19.67	16.71
standard deviation	± 14.57	± 13.72	± 13.48
Psoriasis Scalp Surface Area (SSA) Involvement			
Data are available for 219, 219 and 222 subjects in each group respectively.			
Units: percent			
arithmetic mean	32.42	34.6	28.68
standard deviation	± 28.64	± 29.24	± 27.53
Nail Psoriasis Severity Index (NAPSI)			
The NAPSI scale is an objective, numeric, and reproducible grading system for nail psoriasis that incorporates the many different features of nail psoriasis. Each quarter of the nail was scored for the presence (1) or absence (0) of 8 clinical features for a score of 0-4 for each feature. The total score for each nail ranges from 0 (absent) to 32 (worst). Data are reported for the worst nail for subjects with			

baseline nail involvement; 59, 66 and 62 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	9.54	9.26	9.16
standard deviation	± 3.78	± 4.02	± 3.99
Dermatology Life Quality Index (DLQI)			
The DLQI is a skin disease-specific instrument to evaluate health-related quality of life. Participants evaluate the degree that psoriasis has affected their quality of life in the last week, including symptoms and feelings, daily and leisure activities, work or school activities, personal relationships and treatment related feelings. Participants answer 10 questions on a scale from 0 (not at all) to 3 (very much); the total score ranges from 0 (best possible score) to 30 (worst possible score). Data are available for 217, 216, and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	13.9	14.3	14.2
standard deviation	± 6.8	± 7.5	± 7.3
EuroQol-5D (EQ-5D)			
The EQ-5D captures 2 types of information, a descriptive profile, or health state, and an overall health rating using a visual analog scale. The health states include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, answered as 1 (no problem), 2 (some problem), or 3 (major problem). A weighted index score is calculated by applying coefficients from a validated value set and ranges from -0.594 to 1, with -0.594 representing death and 1 representing the perfect health state. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	0.62	0.61	0.6
standard deviation	± 0.29	± 0.32	± 0.32
Hospital Anxiety and Depression Scale (HADS) Anxiety Score			
The HADS is a 14-item questionnaire assessing subject's symptoms of depression and anxiety. The measure consists of 7 items reflecting anxiety and 7 items reflecting depression. Each item can be answered by the patient on a 4-point (0–3) response category so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	6.42	6.59	6.68
standard deviation	± 3.81	± 4.2	± 4.28
HADS Depression Score			
The HADS is a 14-item questionnaire assessing subject's symptoms of depression and anxiety. The measure consists of 7 items reflecting anxiety and 7 items reflecting depression. Each item can be answered by the patient on a 4-point (0–3) response category so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	5.28	5.18	5.47
standard deviation	± 3.92	± 4.11	± 4.17
Medical Outcomes Short Form-36 (SF-36) Physical Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant.. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	46.73	47.7	46.99
standard deviation	± 9.44	± 9.24	± 9.25
SF-36 Mental Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant.. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning.			

Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	45.98	45.3	45.48
standard deviation	± 11.23	± 11.22	± 11.65
Psoriasis Symptom Inventory Total Score Weekly Average			
The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. Data are available for 211, 210 and 209 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean	19	19.7	18.9
standard deviation	± 6.7	± 7.3	± 6.7

Reporting group values	Total		
Number of subjects	661		
Age Categorical			
Units: Subjects			
< 65 years	607		
≥ 65 years	54		
Age Continuous			
Units: years			
arithmetic mean	-		
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	177		
Male	484		
Race			
Units: Subjects			
American Indian or Alaska Native	2		
Asian	28		
Black (or African American)	17		
Native Hawaiian/Other Pacific Islander	5		
White	601		
Other	8		
Weight			
Units: Subjects			
≤ 100 kg	471		
> 100 kg	190		
Prior Biologic Use			
Units: Subjects			
Yes	305		
No	356		
Region			
Units: Subjects			
Canada	144		
France	36		
Germany	61		
Poland	135		

Switzerland	24		
United States-Midwest	29		
United States-Northeast	32		
United States-South	56		
United States-West	144		
Static Physician Global Assessment of Psoriasis (sPGA)			
The sPGA is a 6-point scale ranging from 0 (clear) to 5 (very severe) used to measure the severity of disease (induration, scaling, and erythema).			
Units: Subjects			
Clear	0		
Almost Clear	0		
Mild	0		
Moderate	364		
Severe	258		
Very Severe	39		
Duration of Psoriasis			
Units: years			
arithmetic mean			
standard deviation	-		
Psoriasis Area and Severity Index (PASI) Score			
The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement. The total PASI score ranges from 0 to 72. The higher the total score, the more severe the disease.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
Psoriasis Body Surface Area (BSA) Involvement			
Units: percent			
arithmetic mean			
standard deviation	-		
Psoriasis Scalp Severity Index (PSSI)			
The Psoriasis Scalp Severity Index (PSSI) measures the extent of psoriasis involvement and the severity of erythema, infiltration, and desquamation of the scalp. Involvement and severity of psoriasis for the PSSI is scored by physicians using a scale from 0 to 72, where 0 = no psoriasis, and higher scores indicating more severe disease. The PSSI calculation does not include the face or neck area. Data were available for 219, 219 and 222 subjects in each group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
Psoriasis Scalp Surface Area (SSA) Involvement			
Data are available for 219, 219 and 222 subjects in each group respectively.			
Units: percent			
arithmetic mean			
standard deviation	-		
Nail Psoriasis Severity Index (NAPSI)			
The NAPSI scale is an objective, numeric, and reproducible grading system for nail psoriasis that incorporates the many different features of nail psoriasis. Each quarter of the nail was scored for the presence (1) or absence (0) of 8 clinical features for a score of 0-4 for each feature. The total score for each nail ranges from 0 (absent) to 32 (worst). Data are reported for the worst nail for subjects with baseline nail involvement; 59, 66 and 62 subjects in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			

standard deviation	-		
Dermatology Life Quality Index (DLQI)			
The DLQI is a skin disease-specific instrument to evaluate health-related quality of life. Participants evaluate the degree that psoriasis has affected their quality of life in the last week, including symptoms and feelings, daily and leisure activities, work or school activities, personal relationships and treatment related feelings. Participants answer 10 questions on a scale from 0 (not at all) to 3 (very much); the total score ranges from 0 (best possible score) to 30 (worst possible score). Data are available for 217, 216, and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
EuroQol-5D (EQ-5D)			
The EQ-5D captures 2 types of information, a descriptive profile, or health state, and an overall health rating using a visual analog scale. The health states include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, answered as 1 (no problem), 2 (some problem), or 3 (major problem). A weighted index score is calculated by applying coefficients from a validated value set and ranges from -0.594 to 1, with -0.594 representing death and 1 representing the perfect health state. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
Hospital Anxiety and Depression Scale (HADS) Anxiety Score			
The HADS is a 14-item questionnaire assessing subject's symptoms of depression and anxiety. The measure consists of 7 items reflecting anxiety and 7 items reflecting depression. Each item can be answered by the patient on a 4-point (0-3) response category so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
HADS Depression Score			
The HADS is a 14-item questionnaire assessing subject's symptoms of depression and anxiety. The measure consists of 7 items reflecting anxiety and 7 items reflecting depression. Each item can be answered by the patient on a 4-point (0-3) response category so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
Medical Outcomes Short Form-36 (SF-36) Physical Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant.. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		
SF-36 Mental Component Score			
The SF-36 assesses the general quality of life by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant.. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning. Data are available for 216, 216 and 221 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			

standard deviation	-		
Psoriasis Symptom Inventory Total Score Weekly Average			
The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. Data are available for 211, 210 and 209 participants in each treatment group respectively.			
Units: units on a scale			
arithmetic mean			
standard deviation	-		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Participants received placebo matching brodalumab administered via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.	
Reporting group title	Brodalumab 140 mg
Reporting group description: Participants received 140 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.	
Reporting group title	Brodalumab 210 mg
Reporting group description: Participants received 210 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.	
Reporting group title	Non-rerandomized Subjects
Reporting group description: Participants who received placebo in the Induction Phase or who did not have an sPGA = 0 or 1 at the week 12 visit received 210 mg brodalumab every 2 weeks (Q2W) from week 12 in the Withdrawal Phase.	
Reporting group title	Brodalumab 140 mg / Placebo
Reporting group description: Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal phase.	
Reporting group title	Brodalumab 140 mg / Brodalumab 140 mg
Reporting group description: Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive 140 mg brodalumab from week 12 in the Withdrawal phase.	
Reporting group title	Brodalumab 210 mg / Placebo
Reporting group description: Participants who received 210 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal Phase.	
Reporting group title	Brodalumab 210 mg / Brodalumab 210 mg
Reporting group description: Participants who received 210 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive 210 mg brodalumab Q2W from week 12 in the Withdrawal Phase.	
Reporting group title	Brodalumab 140 mg / Placebo / Brodalumab 140 mg
Reporting group description: Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal Phase and then received 140 mg brodalumab in the Retreatment Phase.	
Reporting group title	Brodalumab 140 mg / Brodalumab 140 mg / Brodalumab 140 mg
Reporting group description: Participants who received 140 mg Q2W brodalumab in the Induction Phase who were re-randomized to receive 140 mg brodalumab from week 12 in the Withdrawal phase and continued to receive 140 mg brodalumab in the Retreatment Phase.	
Reporting group title	Brodalumab 210 mg / Placebo / Brodalumab 210 mg
Reporting group description: Participants who received 210 mg brodalumab Q2W in the Induction Phase who were re-randomized to receive placebo from week 12 in the Withdrawal Phase and then received 210 mg brodalumab Q2W in the Retreatment Phase.	
Reporting group title	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Reporting group description: Participants who received 210 mg Q2W brodalumab in the Induction Phase who were re-randomized to	

Primary: Percentage of Participants with a 75% or Greater Improvement from Baseline in Psoriasis Area and Severity Index (PASI 75) at Week 12

End point title	Percentage of Participants with a 75% or Greater Improvement from Baseline in Psoriasis Area and Severity Index (PASI 75) at Week 12
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis. Non-responder imputation (NRI) was used to impute missing data.

End point type	Primary
End point timeframe:	
Baseline and week 12	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)	2.7 (1 to 5.8)	60.3 (53.5 to 66.8)	83.3 (77.8 to 88)	

Statistical analyses

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 210 mg v Placebo
Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	< 0.001 ^[2]
Method	Cochran-Mantel-Haenszel

Notes:

[1] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[2] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline PASI score ($\leq$ median, $>$ median).

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 140 mg v Placebo

Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	< 0.001 ^[4]
Method	Cochran-Mantel-Haenszel

Notes:

[3] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[4] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline PASI score ($\leq$ median, $>$ median).

Primary: Percentage of Participants with a Static Physician's Global Assessment (sPGA) of Clear or Almost Clear at Week 12

End point title	Percentage of Participants with a Static Physician's Global Assessment (sPGA) of Clear or Almost Clear at Week 12
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End point description:

Physician's global assessment of the subject's psoriasis based on the severity of induration, scaling, and erythema assessed on a 6-point scale ranging from 0 (clear) to 5 (very severe). A sPGA response is defined as a sPGA value of clear (score 0) or almost clear (score 1). Non-responder imputation (NRI) was used to impute missing data.

End point type	Primary
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End point timeframe:

Week 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)	1.4 (0.3 to 3.9)	53.9 (47 to 60.6)	75.7 (69.5 to 81.2)	

Statistical analyses

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 210 mg v Placebo
Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	superiority ^[5]
P-value	< 0.001 ^[6]
Method	Cochran-Mantel-Haenszel

Notes:

[5] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[6] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline sPGA score (3, 4, 5).

Statistical analysis title	Difference in Response rates
Comparison groups	Brodalumab 140 mg v Placebo

Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	superiority ^[7]
P-value	< 0.001 ^[8]
Method	Cochran-Mantel-Haenszel

Notes:

[7] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[8] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline sPGA score (3, 4, 5).

Secondary: Percentage of Participants with a 100% Improvement from Baseline in PASI (PASI 100) at Week 12

End point title	Percentage of Participants with a 100% Improvement from Baseline in PASI (PASI 100) at Week 12
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

Non-responder imputation (NRI) was used to impute missing data.

End point type	Secondary
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End point timeframe:

Baseline and week 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)	0.5 (0 to 2.5)	23.3 (17.9 to 29.5)	41.9 (35.3 to 48.7)	

Statistical analyses

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 210 mg v Placebo
Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	superiority ^[9]
P-value	< 0.001 ^[10]
Method	Cochran-Mantel-Haenszel

Notes:

[9] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[10] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline PASI score ($\leq$ median, $>$ median).

Statistical analysis title	Difference in Response rates
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Comparison groups	Brodalumab 140 mg v Placebo
Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	superiority ^[11]
P-value	< 0.001 ^[12]
Method	Cochran-Mantel-Haenszel

Notes:

[11] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[12] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline PASI score ($\leq$ median, $>$ median).

Secondary: Percentage of Participants with an sPGA of Clear at Week 12

End point title	Percentage of Participants with an sPGA of Clear at Week 12
End point description:	
Physician's global assessment of the subject's psoriasis based on the severity of induration, scaling, and erythema assessed on a 6-point scale ranging from 0 (clear) to 5 (very severe). A sPGA response is defined as a sPGA value of clear (score 0).	
Non-responder imputation (NRI) was used to impute missing data.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)	0.5 (0 to 2.5)	23.3 (17.9 to 29.5)	41.9 (35.3 to 48.7)	

Statistical analyses

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 210 mg v Placebo
Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	superiority ^[13]
P-value	< 0.001 ^[14]
Method	Cochran-Mantel-Haenszel

Notes:

[13] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[14] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline sPGA score (3, 4, 5).

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 140 mg v Placebo

Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	superiority ^[15]
P-value	< 0.001 ^[16]
Method	Cochran-Mantel-Haenszel

Notes:

[15] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[16] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline sPGA score (3, 4, 5).

Secondary: Percentage of Rerandomized Participants with an sPGA of Clear or Almost Clear at Week 52

End point title	Percentage of Rerandomized Participants with an sPGA of Clear or Almost Clear at Week 52
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End point description:

Physician's global assessment of the subject's psoriasis based on the severity of induration, scaling, and erythema assessed on a 6-point scale ranging from 0 (clear) to 5 (very severe). A sPGA response is defined as a sPGA value of clear (score 0) or almost clear (score 1).

This endpoint was analyzed in subjects rerandomized into the withdrawal phase. Non-responder imputation (NRI) was used to impute missing data; subjects who experienced return of disease through week 52 were imputed as non-responders at the time of qualification.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	57	84	83
Units: percentage of participants				
number (confidence interval 95%)	5.1 (1.1 to 14.1)	70.2 (56.6 to 81.6)	0 (0 to 4.3)	83.1 (73.3 to 90.5)

Statistical analyses

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 210 mg / Brodalumab 210 mg v Brodalumab 210 mg / Placebo
Number of subjects included in analysis	167
Analysis specification	Pre-specified
Analysis type	superiority ^[17]
P-value	< 0.001 ^[18]
Method	Cochran-Mantel-Haenszel

Notes:

[17] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[18] - CMH test adjusted for week 12 total body weight (≤ 100 kg, > 100 kg) and week 12 sPGA (0, ≥ 1).

Statistical analysis title	Difference in Response Rates
Comparison groups	Brodalumab 140 mg / Brodalumab 140 mg v Brodalumab 140 mg / Placebo
Number of subjects included in analysis	116
Analysis specification	Pre-specified
Analysis type	superiority ^[19]
P-value	< 0.001 ^[20]
Method	Cochran-Mantel-Haenszel

Notes:

[19] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[20] - CMH test adjusted for week 12 total body weight (≤ 100 kg, > 100 kg) and week 12 sPGA (0, ≥ 1).

Secondary: Percentage of Participants with a Psoriasis Symptom Inventory (PSI) Response at Week 12

End point title	Percentage of Participants with a Psoriasis Symptom Inventory (PSI) Response at Week 12
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End point description:

The Psoriasis Symptom Inventory consists of eight psoriasis-specific items. Participants rated the severity of their symptoms in the last 24 hours on a scale from 'not at all' (0) to 'very severe' (4) in an electronic diary once a day. Total scores range from 0 to 32 with higher scores indicating worse symptoms. The daily assessment of the Psoriasis Symptom Inventory was analyzed as a weekly average. A PSI response is defined a total score ≤ 8 with no item scores > 1 .

Non-responder imputation was used to impute missing data.

End point type	Secondary
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End point timeframe:

Week 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)	4.1 (1.9 to 7.6)	53 (46.1 to 59.7)	60.8 (54.1 to 67.3)	

Statistical analyses

Statistical analysis title	Difference in Response Rate
Comparison groups	Brodalumab 210 mg v Placebo

Number of subjects included in analysis	442
Analysis specification	Pre-specified
Analysis type	superiority ^[21]
P-value	< 0.001 ^[22]
Method	Cochran-Mantel-Haenszel

Notes:

[21] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[22] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline PSI score ($\leq$ median, $>$ median).

Statistical analysis title	Difference in Response Rate
Comparison groups	Brodalumab 140 mg v Placebo
Number of subjects included in analysis	439
Analysis specification	Pre-specified
Analysis type	superiority ^[23]
P-value	< 0.001 ^[24]
Method	Cochran-Mantel-Haenszel

Notes:

[23] - To maintain the family-wise type-1 error rate for all co-primary and key secondary endpoints at 5% 2-sided, a sequential testing approach was followed. Reported p-values were adjusted for multiplicity.

[24] - CMH test adjusted for baseline weight (≤ 100 kg, > 100 kg), prior biologic use (yes, no), and geographic region (US, Canada, outside North America) and baseline PSI score ($\leq$ median, $>$ median).

Secondary: Time to sPGA Response During the Induction Phase

End point title	Time to sPGA Response During the Induction Phase
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End point description:

Time to sPGA response is calculated from the first dose of study drug to the assessment day of first sPGA response. Response is an sPGA score of 0 (clear) or 1 (almost clear). Time to sPGA response was analyzed using Kaplan-Meier methods. Subjects who discontinued prior to the study day 91 assessment and subjects who reached the study day 91 without achieving response were censored at the date of their last assessment. "99999" indicates data not estimable due to the low number of events.

End point type	Secondary
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End point timeframe:

12 weeks

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	6.14 (5.71 to 6.43)	4.29 (4.14 to 6.14)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PASI Response During the Induction Phase

End point title	Time to PASI Response During the Induction Phase
End point description: Time to PASI 75/90/100 response is calculated as the time from first dose of study drug to assessment day of first PASI 75/90/100 response. Time to PASI response was analyzed using Kaplan-Meier methods. Subjects who discontinued prior to the study day 91 assessment and subjects who reached the study day 91 without achieving response were censored at the date of their last assessment. "99999" indicates data not estimable due to the low number of events.	
End point type	Secondary
End point timeframe: 12 weeks	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: weeks				
median (confidence interval 95%)				
PASI 75	99999 (99999 to 99999)	6.14 (4.57 to 6.14)	4.14 (4.14 to 4.29)	
PASI 90	99999 (99999 to 99999)	10.14 (8.14 to 12.14)	6.29 (6.14 to 8.14)	
PASI 100	99999 (99999 to 99999)	99999 (99999 to 99999)	12.14 (10.14 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an sPGA of Clear or Almost Clear at Each Visit in the Induction Phase

End point title	Percentage of Participants with an sPGA of Clear or Almost Clear at Each Visit in the Induction Phase
End point description: Physician's global assessment of the subject's psoriasis based on the severity of induration, scaling, and erythema assessed on a 6-point scale ranging from 0 (clear) to 5 (very severe). A sPGA response is defined as a sPGA value of clear (score 0) or almost clear (score 1). Non-responder imputation (NRI) was used to impute missing data.	
End point type	Secondary
End point timeframe: Weeks 1, 2, 4, 6, 8, and 10	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0 (0 to 1.7)	2.3 (0.7 to 5.2)	5.4 (2.8 to 9.3)	

Week 2	0 (0 to 1.7)	15.1 (10.6 to 20.5)	18.9 (14 to 24.7)	
Week 4	0 (0 to 1.7)	40.2 (33.6 to 47)	52.7 (45.9 to 59.4)	
Week 6	0 (0 to 1.7)	51.6 (44.8 to 58.4)	66.7 (60 to 72.8)	
Week 8	1.8 (0.5 to 4.6)	55.3 (48.4 to 62)	74.3 (68.1 to 79.9)	
Week 10	2.3 (0.7 to 5.2)	56.2 (49.3 to 62.8)	77.5 (71.4 to 82.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an sPGA of Clear at Each Visit in the Induction Phase

End point title	Percentage of Participants with an sPGA of Clear at Each Visit in the Induction Phase
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End point description:

Physician's global assessment of the subject's psoriasis based on the severity of induration, scaling, and erythema assessed on a 6-point scale ranging from 0 (clear) to 5 (very severe). A sPGA response is defined as a sPGA value of clear (score 0).

Non-responder imputation (NRI) was used to impute missing data.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 4, 6, 8 and 10

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0 (0 to 1.7)	0 (0 to 1.7)	0 (0 to 1.6)	
Week 2	0 (0 to 1.7)	1.4 (0.3 to 4)	0.9 (0.1 to 3.2)	
Week 4	0 (0 to 1.7)	7.8 (4.6 to 12.1)	10.4 (6.7 to 15.1)	
Week 6	0 (0 to 1.7)	15.5 (11 to 21)	25.2 (19.7 to 31.5)	
Week 8	0 (0 to 1.7)	20.1 (15 to 26)	30.6 (24.6 to 37.1)	
Week 10	0.5 (0 to 2.5)	21.5 (16.2 to 27.5)	39.6 (33.2 to 46.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 75 at Each Visit in the Induction Phase

End point title	Percentage of Participants with a PASI 75 at Each Visit in the Induction Phase
End point description: The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis. Non-responder imputation (NRI) was used to impute missing data.	
End point type	Secondary
End point timeframe: Baseline and Weeks 1, 2, 4, 6, 8, and 10	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0 (0 to 1.7)	1.4 (0.3 to 4)	3.2 (1.3 to 6.4)	
Week 2	0.5 (0 to 2.5)	14.6 (10.2 to 20)	23 (17.6 to 29.1)	
Week 4	1.4 (0.3 to 3.9)	41.6 (35 to 48.4)	62.2 (55.4 to 68.6)	
Week 6	2.3 (0.7 to 5.2)	62.1 (55.3 to 68.6)	75.7 (69.5 to 81.2)	
Week 8	2.3 (0.7 to 5.2)	63.5 (56.7 to 69.9)	80.6 (74.8 to 85.6)	
Week 10	3.2 (1.3 to 6.4)	62.6 (55.8 to 69)	82 (76.3 to 86.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 100 at Each Visit in the Induction Phase

End point title	Percentage of Participants with a PASI 100 at Each Visit in the Induction Phase
End point description: The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis. Non-responder imputation was used to impute missing data.	
End point type	Secondary
End point timeframe: Baseline and Weeks 1, 2, 4, 6, 8 and 10	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0 (0 to 1.7)	0 (0 to 1.7)	0 (0 to 1.6)	
Week 2	0 (0 to 1.7)	1.4 (0.3 to 4)	0.9 (0.1 to 3.2)	
Week 4	0 (0 to 1.7)	7.8 (4.6 to 12.1)	10.4 (6.7 to 15.1)	
Week 6	0 (0 to 1.7)	15.5 (11 to 21)	25.2 (19.7 to 31.5)	
Week 8	0 (0 to 1.7)	20.1 (15 to 26)	30.6 (24.6 to 37.1)	
Week 10	0.5 (0 to 2.5)	21.5 (16.2 to 27.5)	39.2 (32.7 to 45.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 50 at Each Visit in the Induction Phase

End point title	Percentage of Participants with a PASI 50 at Each Visit in the Induction Phase
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis. A PASI 50% response is a 50% or greater improvement from baseline. Non-responder imputation (NRI) was used to impute missing data.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 1, 2, 4, 6, 8, 10 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0.9 (0.1 to 3.2)	10 (6.4 to 14.8)	26.1 (20.5 to 32.4)	
Week 2	2.7 (1 to 5.8)	47.9 (41.2 to 54.8)	62.2 (55.4 to 68.6)	

Week 4	5.5 (2.8 to 9.3)	69.9 (63.3 to 75.9)	87.4 (82.3 to 91.5)	
Week 6	7.3 (4.2 to 11.5)	75.3 (69.1 to 80.9)	88.3 (83.3 to 92.2)	
Week 8	9.5 (6 to 14.2)	75.3 (69.1 to 80.9)	86.5 (81.3 to 90.7)	
Week 10	7.7 (4.6 to 12.1)	73.5 (67.1 to 79.2)	85.1 (79.8 to 89.5)	
Week 12	7.7 (4.6 to 12.1)	73.5 (67.1 to 79.2)	88.3 (83.3 to 92.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 90 at Each Visit in the Induction Phase

End point title	Percentage of Participants with a PASI 90 at Each Visit in the Induction Phase
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis. A PASI 90% response is a 90% or greater improvement from baseline. Non-responder imputation (NRI) was used to impute missing data.

End point type	Secondary
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End point timeframe:

Baseline and Weeks 1, 2, 4, 6, 8, 10, and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percentage of participants				
number (confidence interval 95%)				
Week 1	0 (0 to 1.7)	0.5 (0 to 2.5)	0 (0 to 1.6)	
Week 2	0 (0 to 1.7)	3.2 (1.3 to 6.5)	5.4 (2.8 to 9.3)	
Week 4	0.5 (0 to 2.5)	21.5 (16.2 to 27.5)	30.2 (24.2 to 36.7)	
Week 6	0.5 (0 to 2.5)	32.9 (26.7 to 39.5)	49.1 (42.3 to 55.9)	
Week 8	0.5 (0 to 2.5)	39.7 (33.2 to 46.5)	62.6 (55.9 to 69)	
Week 10	0.9 (0.1 to 3.2)	43.4 (36.7 to 50.2)	67.1 (60.5 to 73.3)	
Week 12	0.9 (0.1 to 3.2)	42.5 (35.8 to 49.3)	70.3 (63.8 to 76.2)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Baseline in PASI During the Induction Phase

End point title	Percent Improvement From Baseline in PASI During the Induction Phase
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

This endpoint was analyzed in subjects with a valid measurement value at each time point.

Percent improvement from baseline is calculated as: $(\text{Baseline} - \text{Post-baseline}) / \text{Baseline} * 100$.

End point type	Secondary
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End point timeframe:

Baseline and weeks 1, 2, 4, 6, 8, 10 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 1 (N = 215, 215, 219)	1.95 (± 15.03)	22.1 (± 21.06)	32.6 (± 23.09)	
Week 2 (N = 213, 215, 213)	1.52 (± 23.23)	45.5 (± 27.67)	55.59 (± 24.75)	
Week 4 (N = 216, 214, 216)	1.12 (± 28.59)	63.1 (± 30.38)	75.16 (± 26.63)	
Week 6 (N = 210, 215, 211)	3.46 (± 30.87)	70.11 (± 32.27)	83.78 (± 21.55)	
Week 8 (N = 212, 206, 206)	0.94 (± 37.11)	73.21 (± 32.23)	87.19 (± 21.37)	
Week 10 (N = 203, 202, 206)	-1.26 (± 38.96)	74.33 (± 33.43)	88.29 (± 22.18)	
Week 12 (N = 209, 208, 212)	-3.15 (± 40.53)	70.69 (± 37.24)	87.58 (± 25.56)	

Statistical analyses

No statistical analyses for this end point

Secondary: Absolute PASI Score During the Induction Phase

End point title	Absolute PASI Score During the Induction Phase
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

This endpoint was analyzed in subjects with a valid measurement value at each time point.

End point type	Secondary
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End point timeframe:

Weeks 1, 2, 4, 6, 8, 10 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: units on a scale				
arithmetic mean (standard deviation)				
Week 1 (N = 215, 215, 219)	19.16 (± 7.53)	15.58 (± 7.16)	13.3 (± 7.13)	
Week 2 (N = 213, 215, 213)	19.35 (± 8.32)	10.98 (± 7.08)	8.7 (± 5.83)	
Week 4 (N = 216, 214, 216)	19.33 (± 8.74)	7.34 (± 7)	4.85 (± 5.28)	
Week 6 (N = 210, 215, 211)	18.89 (± 8.96)	6.13 (± 7.46)	3.21 (± 4.68)	
Week 8 (N = 212, 206, 206)	19.34 (± 10.03)	5.59 (± 7.69)	2.6 (± 4.74)	
Week 10 (N = 203, 202, 206)	19.85 (± 10.36)	5.49 (± 8.02)	2.34 (± 4.8)	
Week 12 (N = 209, 208, 212)	19.99 (± 10.49)	6.08 (± 8.59)	2.52 (± 5.74)	

Statistical analyses

No statistical analyses for this end point

Secondary: Body Surface Area Involvement During the Induction Phase

End point title Body Surface Area Involvement During the Induction Phase

End point description:

This endpoint was analyzed in subjects with a valid measurement value at each time point.

End point type Secondary

End point timeframe:

Weeks 1, 2, 4, 6, 8, 10 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	220	219	222	
Units: Percent involvement				
arithmetic mean (standard deviation)				
Week 1 (N = 215, 215, 219)	26.92 (± 16.98)	25.81 (± 16.78)	22.48 (± 15.01)	
Week 2 (N = 213, 215, 213)	27.83 (± 17.61)	21.33 (± 15.62)	17.74 (± 13.31)	
Week 4 (N = 216, 214, 216)	28.55 (± 18.26)	15.34 (± 14.59)	11.84 (± 12.88)	
Week 6 (N = 210, 215, 211)	28.27 (± 18.42)	12.64 (± 15.78)	8.37 (± 12.3)	

Week 8 (N = 212, 206, 206)	29.16 (± 19.03)	11.05 (± 15.78)	6.71 (± 11.17)	
Week 10 (N = 203, 202, 206)	29.68 (± 19.76)	10.38 (± 16.2)	5.77 (± 11.18)	
Week 12 (N = 208, 208, 212)	29.8 (± 20.2)	11.03 (± 16.73)	5.39 (± 11.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement From Baseline in NAPS I Score at Week 12

End point title	Improvement From Baseline in NAPS I Score at Week 12
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End point description:

The NAPS I scale is an objective, numeric, and reproducible grading system for nail psoriasis that incorporates the many different features of nail psoriasis. Each quarter of the nail was scored for the presence (1) or absence (0) of 8 clinical features for a score of 0-4 for each feature. The total score for each nail ranges from 0 (absent) to 32 (worst). Results are reported for the worst nail for subjects with baseline nail involvement (NAPS I score ≥ 6) with a valid measurement at week 12. Improvement from baseline is calculated as: Baseline value – Post-baseline value.

End point type	Secondary
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End point timeframe:

Baseline and week 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	56	62	59	
Units: units on a scale				
arithmetic mean (standard deviation)	0.6 (± 3)	3.6 (± 4)	4.6 (± 3.5)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Baseline in Psoriasis Scalp Severity Index Score

End point title	Percent Improvement From Baseline in Psoriasis Scalp Severity Index Score
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End point description:

The Psoriasis Scalp Severity Index (PSSI) measures the extent of psoriasis involvement and the severity of erythema, infiltration, and desquamation of the scalp. Involvement and severity of psoriasis for the PSSI is scored by physicians using a scale from 0 to 72, where 0 = no psoriasis, and higher scores indicating more severe disease. The PSSI calculation does not include the face or neck area. Results are reported for subjects with a PSSI ≥ 15 and SSA ≥ 30 at baseline and with a valid measurement value at each time point.

Percent improvement from baseline is calculated as: (Baseline – Post-baseline) / Baseline * 100.

End point type	Secondary
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End point timeframe:

Baseline and weeks 2, 4, 8, and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	105	82	
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 2 (N = 91, 102, 78)	6.69 (± 33.91)	59.02 (± 37.94)	67.58 (± 28.83)	
Week 4 (N = 94, 102, 79)	7.06 (± 37.54)	75.12 (± 32.81)	87.54 (± 20.87)	
Week 8 (N = 91, 99, 77)	13.42 (± 47.91)	75.3 (± 37.04)	92.97 (± 14.04)	
Week 12 (N = 90, 100, 81)	14.42 (± 42.77)	73.28 (± 40.24)	92.83 (± 13.94)	

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement From Study Baseline in Scalp Surface Area (SSA) During the Induction Phase

End point title	Improvement From Study Baseline in Scalp Surface Area (SSA) During the Induction Phase
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End point description:

Results are reported for subjects with a PSSI ≥ 15 and SSA ≥ 30 at baseline with a valid measurement value at each time point.

End point type	Secondary
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End point timeframe:

Baseline and weeks 2, 4, 8 and 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	95	105	82	
Units: percent				
arithmetic mean (standard deviation)				
Week 2 (N = 91, 102, 78)	7.58 (± 21.54)	26.3 (± 28.56)	29.56 (± 26.38)	
Week 4 (N = 94, 102, 79)	6.19 (± 21.23)	38.07 (± 28.49)	44.53 (± 26.38)	
Week 8 (N = 91, 99, 77)	8.61 (± 23.11)	41.98 (± 29.09)	52.58 (± 24.71)	
Week 12 (N = 90, 100, 81)	8.68 (± 26.5)	41.92 (± 29.48)	52.53 (± 22.92)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an sPGA of Clear at Week 52

End point title	Percentage of Participants with an sPGA of Clear at Week 52
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End point description:

Physician's global assessment of the subject's psoriasis based on the severity of induration, scaling, and erythema assessed on a 6-point scale ranging from 0 (clear) to 5 (very severe). A sPGA response is defined as a sPGA value of clear (score 0) at week 52.

This endpoint was analyzed in subjects rerandomized into the withdrawal phase. Non-responder imputation (NRI) was used to impute missing data; subjects who experienced return of disease through week 52 were imputed as non-responders at the time of qualification.

End point type	Secondary
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End point timeframe:

Week 52

End point values	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	57	84	83
Units: percentage of participants				
number (confidence interval 95%)	1.7 (0 to 9.1)	43.9 (30.7 to 57.6)	0 (0 to 4.3)	67.5 (56.3 to 77.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 75 at Week 52

End point title	Percentage of Participants with a PASI 75 at Week 52
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

This endpoint was analyzed in subjects rerandomized into the withdrawal phase. Non-responder imputation was used to impute missing data; subjects who experienced return of disease and/or inadequate response that resulted in a protocol-specified treatment change at or before week 52 were also imputed as non-responders.

End point type	Secondary
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End point timeframe:

Baseline and week 52

End point values	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	57	84	83
Units: percentage of participants				
number (confidence interval 95%)	8.5 (2.8 to 18.7)	82.5 (70.1 to 91.3)	0 (0 to 4.3)	90.4 (81.9 to 95.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 90 at Week 52

End point title	Percentage of Participants with a PASI 90 at Week 52
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

This endpoint was analyzed in subjects rerandomized into the withdrawal phase. Non-responder imputation was used to impute missing data; subjects who experienced return of disease and/or inadequate response that resulted in a protocol-specified treatment change at or before week 52 were also imputed as non-responders.

End point type	Secondary
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End point timeframe:

Baseline and week 52

End point values	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	57	84	83
Units: percentage of participants				
number (confidence interval 95%)	3.4 (0.4 to 11.7)	66.7 (52.9 to 78.6)	0 (0 to 4.3)	79.5 (69.2 to 87.6)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 100 at Week 52

End point title	Percentage of Participants with a PASI 100 at Week 52
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis.

This endpoint was analyzed in subjects rerandomized into the withdrawal phase. Non-responder imputation was used to impute missing data; subjects who experienced return of disease and/or inadequate response that resulted in a protocol-specified treatment change at or before week 52 were also imputed as non-responders.

End point type	Secondary
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End point timeframe:

Baseline and week 52

End point values	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	57	84	83
Units: percentage of participants				
number (confidence interval 95%)	1.7 (0 to 9.1)	43.9 (30.7 to 57.6)	0 (0 to 4.3)	67.5 (56.3 to 77.4)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Improvement From Baseline in PASI Score During the Withdrawal Phase

End point title	Percent Improvement From Baseline in PASI Score During the Withdrawal Phase
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End point description:

The PASI measures the average redness (erythema), thickness (induration), and scaliness (each graded on a 0 to 4 scale) of psoriasis lesions, weighted by the area of involvement in the four main body areas (i.e., head and neck, trunk, upper extremities, and lower extremities). PASI scores can range from 0.0 to 72.0, with higher scores indicating greater severity and/or more extensive psoriasis. This endpoint was analyzed in subjects re-randomized into the withdrawal phase with a valid measurement at each time point. Percent improvement from baseline is calculated as: $(\text{Baseline} - \text{Post-baseline}) / \text{Baseline} * 100$.

End point type	Secondary
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End point timeframe:

Baseline and weeks 12, 16, 24, 36, and 52

End point values	Brodalumab 140 mg / Placebo	Brodalumab 140 mg / Brodalumab 140 mg	Brodalumab 210 mg / Placebo	Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	59	57	84	83
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 12 (N = 59, 57, 84, 83)	94.72 (± 7.69)	94.16 (± 7.1)	97.07 (± 4.42)	96.43 (± 6.87)
Week 16 (N = 58, 54, 82, 83)	76.53 (± 23.41)	94.73 (± 7.23)	84.45 (± 23.27)	95.76 (± 6.96)
Week 24 (N = 20, 53, 26, 78)	78.15 (± 21.07)	94.84 (± 8.41)	67.94 (± 22.29)	96.83 (± 5.41)
Week 36 (N = 11, 48, 9, 77)	76.25 (± 28.41)	94.9 (± 9.45)	57.53 (± 46.43)	97.57 (± 7.38)
Week 52 (N = 6, 47, 2, 72)	84 (± 14.33)	94.69 (± 9.13)	61.51 (± 5.17)	98.18 (± 3.82)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to sPGA Response During the Retreatment Phase

End point title	Time to sPGA Response During the Retreatment Phase
End point description:	
Time to sPGA success is calculated as the time from qualification for retreatment to the assessment day of first sPGA response. Response is an sPGA score of 0 (clear) or 1 (almost clear). Time to sPGA response was analyzed using Kaplan-Meier methods in subjects who entered the retreatment phase. Subjects who discontinued prior to study day 392 or qualified for rescue were censored at the date of the last assessment taken prior to or on the early termination visit or last assessment taken prior to or on the date of qualification for rescue treatment, whichever occurred first. Continuing subjects who reached study day 392 or qualified for rescue treatment without achieving response were censored at the date of the last assessment taken prior to or on day 392 or at the rescue qualification date, whichever occurred first. "99999" indicates data that could not be estimated due to the low number of events.	
End point type	Secondary
End point timeframe:	
Week 16 to week 52	

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: weeks				
median (confidence interval 95%)	4.14 (4.14 to 4.29)	15 (2.29 to 99999)	4.14 (4.14 to 4.86)	99999 (2 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PASI 75 Response During the Retreatment Phase

End point title	Time to PASI 75 Response During the Retreatment Phase
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End point description:

Time to PASI 75 response was calculated from the date of qualification for retreatment to the assessment day of first PASI 75 response. The analysis includes subjects who entered the retreatment phase and were not PASI 75 responders at the retreatment qualification date. Time to PASI response was analyzed using Kaplan-Meier methods. Subjects who discontinued prior to study day 392 or qualified for rescue were censored at the date of the last assessment taken prior to or on the early termination visit or last assessment taken prior to or on the date of qualification for rescue treatment, whichever occurred first. Continuing subjects who reached study day 392 or qualified for rescue treatment without achieving response were censored at the date of the last assessment taken prior to or on day 392 or at the rescue qualification date, whichever occurred first. "99999" indicates data that could not be estimated due to the low number of events.

End point type	Secondary
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End point timeframe:

Week 16 to week 52

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	47	5	70	2
Units: weeks				
median (confidence interval 95%)	3.71 (2.14 to 4.14)	99999 (11.14 to 99999)	4.14 (2.29 to 4.14)	9.36 (8.57 to 10.14)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PASI 90 Response During the Retreatment Phase

End point title	Time to PASI 90 Response During the Retreatment Phase
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End point description:

Time to PASI 90 response was calculated from the date of qualification for retreatment to the assessment day of first PASI 90 response. The analysis includes subjects who entered the retreatment phase and were not PASI 90 responders at the retreatment qualification date. Time to PASI response was analyzed using Kaplan-Meier methods. Subjects who discontinued prior to study day 392 or qualified for rescue were censored at the date of the last assessment taken prior to or on the early termination visit or last assessment taken prior to or on the date of qualification for rescue treatment, whichever occurred first. Continuing subjects who reached study day 392 or qualified for rescue treatment without achieving response were censored at the date of the last assessment taken prior to or on day 392 or at the rescue qualification date, whichever occurred first. "99999" indicates data that could not be estimated due to the low number of events.

End point type	Secondary
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End point timeframe:

Week 16 to week 52

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: weeks				
median (confidence interval 95%)	4.21 (4.14 to 6.14)	15 (2.29 to 99999)	4.43 (4.14 to 6.14)	10.14 (2 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PASI 100 Response During the Retreatment Phase

End point title	Time to PASI 100 Response During the Retreatment Phase
End point description:	
Time to PASI 100 response was calculated from the date of qualification for retreatment to the assessment day of first PASI 100 response. The analysis includes subjects who entered the retreatment phase and were not PASI 100 responders at the retreatment qualification date. Time to PASI response was analyzed using Kaplan-Meier methods. Subjects who discontinued prior to study day 392 or qualified for rescue were censored at the date of the last assessment taken prior to or on the early termination visit or last assessment taken prior to or on the date of qualification for rescue treatment, whichever occurred first. Continuing subjects who reached study day 392 or qualified for rescue treatment without achieving response were censored at the date of the last assessment taken prior to or on day 392 or at the rescue qualification date, whichever occurred first. "99999" indicates data that could not be estimated due to the low number of events.	
End point type	Secondary
End point timeframe:	
Week 16 to week 52	

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: weeks				
median (confidence interval 95%)	11.71 (6.43 to 20.14)	99999 (4.14 to 99999)	8.14 (6.14 to 9)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with an sPGA Response During the Retreatment Phase

End point title	Percentage of Participants with an sPGA Response During the Retreatment Phase
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End point description:

A sPGA response is defined as a sPGA value of clear (score 0) or almost clear (score 1). Results are reported by weeks since return of disease."N" indicates the number of subjects who entered the retreatment phase and had a valid measurement value at the specified week of retreatment.

End point type	Secondary
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End point timeframe:

Week 16 to week 52

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: percentage of participants				
number (confidence interval 95%)				
2 weeks (N = 39, 4, 56, 2)	30.8 (17 to 47.6)	25 (0.6 to 80.6)	33.9 (21.8 to 47.8)	50 (1.3 to 98.7)
4 weeks (N = 48, 7, 62, 4)	70.8 (55.9 to 83)	14.3 (0.4 to 57.9)	69.4 (56.3 to 80.4)	25 (0.6 to 80.6)
8 weeks (N = 36, 7, 45, 3)	77.8 (60.8 to 89.9)	14.3 (0.4 to 57.9)	80 (65.4 to 90.4)	66.7 (9.4 to 99.2)
12 weeks (N = 33, 7, 40, 2)	72.7 (54.5 to 86.7)	14.3 (0.4 to 57.9)	80 (64.4 to 90.9)	100 (15.8 to 100)
16 weeks (N = 33, 3, 38, 2)	81.8 (64.5 to 93)	0 (0 to 70.8)	81.6 (65.7 to 92.3)	100 (15.8 to 100)
20 weeks (N = 27, 3, 34, 2)	81.5 (61.9 to 93.7)	66.7 (9.4 to 99.2)	88.2 (72.5 to 96.7)	0 (0 to 84.2)
24 weeks (N = 19, 1, 32, 1)	84.2 (60.4 to 96.6)	0 (0 to 97.5)	96.9 (83.8 to 99.9)	0 (0 to 97.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 75 Response During the Retreatment Phase

End point title	Percentage of Participants with a PASI 75 Response During the Retreatment Phase
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End point description:

Results are reported by weeks since return of disease."N" indicates the number of subjects who entered the retreatment phase and had a valid measurement value at the specified week of retreatment.

End point type	Secondary
End point timeframe:	
Week 16 to week 52	

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: percentage of participants				
number (confidence interval 95%)				
2 weeks (N = 39, 4, 56, 2)	66.7 (49.8 to 80.9)	75 (19.4 to 99.4)	67.9 (54 to 79.7)	50 (1.3 to 98.7)
4 weeks (N = 48, 7, 62, 4)	85.4 (72.2 to 93.9)	42.9 (9.9 to 81.6)	83.9 (72.3 to 92)	50 (6.8 to 93.2)
8 weeks (N = 36, 7, 45, 3)	86.1 (70.5 to 95.3)	14.3 (0.4 to 57.9)	91.1 (78.8 to 97.5)	100 (29.2 to 100)
12 weeks (N = 33, 7, 40, 2)	78.8 (61.1 to 91)	57.1 (18.4 to 90.1)	92.5 (79.6 to 98.4)	100 (15.8 to 100)
16 weeks (N = 33, 3, 38, 2)	84.8 (68.1 to 94.9)	66.7 (9.4 to 99.2)	92.1 (78.6 to 98.3)	100 (15.8 to 100)
20 weeks (N = 27, 3, 34, 2)	100 (87.2 to 100)	100 (29.2 to 100)	94.1 (80.3 to 99.3)	50 (1.3 to 98.7)
24 weeks (N = 19, 1, 32, 1)	94.7 (74 to 99.9)	100 (2.5 to 100)	100 (89.1 to 100)	100 (2.5 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 90 Response During the Retreatment Phase

End point title	Percentage of Participants with a PASI 90 Response During the Retreatment Phase
End point description:	
Results are reported by weeks since return of disease.	
"N" indicates the number of subjects who entered the retreatment phase and had a valid measurement value at the specified week of retreatment.	
End point type	Secondary
End point timeframe:	
Week 16 to week 52	

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: percentage of participants				
number (confidence interval 95%)				
2 weeks (N = 39, 4, 56, 2)	23.1 (11.1 to 39.3)	25 (0.6 to 80.6)	28.6 (17.3 to 42.2)	50 (1.3 to 98.7)
4 weeks (N = 48, 7, 62, 4)	62.5 (47.4 to 76)	28.6 (3.7 to 71)	59.7 (46.4 to 71.9)	25 (0.6 to 80.6)
8 weeks (N = 36, 7, 45, 3)	75 (57.8 to 87.9)	0 (0 to 41)	88.9 (75.9 to 96.3)	66.7 (9.4 to 99.2)
12 weeks (N = 33, 7, 40, 2)	63.6 (45.1 to 79.6)	14.3 (0.4 to 57.9)	85 (70.2 to 94.3)	50 (1.3 to 98.7)
16 weeks (N = 33, 3, 38, 2)	72.7 (54.5 to 86.7)	33.3 (0.8 to 90.6)	86.8 (71.9 to 95.6)	50 (1.3 to 98.7)
20 weeks (N = 27, 3, 34, 2)	70.4 (49.8 to 86.2)	0 (0 to 70.8)	91.2 (76.3 to 98.1)	0 (0 to 84.2)
24 weeks (N = 19, 1, 32, 1)	78.9 (54.4 to 93.9)	0 (0 to 97.5)	96.9 (83.8 to 99.9)	0 (0 to 97.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a PASI 100 Response During the Retreatment Phase

End point title	Percentage of Participants with a PASI 100 Response During the Retreatment Phase
End point description:	
Results are reported by weeks since return of disease.	
"N" indicates the number of subjects who entered the retreatment phase and had a valid measurement value at the specified week of retreatment.	
End point type	Secondary
End point timeframe:	
Week 16 to week 52	

End point values	Brodalumab 140 mg / Placebo / Brodalumab 140 mg	Brodalumab 140 mg / Brodalumab 140 mg /Brodalumab 140 mg	Brodalumab 210 mg / Placebo / Brodalumab 210 mg	Brodalumab 210 mg / Brodalumab 210 mg / Brodalumab 210 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	53	12	79	5
Units: percentage of participants				
number (confidence interval 95%)				
2 weeks (N = 39, 4, 56, 2)	5.1 (0.6 to 17.3)	0 (0 to 60.2)	10.7 (4 to 21.9)	0 (0 to 84.2)

4 weeks (N = 48, 7, 62, 4)	27.1 (15.3 to 41.8)	14.3 (0.4 to 57.9)	33.9 (22.3 to 47)	0 (0 to 60.2)
8 weeks (N = 36, 7, 45, 3)	38.9 (23.1 to 56.5)	0 (0 to 41)	64.4 (48.8 to 78.1)	0 (0 to 70.8)
12 weeks (N = 33, 7, 40, 2)	45.5 (28.1 to 63.6)	0 (0 to 41)	60 (43.3 to 75.1)	0 (0 to 84.2)
16 weeks (N = 33, 3, 38, 2)	60.6 (42.1 to 77.1)	0 (0 to 70.8)	65.8 (48.6 to 80.4)	0 (0 to 84.2)
20 weeks (N = 27, 3, 34, 2)	63 (42.4 to 80.6)	0 (0 to 70.8)	79.4 (62.1 to 91.3)	0 (0 to 84.2)
24 weeks (N = 19, 1, 32, 1)	68.4 (43.4 to 87.4)	0 (0 to 97.5)	84.4 (67.2 to 94.7)	0 (0 to 97.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a Dermatology Life Quality Index (DLQI) Response at Week 12

End point title	Percentage of Participants with a Dermatology Life Quality Index (DLQI) Response at Week 12
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End point description:

The dermatology life quality index (DLQI) is a skin disease-specific instrument to evaluate health-related quality of life. The DLQI questionnaire asks participants to evaluate the degree that psoriasis has affected their quality of life in the last week, and includes the following parameters: symptoms and feelings, daily activities, leisure activities, work or school activities, personal relationships and treatment related feelings. Participants answered 10 questions on a scale from 0 (not at all) to 3 (very much); the range of the total score is from 0 (best possible score) to 30 (worst possible score). A DLQI response is defined as achieving at least a 5-point improvement from baseline. This endpoint was analyzed in subjects with a baseline DLQI ≥ 5 . Non-responder imputation was used to impute missing data.

End point type	Secondary
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End point timeframe:

Baseline and week 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	199	191	201	
Units: percentage of participants				
number (confidence interval 95%)	21.6 (16.1 to 28)	73.8 (67 to 79.9)	83.6 (77.7 to 88.4)	

Statistical analyses

No statistical analyses for this end point

Secondary: Treatment Satisfaction at Week 12

End point title	Treatment Satisfaction at Week 12
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End point description:

Subjects assessed their satisfaction with their treatment as dissatisfied, very dissatisfied, neither satisfied nor dissatisfied, satisfied, or very satisfied.

This endpoint was analyzed in subjects who had a valid measurement value at week 12.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	205	208	209	
Units: participants				
number (not applicable)				
Very dissatisfied	60	15	16	
Dissatisfied	55	21	5	
Neither satisfied nor dissatisfied	48	20	10	
Satisfied	28	52	57	
Very satisfied	14	100	121	

Statistical analyses

No statistical analyses for this end point

Secondary: Medical Outcomes Short Form-36 (SF-36) Mental and Physical Component Scores at Week 12

End point title	Medical Outcomes Short Form-36 (SF-36) Mental and Physical Component Scores at Week 12
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End point description:

The SF-36 assesses the general quality of life (QOL) of participants by evaluating the domains of physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. The questionnaire consists of 36 questions that are completed by the participant. The SF-36 is split into two major components: physical health and mental health. Under physical health are the following four domains: physical health, bodily pain, physical functioning and physical role limitations. Under the mental health domain there are four domains; mental health, vitality, social functioning, and emotional role limitation. The individual domain scores are aggregated to derive a physical-component summary score and a mental-component summary score which range from 0 to 100, with higher scores indicating a better level of functioning.

This endpoint was analyzed in subjects who had a valid measurement value at week 12.

End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	205	207	208	
Units: units on a scale				
arithmetic mean (standard deviation)				
Physical Component Score	46.52 (± 9.82)	51.96 (± 7.8)	51.03 (± 8.98)	
Mental Component Score	46.43 (± 11.48)	50.82 (± 9.19)	51.86 (± 8.88)	

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQoL-5 Dimension (EQ-5D) Score at Week 12

End point title	EuroQoL-5 Dimension (EQ-5D) Score at Week 12
End point description:	
The EQ-5D questionnaire captures 2 types of information, a descriptive "profile," (health state), and an overall health rating using a visual analog scale. The health states include mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, which are combined to produce a single weighted index score by applying coefficients from a validated value set. The visual analog scale is a linear, thermometer-like scale that respondents can use to rate their health status, with zero representing the worst imaginable health status and 100 the best. The EQ-5D score was calculated based on the five attributes on the EQ-5D questionnaire, each answered 1, 2, or 3, with 1 signifying no problem, 2 signifying some problem, and 3 signifying major problem. The calculated EQ-5D score ranges from -0.594 to 1, with -0.594 representing death and 1 representing the perfect health state. This endpoint was analyzed in subjects who had a valid measurement value at week 12.	
End point type	Secondary
End point timeframe:	
Week 12	

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	205	207	209	
Units: units on a scale				
arithmetic mean (standard deviation)	0.6226 (± 0.3196)	0.8322 (± 0.2391)	0.8584 (± 0.2135)	

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement From Baseline in Hospital Anxiety and Depression Scale (HADS) Score at Week 12

End point title	Improvement From Baseline in Hospital Anxiety and Depression Scale (HADS) Score at Week 12
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End point description:

The HADS is a 14-item questionnaire assessing subject's symptoms of depression and anxiety. The measure consists of 7 items reflecting anxiety and 7 items reflecting depression. Each item is answered by the patient on a 4-point (0–3) response category so the possible scores ranged from 0 to 21 for anxiety and 0 to 21 for depression.

This endpoint was analyzed in subjects who had a valid measurement value at week 12.

Improvement from baseline was calculated as Baseline value - Post-baseline value.

End point type	Secondary
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End point timeframe:

Baseline and week 12

End point values	Placebo	Brodalumab 140 mg	Brodalumab 210 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	204	204	208	
Units: units on a scale				
arithmetic mean (standard deviation)				
Depression Score	-0.1 (± 3)	1.7 (± 3.4)	2 (± 3.4)	
Anxiety Score	0.2 (± 2.8)	1.4 (± 3.4)	1.8 (± 3.3)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Induction Phase: 12 weeks

Overall Study: Up to 266 weeks

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.0
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Reporting groups

Reporting group title	Induction Phase: Placebo
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Reporting group description:

Participants received placebo matching brodalumab administered via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Reporting group title	Induction Phase: Brodalumab 140 mg
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Reporting group description:

Participants received 140 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Reporting group title	Induction Phase: Brodalumab 210 mg
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Reporting group description:

Participants received 210 mg brodalumab via subcutaneous injection on day 1 and at weeks 1, 2, 4, 6, 8, and 10.

Reporting group title	Overall Study: Brodalumab Variable Dosing
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Reporting group description:

Participants who received either combination dosing of brodalumab (140 mg and 210 mg) during the overall study or who received fewer than 75% of doses of brodalumab after first dose of active treatment.

Reporting group title	Overall Study: Brodalumab 140 mg
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Reporting group description:

Participants who received at least 75% of doses with brodalumab 140 mg after the first active dose and no doses of 210 mg during the overall study.

Reporting group title	Overall Study: Brodalumab 210 mg
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Reporting group description:

Participants who received at least 75% of doses with brodalumab 210 mg after the first active dose and no doses of 140 mg during the overall study.

Serious adverse events	Induction Phase: Placebo	Induction Phase: Brodalumab 140 mg	Induction Phase: Brodalumab 210 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 220 (1.36%)	6 / 219 (2.74%)	4 / 222 (1.80%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenolymphoma			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesterol granuloma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestine carcinoma metastatic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal death			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Sudden death			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung perforation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional overdose			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Limb injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scapula fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriospasm coronary			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nodal arrhythmia			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratopathy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammatory bowel disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			

subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus of small bowel			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropathy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoroacetabular impingement			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Foot deformity			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis stenosans			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess of salivary gland			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coccidioidomycosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Overall Study:	Overall Study:	Overall Study:
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	Brodalumab Variable Dosing	Brodalumab 140 mg	Brodalumab 210 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 179 (19.55%)	11 / 71 (15.49%)	57 / 398 (14.32%)
number of deaths (all causes)	1	0	6
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenolymphoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesterol granuloma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipoma			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal cancer			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestine carcinoma metastatic			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foetal death			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Cyst			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperthermia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Apnoea			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung perforation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Completed suicide			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Depression			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intentional overdose			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Limb injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple injuries			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scapula fracture			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arteriospasm coronary			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Myocardial infarction			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Nodal arrhythmia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratopathy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Abdominal adhesions			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inflammatory bowel disease			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritable bowel syndrome			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal varices haemorrhage			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pancreatitis acute			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varices oesophageal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus of small bowel			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Psoriasis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthropathy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Femoroacetabular impingement subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal osteoarthritis subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis stenosans subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess of salivary gland subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic tonsillitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coccidioidomycosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Induction Phase: Placebo	Induction Phase: Brodalumab 140 mg	Induction Phase: Brodalumab 210 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	111 / 220 (50.45%)	124 / 219 (56.62%)	131 / 222 (59.01%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Basal cell carcinoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Breast neoplasm			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dysplastic naevus			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Enchondroma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Fibroma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Keratoacanthoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lipoma			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Melanocytic naevus			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neoplasm			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neurofibroma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pyogenic granuloma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic keratosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Deep vein thrombosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Diastolic hypertension			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Embolism			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Flushing			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Hot flush			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	4 / 220 (1.82%)	8 / 219 (3.65%)	2 / 222 (0.90%)
occurrences (all)	4	8	2
Hypertensive crisis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypotension			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neurogenic shock			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	2	0
Orthostatic hypotension			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Peripheral vascular disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Peripheral venous disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Phlebitis superficial			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Post thrombotic syndrome			

subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Raynaud's phenomenon			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Systolic hypertension			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Varicose vein			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Surgical and medical procedures			
Abdominal hernia repair			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Arthroscopic surgery			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Bunion operation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Carpal tunnel decompression			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cataract operation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dental care			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dental implantation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Dental operation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermabrasion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Endodontic procedure			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	2	0	0
Endometrial ablation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Internal fixation of spine			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Joint surgery			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Knee arthroplasty			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Mole excision			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oophorectomy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Peripheral nerve operation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sinus operation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Skin lesion excision			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Tooth extraction subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	1 / 219 (0.46%) 1	1 / 222 (0.45%) 1
Tooth repair subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Vitrectomy subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Wedge resection toenail subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	1 / 219 (0.46%) 1	0 / 222 (0.00%) 0
Wisdom teeth removal subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
General disorders and administration site conditions			
Adverse drug reaction subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	2 / 219 (0.91%) 2	1 / 222 (0.45%) 1
Chest discomfort subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Chills subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	1 / 219 (0.46%) 1	0 / 222 (0.00%) 0
Cyst subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	1 / 222 (0.45%) 1
Device failure			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Discomfort			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	1
Feeling cold			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	2	0	0
Feeling of body temperature change			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Gravitational oedema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Impaired healing			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	4 / 222 (1.80%)
occurrences (all)	1	0	4
Injection site bruising			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Injection site extravasation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injection site haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Injection site induration			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injection site irritation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injection site oedema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	0	3	0
Injection site swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injury associated with device			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Local swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Metaplasia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nodule			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	2 / 220 (0.91%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	2	1	0
Oedema			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			
subjects affected / exposed	5 / 220 (2.27%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	5	1	1
Pain			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Peripheral swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Puncture site reaction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	2 / 220 (0.91%)	3 / 219 (1.37%)	0 / 222 (0.00%)
occurrences (all)	2	3	0
Ulcer			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Xerosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Drug hypersensitivity subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Flour sensitivity subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Food allergy subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Hypersensitivity subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Social circumstances Dental prosthesis user subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Reproductive system and breast disorders Balanoposthitis subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	1 / 219 (0.46%) 1	0 / 222 (0.00%) 0
Breast cyst subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Breast mass subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Dysmenorrhoea subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	1 / 222 (0.45%) 1
Erectile dysfunction			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Fibrocystic breast disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Haematospermia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Menopausal symptoms			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Menstruation irregular			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Nipple pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	1	0	3
Prostatitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Testicular pain			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Uterine cervical erosion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal dryness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Vulvovaginal pain			

subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Asthma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Bronchial hyperreactivity			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 220 (0.00%)	6 / 219 (2.74%)	3 / 222 (1.35%)
occurrences (all)	0	6	3
Dry throat			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dysphonia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Emphysema			

subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Haemothorax			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lung infiltration			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	2 / 222 (0.90%)
occurrences (all)	0	1	2
Nasal dryness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nasal inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nasal septum deviation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 220 (0.91%)	4 / 219 (1.83%)	2 / 222 (0.90%)
occurrences (all)	3	5	2
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Pharyngeal inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Productive cough			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Respiratory disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	1	1	1
Rhinorrhoea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sinus congestion			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Sinusitis noninfective			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Sleep apnoea syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Acute stress disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Anxiety disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Apathy			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Bipolar disorder			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Depressed mood			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	1	1	1
Initial insomnia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Libido decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Mood altered			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Panic attack			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Stress			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Arthroscopy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood chloride decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood creatinine abnormal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood creatinine increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			

subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Blood immunoglobulin E increased			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Blood pressure diastolic increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	1	0	1
Blood sodium decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood testosterone decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood triglycerides increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Blood urine present			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Colonoscopy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram abnormal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Endoscopy upper gastrointestinal			

tract			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eosinophil count increased			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	0	2	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Grip strength decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Haemoglobin decreased			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lipids abnormal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lipids increased			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Lymph node palpable			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lymphocyte morphology abnormal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Neutrophil count increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	1	0	2
Urine analysis abnormal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	0	2	0
White blood cell count increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
White blood cells urine positive			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Wound healing normal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Animal bite			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Ankle fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Burns second degree			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cartilage injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Chemical injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Concussion			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	2	0	1
Dislocation of vertebra			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Epicondylitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eye injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Fall			

subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Gingival injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Heat stroke			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	2	0	1
Laceration			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Ligament injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ligament rupture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	1 / 220 (0.45%)	3 / 219 (1.37%)	0 / 222 (0.00%)
occurrences (all)	1	3	0
Limb injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Muscle injury			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Muscle rupture			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	2	0	1
Nail avulsion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nail injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neck injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Post procedural inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Post-traumatic neck syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	2	0	0
Postoperative wound complication			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Procedural site reaction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Radius fracture			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rib fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Road traffic accident			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Skeletal injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Skin injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Soft tissue injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Sunburn			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Synovial rupture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tendon injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tibia fracture			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	1	0	2
Traumatic haematoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ulnar nerve injury			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Upper limb fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Atrial hypertrophy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block first degree			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Bundle branch block left			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cardiac failure congestive			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cardiomegaly			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Coronary artery disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypertensive heart disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Left ventricular hypertrophy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Myocardial ischaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sinus arrhythmia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Amnesia subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Burning sensation subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	1 / 222 (0.45%) 1
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Cerebral cyst subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Cerebral ischaemia subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Demyelination subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Diabetic neuropathy subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	3 / 219 (1.37%) 3	0 / 222 (0.00%) 0
Dizziness postural subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Epilepsy			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Formication			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	7 / 220 (3.18%)	12 / 219 (5.48%)	12 / 222 (5.41%)
occurrences (all)	7	15	15
Hypoaesthesia			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Hypotonia			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Intercostal neuralgia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	1 / 222 (0.45%)
occurrences (all)	0	2	1
Morton's neuralgia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Occipital neuralgia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Polyneuropathy			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	1
Restless legs syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	1	2	1
Sinus headache			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	2	0	0
Somnolence			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tension headache			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tongue biting			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0

Eosinophilia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Leukocytosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Neutrophilia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Sickle cell anaemia with crisis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1

Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Deafness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ear pain			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Inner ear inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	2 / 220 (0.91%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	3	0	0
Vertigo positional			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Asthenopia			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Blepharitis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cataract			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Chalazion			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Conjunctival hyperaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Eczema eyelids			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eye discharge			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eye movement disorder			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	0	2	0
Eye swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Glaucoma			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Iritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Lacrimation increased			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Macular degeneration			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Retinal telangiectasia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Uveitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal discomfort			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	2 / 220 (0.91%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	2	1	0
Abdominal pain lower			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	2 / 222 (0.90%)
occurrences (all)	1	1	3
Abdominal tenderness			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Abnormal faeces			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Anal fissure			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Aphthous stomatitis			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Cheilitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Chronic gastritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	0	2	0

Dental caries			
subjects affected / exposed	2 / 220 (0.91%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	2	1	0
Diarrhoea			
subjects affected / exposed	1 / 220 (0.45%)	4 / 219 (1.83%)	4 / 222 (1.80%)
occurrences (all)	2	4	5
Diarrhoea haemorrhagic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Diverticulum intestinal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	2	1
Duodenitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	1 / 222 (0.45%)
occurrences (all)	0	2	1
Dysphagia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Epigastric discomfort			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eructation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0

Gastric ulcer			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Gingival cyst			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Glossodynia			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Haematochezia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyperchlorhydria			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Inflammatory bowel disease			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Inguinal hernia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Irritable bowel syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Large intestine polyp			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lip blister			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Lip dry			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Lip pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Mouth swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 220 (0.91%)	5 / 219 (2.28%)	5 / 222 (2.25%)
occurrences (all)	2	6	14
Noninfective gingivitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oesophageal obstruction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oesophageal spasm			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oesophagitis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Parotid gland enlargement			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Plicated tongue			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Poor dental condition			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Salivary duct inflammation			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Sensitivity of teeth			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tongue blistering			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tooth disorder			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	2 / 220 (0.91%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	3	2	0
Umbilical hernia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	1 / 220 (0.45%)	4 / 219 (1.83%)	2 / 222 (0.90%)
occurrences (all)	1	4	2
Hepatobiliary disorders			
Biliary colic			

subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Cholecystitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Gallbladder polyp			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Non-alcoholic steatohepatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Portal hypertension			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Actinic keratosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	1 / 222 (0.45%)
occurrences (all)	0	2	1
Alopecia areata			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1

Angioedema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Angiokeratoma			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Diffuse alopecia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	2	1
Dyshidrotic eczema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Eczema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Eczema asteatotic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Guttate psoriasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hidradenitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Hyperkeratosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Intertrigo			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lichen planus			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lichenification			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Nail psoriasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Neurodermatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Onycholysis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Papule			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pityriasis rosea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Polymorphic light eruption			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Prurigo			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	5 / 220 (2.27%)	5 / 219 (2.28%)	5 / 222 (2.25%)
occurrences (all)	6	5	6
Pruritus generalised			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	2	1
Psoriasis			
subjects affected / exposed	3 / 220 (1.36%)	2 / 219 (0.91%)	1 / 222 (0.45%)
occurrences (all)	4	2	2
Pustular psoriasis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	4 / 222 (1.80%)
occurrences (all)	0	0	5
Rash pruritic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rebound psoriasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rosacea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Scab			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Skin discomfort			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Skin fissures			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Skin hyperpigmentation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Skin odour abnormal			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Stasis dermatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Vitiligo			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Glycosuria			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Hydronephrosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Micturition frequency decreased			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Nephrolithiasis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0

Pollakiuria			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Renal colic			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ureterocele			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Urinary tract inflammation			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Hyperthyroidism			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypogonadism			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Hypothyroidism			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Thyroid cyst			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			

Ankylosing spondylitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	6 / 220 (2.73%)	11 / 219 (5.02%)	7 / 222 (3.15%)
occurrences (all)	7	12	8
Arthritis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	2 / 222 (0.90%)
occurrences (all)	0	1	2
Arthropathy			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	4 / 220 (1.82%)	2 / 219 (0.91%)	5 / 222 (2.25%)
occurrences (all)	4	2	5
Bone pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	2
Bursitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Chondromalacia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Costochondritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dactylitis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	1	0	1
Dupuytren's contracture			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Exostosis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0

Fibromyalgia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Intervertebral disc degeneration			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Intervertebral disc disorder			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Joint effusion			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Joint stiffness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Metatarsalgia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Muscle tightness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Muscle twitching			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	2 / 220 (0.91%)	1 / 219 (0.46%)	3 / 222 (1.35%)
occurrences (all)	3	1	3
Musculoskeletal stiffness			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	4 / 222 (1.80%)
occurrences (all)	0	2	5
Neck pain			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Osteoarthritis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	2 / 220 (0.91%)	1 / 219 (0.46%)	4 / 222 (1.80%)
occurrences (all)	2	1	6
Pain in jaw			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Periarthritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Plantar fasciitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Polyarthrititis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Polymyalgia rheumatica			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Psoriatic arthropathy			
subjects affected / exposed	4 / 220 (1.82%)	3 / 219 (1.37%)	4 / 222 (1.80%)
occurrences (all)	4	3	5
Rhabdomyolysis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	1
Spinal column stenosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Spinal osteoarthritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Synovial cyst			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Synovitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Temporomandibular joint syndrome subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Tendon pain subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Tendonitis subjects affected / exposed occurrences (all)	1 / 220 (0.45%) 1	1 / 219 (0.46%) 1	2 / 222 (0.90%) 2
Tenosynovitis subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Torticollis subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	1 / 219 (0.46%) 1	0 / 222 (0.00%) 0
Infections and infestations			
Abdominal abscess subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	1 / 219 (0.46%) 1	0 / 222 (0.00%) 0
Abscess subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Abscess limb subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	1 / 222 (0.45%) 1
Acarodermatitis subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Acne pustular subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	1 / 222 (0.45%) 1
Acute sinusitis subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Acute tonsillitis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Appendicitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Bacteriuria			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Balanitis candida			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Body tinea			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Bronchitis			
subjects affected / exposed	3 / 220 (1.36%)	3 / 219 (1.37%)	3 / 222 (1.35%)
occurrences (all)	3	3	3
Bronchitis bacterial			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Bronchitis viral			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	1	1	1
Chlamydial infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Chronic tonsillitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			

subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	5 / 222 (2.25%)
occurrences (all)	0	2	5
Conjunctivitis bacterial			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Corneal infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Cystitis			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	1	0	1
Cystitis bacterial			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Dacryocanaliculitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Dermo-hypodermatitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Diarrhoea infectious			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Diverticulitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Eczema infected			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Enteritis infectious			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Erysipelas			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
External ear cellulitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	1 / 220 (0.45%)	2 / 219 (0.91%)	1 / 222 (0.45%)
occurrences (all)	1	2	1
Fungal infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Furuncle			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Gastroenteritis			
subjects affected / exposed	3 / 220 (1.36%)	0 / 219 (0.00%)	3 / 222 (1.35%)
occurrences (all)	4	0	3
Gastroenteritis viral			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal infection			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal viral infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Genital herpes			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Gingivitis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Herpes oesophagitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Herpes simplex			
subjects affected / exposed	1 / 220 (0.45%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	1	2	0
Herpes virus infection			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Influenza			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	4 / 222 (1.80%)
occurrences (all)	1	1	4
Labyrinthitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Laryngitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	22 / 220 (10.00%)	20 / 219 (9.13%)	22 / 222 (9.91%)
occurrences (all)	24	21	27
Oesophageal candidiasis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Omphalitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oral fungal infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	0 / 222 (0.00%)
occurrences (all)	0	2	0
Oral infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Orchitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Oropharyngitis fungal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Osteomyelitis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Otitis media			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	1	0	1
Otitis media acute			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Papilloma viral infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Pericarditis infective			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Peritonsillar abscess			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	2 / 220 (0.91%)	3 / 219 (1.37%)	3 / 222 (1.35%)
occurrences (all)	2	3	3
Pharyngitis bacterial			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Pharyngitis streptococcal			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pilonidal cyst			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Post procedural infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pulpitis dental			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	1
Pyelonephritis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Pyuria			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rash pustular			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	2 / 220 (0.91%)	2 / 219 (0.91%)	5 / 222 (2.25%)
occurrences (all)	2	2	5
Sinusitis			
subjects affected / exposed	4 / 220 (1.82%)	2 / 219 (0.91%)	4 / 222 (1.80%)
occurrences (all)	4	2	4
Skin bacterial infection			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Skin candida			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tinea cruris			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tinea infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tinea manuum			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tinea pedis			
subjects affected / exposed	0 / 220 (0.00%)	2 / 219 (0.91%)	2 / 222 (0.90%)
occurrences (all)	0	2	2
Tonsillitis			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	2
Tooth abscess			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	1
Tooth infection			

subjects affected / exposed	2 / 220 (0.91%)	6 / 219 (2.74%)	1 / 222 (0.45%)
occurrences (all)	2	6	1
Toxocariasis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Tracheitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	14 / 220 (6.36%)	18 / 219 (8.22%)	18 / 222 (8.11%)
occurrences (all)	18	20	21
Upper respiratory tract infection bacterial			
subjects affected / exposed	1 / 220 (0.45%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	1	1	0
Urinary tract infection			
subjects affected / exposed	0 / 220 (0.00%)	3 / 219 (1.37%)	1 / 222 (0.45%)
occurrences (all)	0	3	1
Vaginal infection			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Vaginitis bacterial			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	1 / 222 (0.45%)
occurrences (all)	0	1	1
Viral infection			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Viral pharyngitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 220 (1.36%)	2 / 219 (0.91%)	2 / 222 (0.90%)
occurrences (all)	3	2	2
Vulvitis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0

Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Vulvovaginal mycotic infection subjects affected / exposed occurrences (all)	2 / 220 (0.91%) 2	0 / 219 (0.00%) 0	2 / 222 (0.90%) 2
Wound infection subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Metabolism and nutrition disorders			
Abnormal loss of weight subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Carbohydrate intolerance subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Decreased appetite subjects affected / exposed occurrences (all)	2 / 220 (0.91%) 2	1 / 219 (0.46%) 1	1 / 222 (0.45%) 1
Dehydration subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 220 (0.91%) 2	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Glucose tolerance impaired subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Gout subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 220 (0.00%) 0	0 / 219 (0.00%) 0	0 / 222 (0.00%) 0
Hypercholesterolaemia			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyperlipidaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	2 / 222 (0.90%)
occurrences (all)	0	0	2
Hyperuricaemia			
subjects affected / exposed	1 / 220 (0.45%)	2 / 219 (0.91%)	1 / 222 (0.45%)
occurrences (all)	1	2	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	1 / 222 (0.45%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			

subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Lactose intolerance			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Obesity			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 220 (0.00%)	1 / 219 (0.46%)	0 / 222 (0.00%)
occurrences (all)	0	1	0
Vitamin B12 deficiency			
subjects affected / exposed	0 / 220 (0.00%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	1 / 220 (0.45%)	0 / 219 (0.00%)	0 / 222 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Overall Study: Brodalumab Variable Dosing	Overall Study: Brodalumab 140 mg	Overall Study: Brodalumab 210 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	160 / 179 (89.39%)	61 / 71 (85.92%)	345 / 398 (86.68%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Basal cell carcinoma			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Breast neoplasm			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Dysplastic naevus			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Enchondroma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Fibroma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Keratoacanthoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Lipoma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Melanocytic naevus			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Neoplasm			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Neurofibroma			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Pyogenic granuloma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Seborrhoeic keratosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Skin papilloma			

subjects affected / exposed	6 / 179 (3.35%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	6	0	4
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Deep vein thrombosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Diastolic hypertension			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	4	0	1
Embolism			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Haematoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	0	0	4
Hot flush			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	15 / 179 (8.38%)	7 / 71 (9.86%)	23 / 398 (5.78%)
occurrences (all)	22	7	26
Hypertensive crisis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hypotension			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Lymphoedema			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Neurogenic shock			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Peripheral vascular disorder			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Peripheral venous disease			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Phlebitis superficial			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Post thrombotic syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Raynaud's phenomenon			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Systolic hypertension			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Thrombophlebitis superficial			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Varicose vein			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			

Abdominal hernia repair			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Arthroscopic surgery			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Bunion operation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Carpal tunnel decompression			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Cataract operation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Dental care			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dental implantation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dental operation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Dermabrasion			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Endodontic procedure			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Endometrial ablation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Internal fixation of spine			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0

Joint surgery			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Knee arthroplasty			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Mole excision			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Oophorectomy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Peripheral nerve operation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Sinus operation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Skin lesion excision			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tooth extraction			
subjects affected / exposed	5 / 179 (2.79%)	2 / 71 (2.82%)	5 / 398 (1.26%)
occurrences (all)	5	2	5
Tooth repair			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Vitrectomy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Wedge resection toenail			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Wisdom teeth removal			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	1	1	2

General disorders and administration site conditions			
Adverse drug reaction			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	2	1	4
Chest discomfort			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	8 / 398 (2.01%)
occurrences (all)	0	0	8
Chills			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Device failure			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Discomfort			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	8 / 398 (2.01%)
occurrences (all)	2	1	8
Feeling cold			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Feeling of body temperature change			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Gravitational oedema			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Impaired healing			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Inflammation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Influenza like illness			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	5 / 398 (1.26%)
occurrences (all)	2	0	6
Injection site bruising			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Injection site extravasation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Injection site haematoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Injection site haemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Injection site induration			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Injection site irritation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Injection site oedema			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Injection site pain			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Injection site reaction			
subjects affected / exposed	2 / 179 (1.12%)	2 / 71 (2.82%)	3 / 398 (0.75%)
occurrences (all)	2	3	3
Injection site swelling			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Injury associated with device			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Local swelling			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	1	1	1
Malaise			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	3
Metaplasia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Nodule			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	0	1	4
Oedema			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	1	1	1
Oedema peripheral			
subjects affected / exposed	6 / 179 (3.35%)	0 / 71 (0.00%)	8 / 398 (2.01%)
occurrences (all)	8	0	8
Pain			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	3
Peripheral swelling			

subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	6 / 398 (1.51%)
occurrences (all)	1	1	6
Puncture site reaction			
subjects affected / exposed	0 / 179 (0.00%)	2 / 71 (2.82%)	0 / 398 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	3 / 179 (1.68%)	2 / 71 (2.82%)	5 / 398 (1.26%)
occurrences (all)	3	2	10
Ulcer			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Vessel puncture site haematoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Xerosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Drug hypersensitivity			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Flour sensitivity			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Food allergy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	1
Seasonal allergy			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	5 / 398 (1.26%)
occurrences (all)	3	1	5

Social circumstances			
Dental prosthesis user			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 179 (0.00%)	2 / 71 (2.82%)	0 / 398 (0.00%)
occurrences (all)	0	2	0
Breast cyst			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Breast mass			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dysmenorrhoea			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Erectile dysfunction			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	1	0	3
Fibrocystic breast disease			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Haematospermia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Menopausal symptoms			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Menstruation irregular			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	2
Nipple pain			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ovarian cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	4
Prostatitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	2	0	2
Testicular pain			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Uterine cervical erosion			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Vulvovaginal dryness			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Vulvovaginal pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Allergic sinusitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Asthma			
subjects affected / exposed	1 / 179 (0.56%)	2 / 71 (2.82%)	2 / 398 (0.50%)
occurrences (all)	1	2	2
Atelectasis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Bronchial hyperreactivity			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Cough			
subjects affected / exposed	7 / 179 (3.91%)	6 / 71 (8.45%)	21 / 398 (5.28%)
occurrences (all)	7	7	23
Dry throat			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	2	1	1
Dyspnoea			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Dyspnoea exertional			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Emphysema			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 179 (0.56%)	2 / 71 (2.82%)	2 / 398 (0.50%)
occurrences (all)	1	2	2
Haemothorax			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Lung infiltration			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	8 / 398 (2.01%)
occurrences (all)	3	0	9

Nasal dryness			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Nasal inflammation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Nasal septum deviation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	9 / 179 (5.03%)	2 / 71 (2.82%)	14 / 398 (3.52%)
occurrences (all)	10	2	18
Paranasal sinus hypersecretion			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Pharyngeal inflammation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	3
Pleural effusion			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Pulmonary arterial hypertension			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Respiratory disorder			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	5 / 179 (2.79%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	6	0	2

Rhinorrhoea			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	2	1
Sinus congestion			
subjects affected / exposed	1 / 179 (0.56%)	2 / 71 (2.82%)	2 / 398 (0.50%)
occurrences (all)	1	2	2
Sinusitis noninfective			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Sleep apnoea syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Throat irritation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Upper-airway cough syndrome			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Psychiatric disorders			
Acute stress disorder			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Agitation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Anxiety			
subjects affected / exposed	8 / 179 (4.47%)	1 / 71 (1.41%)	6 / 398 (1.51%)
occurrences (all)	8	1	6
Anxiety disorder			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Apathy			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Bipolar disorder			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Depressed mood			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	7 / 179 (3.91%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	7	0	7
Initial insomnia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	4 / 179 (2.23%)	0 / 71 (0.00%)	7 / 398 (1.76%)
occurrences (all)	4	0	7
Libido decreased			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Mood altered			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Sleep disorder			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	2	0	1
Stress			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	5	0	4

Arthroscopy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	3	1	1
Blood bicarbonate decreased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Blood bilirubin increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Blood chloride decreased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Blood creatinine abnormal			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	3 / 179 (1.68%)	2 / 71 (2.82%)	3 / 398 (0.75%)
occurrences (all)	3	3	3
Blood immunoglobulin E increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Blood pressure diastolic increased			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Blood pressure increased			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	4 / 398 (1.01%)
occurrences (all)	1	1	4
Blood sodium decreased			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Blood testosterone decreased			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	2	0	2
Blood triglycerides increased			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	2	0	1
Blood uric acid increased			
subjects affected / exposed	3 / 179 (1.68%)	3 / 71 (4.23%)	5 / 398 (1.26%)
occurrences (all)	4	6	6
Blood urine present			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 179 (0.00%)	2 / 71 (2.82%)	1 / 398 (0.25%)
occurrences (all)	0	2	1
Colonoscopy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Electrocardiogram abnormal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Endoscopy upper gastrointestinal tract			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Eosinophil count increased			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Grip strength decreased			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	0	0	4
Lipids abnormal			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Lipids increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Lymph node palpable			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Lymphocyte morphology abnormal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Neutrophil count decreased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Neutrophil count increased			
subjects affected / exposed	2 / 179 (1.12%)	2 / 71 (2.82%)	1 / 398 (0.25%)
occurrences (all)	2	2	1
Platelet count decreased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Transaminases increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	5 / 398 (1.26%)
occurrences (all)	0	0	9
Urine analysis abnormal			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	0	1	3
Weight increased			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	6 / 398 (1.51%)
occurrences (all)	3	1	10
White blood cell count increased			
subjects affected / exposed	2 / 179 (1.12%)	2 / 71 (2.82%)	2 / 398 (0.50%)
occurrences (all)	2	2	2
White blood cells urine positive			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Wound healing normal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Animal bite			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	0	0	4
Ankle fracture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Arthropod bite			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	6 / 398 (1.51%)
occurrences (all)	3	1	6
Arthropod sting			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Burns second degree			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Cartilage injury			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Chemical injury			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Concussion			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Contusion			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	9 / 398 (2.26%)
occurrences (all)	3	0	9
Dislocation of vertebra			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Epicondylitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Eye injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	7 / 179 (3.91%)	1 / 71 (1.41%)	5 / 398 (1.26%)
occurrences (all)	9	1	5
Foot fracture			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	3	1	0
Gingival injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hand fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Heat stroke			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	7 / 398 (1.76%)
occurrences (all)	1	1	7
Laceration			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	9 / 398 (2.26%)
occurrences (all)	2	1	11
Ligament injury			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Ligament rupture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	5 / 179 (2.79%)	3 / 71 (4.23%)	7 / 398 (1.76%)
occurrences (all)	5	3	8
Limb injury			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	3
Meniscus injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	0	0	6
Muscle injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Muscle rupture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Muscle strain			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	11 / 398 (2.76%)
occurrences (all)	3	1	13
Nail avulsion			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Nail injury			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Neck injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Post procedural inflammation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Postoperative wound complication			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	2	0	6
Procedural site reaction			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	2	1	3
Road traffic accident			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	1
Skeletal injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Skin abrasion			

subjects affected / exposed	1 / 179 (0.56%)	2 / 71 (2.82%)	2 / 398 (0.50%)
occurrences (all)	4	2	2
Skin injury			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Soft tissue injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	0	0	4
Sunburn			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Synovial rupture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tendon injury			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Tendon rupture			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Thermal burn			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	1
Tibia fracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tooth fracture			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	3	0	7
Traumatic haematoma			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Ulnar nerve injury			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Upper limb fracture			

subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Wound subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	1 / 71 (1.41%) 1	1 / 398 (0.25%) 1
Wrist fracture subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Cardiac disorders			
Angina pectoris subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Arrhythmia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	1 / 71 (1.41%) 1	1 / 398 (0.25%) 1
Atrial hypertrophy subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Atrioventricular block first degree subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Bradycardia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Bundle branch block left subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Cardiac failure congestive subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0
Cardiomegaly subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Coronary artery disease subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0

Hypertensive heart disease subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0
Ischaemic cardiomyopathy subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0
Left ventricular hypertrophy subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Myocardial ischaemia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	1 / 71 (1.41%) 1	0 / 398 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	2 / 398 (0.50%) 2
Sinus arrhythmia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	2 / 398 (0.50%) 2
Tachycardia subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	5 / 398 (1.26%) 5
Ventricular extrasystoles subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	1 / 71 (1.41%) 1	0 / 398 (0.00%) 0
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Amnesia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	1 / 71 (1.41%) 2	1 / 398 (0.25%) 1
Burning sensation			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Carpal tunnel syndrome			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	2	1	3
Cerebral cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Cerebral ischaemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Demyelination			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Diabetic neuropathy			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	1
Dizziness			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	7 / 398 (1.76%)
occurrences (all)	6	1	7
Dizziness postural			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Formication			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	17 / 179 (9.50%)	5 / 71 (7.04%)	32 / 398 (8.04%)
occurrences (all)	39	5	60
Hypoaesthesia			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	1	1	4
Hypotonia			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Intercostal neuralgia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Migraine			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	5 / 398 (1.26%)
occurrences (all)	2	1	5
Morton's neuralgia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Nerve compression			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Neuropathy peripheral			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Occipital neuralgia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Polyneuropathy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Presyncope			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Restless legs syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Sciatica			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	7 / 398 (1.76%)
occurrences (all)	2	2	8
Sinus headache			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Syncope			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	5 / 398 (1.26%)
occurrences (all)	0	0	5
Tension headache			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tongue biting			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Transient ischaemic attack			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 179 (0.00%)	2 / 71 (2.82%)	0 / 398 (0.00%)
occurrences (all)	0	3	0
Eosinophilia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Iron deficiency anaemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Leukocytosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2

Lymphadenopathy			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Lymphopenia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Neutropenia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Neutrophilia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	1	0	3
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Pancytopenia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Sickle cell anaemia with crisis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Deafness			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ear discomfort			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ear pain			

subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	3	0	1
Inner ear inflammation			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Otorrhoea			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Tinnitus			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	3	0	6
Vertigo positional			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Asthenopia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Blepharitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Cataract			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Chalazion			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2

Conjunctival hyperaemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	5 / 398 (1.26%)
occurrences (all)	1	0	5
Eczema eyelids			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Eye discharge			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Eye movement disorder			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Eye pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Eye pruritus			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Eye swelling			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Glaucoma			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Iritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Lacrimation increased			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Macular degeneration			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1

Ocular hyperaemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Photopsia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Retinal telangiectasia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Uveitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	3
Vision blurred			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Visual acuity reduced			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Vitreous floaters			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Abdominal distension			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	8 / 398 (2.01%)
occurrences (all)	2	1	8
Abdominal pain lower			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	11 / 398 (2.76%)
occurrences (all)	2	0	12
Abdominal tenderness			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Abnormal faeces			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Anal fissure			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Aphthous stomatitis			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Cheilitis			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	1	1	3
Chronic gastritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	3 / 179 (1.68%)	2 / 71 (2.82%)	4 / 398 (1.01%)
occurrences (all)	3	2	4
Dental caries			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	4	0	4
Diarrhoea			
subjects affected / exposed	9 / 179 (5.03%)	2 / 71 (2.82%)	23 / 398 (5.78%)
occurrences (all)	11	2	35
Diarrhoea haemorrhagic			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	3	0	0
Diverticulum intestinal			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	2	1	3
Duodenitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	5 / 179 (2.79%)	2 / 71 (2.82%)	10 / 398 (2.51%)
occurrences (all)	5	2	14
Dysphagia			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Epigastric discomfort			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Eructation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Gastric ulcer			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	3
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	12 / 398 (3.02%)
occurrences (all)	3	0	12
Gingival cyst			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Glossodynia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Hiatus hernia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Hyperchlorhydria			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Inflammatory bowel disease			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Irritable bowel syndrome			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Large intestine polyp			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Lip blister			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Lip dry			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Lip pain			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Lip swelling			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Mouth swelling			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	7 / 179 (3.91%)	2 / 71 (2.82%)	13 / 398 (3.27%)
occurrences (all)	8	2	25
Noninfective gingivitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Oesophageal obstruction			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Oesophageal spasm			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Parotid gland enlargement			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Plicated tongue			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Poor dental condition			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Salivary duct inflammation			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Sensitivity of teeth			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Tongue blistering			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tooth disorder			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Toothache			
subjects affected / exposed	4 / 179 (2.23%)	1 / 71 (1.41%)	15 / 398 (3.77%)
occurrences (all)	5	1	18
Umbilical hernia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	6 / 179 (3.35%)	1 / 71 (1.41%)	7 / 398 (1.76%)
occurrences (all)	7	1	7
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Cholecystitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Cholelithiasis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Gallbladder polyp			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1

Hepatic steatosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Hyperbilirubinaemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Non-alcoholic steatohepatitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Portal hypertension			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Actinic keratosis			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	1	1	3
Alopecia			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	4	0	2
Alopecia areata			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Angioedema			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Angiokeratoma			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Decubitus ulcer			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dermal cyst			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Dermatitis			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	3 / 398 (0.75%)
occurrences (all)	4	1	3
Dermatitis acneiform			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Dermatitis contact			
subjects affected / exposed	4 / 179 (2.23%)	1 / 71 (1.41%)	8 / 398 (2.01%)
occurrences (all)	5	2	10
Diffuse alopecia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Dry skin			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	3
Dyshidrotic eczema			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	2	0	2
Ecchymosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Eczema			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	10 / 398 (2.51%)
occurrences (all)	2	0	10
Eczema asteatotic			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	0	0	4
Guttate psoriasis			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Hand dermatitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	2
Hidradenitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Hyperkeratosis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Intertrigo			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Lichen planus			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Lichenification			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Nail psoriasis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Neurodermatitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Onycholysis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysesthesia syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0

Papule			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Pityriasis rosea			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Polymorphic light eruption			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Prurigo			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Pruritus			
subjects affected / exposed	8 / 179 (4.47%)	2 / 71 (2.82%)	16 / 398 (4.02%)
occurrences (all)	9	6	23
Pruritus generalised			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	1	2	2
Psoriasis			
subjects affected / exposed	9 / 179 (5.03%)	1 / 71 (1.41%)	6 / 398 (1.51%)
occurrences (all)	10	1	8
Pustular psoriasis			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	5	1	2
Rash			
subjects affected / exposed	4 / 179 (2.23%)	0 / 71 (0.00%)	9 / 398 (2.26%)
occurrences (all)	4	0	11
Rash pruritic			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rebound psoriasis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0

Rosacea			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Scab			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Seborrhoeic dermatitis			
subjects affected / exposed	3 / 179 (1.68%)	3 / 71 (4.23%)	5 / 398 (1.26%)
occurrences (all)	3	4	5
Skin discomfort			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Skin exfoliation			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Skin hyperpigmentation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	3
Skin odour abnormal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Stasis dermatitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	4 / 398 (1.01%)
occurrences (all)	3	1	4

Vitiligo			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	3	0	1
Glycosuria			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	3	0	5
Hydronephrosis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Leukocyturia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Micturition frequency decreased			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Nephrolithiasis			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	10 / 398 (2.51%)
occurrences (all)	1	1	11
Pollakiuria			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Proteinuria			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	1	0	5
Renal colic			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Renal cyst			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ureterocele			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Urinary tract inflammation			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Hyperthyroidism			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Hypogonadism			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Thyroid cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Ankylosing spondylitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	26 / 179 (14.53%)	7 / 71 (9.86%)	50 / 398 (12.56%)
occurrences (all)	35	8	63
Arthritis			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	15 / 398 (3.77%)
occurrences (all)	2	1	15
Arthropathy			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	11 / 179 (6.15%)	4 / 71 (5.63%)	36 / 398 (9.05%)
occurrences (all)	12	4	41
Bone pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Bursitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	3
Chondromalacia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Costochondritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dactylitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	2	0	1
Dupuytren's contracture			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Exostosis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Fibromyalgia			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	2	1	1
Flank pain			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Groin pain			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Intervertebral disc degeneration			

subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Intervertebral disc disorder			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	0	1	3
Joint effusion			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Joint stiffness			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Joint swelling			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	1	1	1
Metatarsalgia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	2	0	2
Muscle tightness			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Muscle twitching			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Musculoskeletal pain			

subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	11 / 398 (2.76%)
occurrences (all)	2	0	11
Musculoskeletal stiffness			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	10 / 398 (2.51%)
occurrences (all)	3	1	13
Neck pain			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	2	0	7
Osteoarthritis			
subjects affected / exposed	0 / 179 (0.00%)	3 / 71 (4.23%)	12 / 398 (3.02%)
occurrences (all)	0	3	12
Pain in extremity			
subjects affected / exposed	7 / 179 (3.91%)	1 / 71 (1.41%)	10 / 398 (2.51%)
occurrences (all)	8	3	12
Pain in jaw			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Patellofemoral pain syndrome			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Periarthritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Plantar fasciitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Polyarthritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	4
Polymyalgia rheumatica			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Psoriatic arthropathy			

subjects affected / exposed	6 / 179 (3.35%)	3 / 71 (4.23%)	15 / 398 (3.77%)
occurrences (all)	10	3	19
Rhabdomyolysis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rheumatoid arthritis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	5 / 398 (1.26%)
occurrences (all)	1	1	5
Spinal column stenosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	0	1	2
Spinal pain			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	5 / 398 (1.26%)
occurrences (all)	0	1	6
Synovial cyst			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Synovitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tendon pain			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	11 / 398 (2.76%)
occurrences (all)	3	0	12
Tenosynovitis			

subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Torticollis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Abscess			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Abscess limb			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Acarodermatitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Acne pustular			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Acute sinusitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	0	0	3
Acute tonsillitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Appendicitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Bacteriuria			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Balanitis candida			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1

Body tinea			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	9 / 179 (5.03%)	6 / 71 (8.45%)	25 / 398 (6.28%)
occurrences (all)	12	8	33
Bronchitis bacterial			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Bronchitis viral			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Candida infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	3
Cellulitis			
subjects affected / exposed	4 / 179 (2.23%)	1 / 71 (1.41%)	9 / 398 (2.26%)
occurrences (all)	4	1	10
Chlamydial infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Chronic tonsillitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	6 / 179 (3.35%)	3 / 71 (4.23%)	11 / 398 (2.76%)
occurrences (all)	6	3	14
Conjunctivitis bacterial			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Corneal infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	4 / 179 (2.23%)	0 / 71 (0.00%)	7 / 398 (1.76%)
occurrences (all)	4	0	8

Cystitis bacterial			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Dacryocanaliculitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Dermo-hypodermatitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Diarrhoea infectious			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Diverticulitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	5 / 179 (2.79%)	3 / 71 (4.23%)	6 / 398 (1.51%)
occurrences (all)	5	3	9
Eczema infected			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Enteritis infectious			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Erysipelas			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
External ear cellulitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Eye infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Folliculitis			
subjects affected / exposed	5 / 179 (2.79%)	1 / 71 (1.41%)	7 / 398 (1.76%)
occurrences (all)	5	1	10

Fungal infection			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	4
Fungal skin infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Furuncle			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	3	0	3
Gastroenteritis			
subjects affected / exposed	7 / 179 (3.91%)	1 / 71 (1.41%)	16 / 398 (4.02%)
occurrences (all)	7	1	20
Gastroenteritis viral			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	8 / 398 (2.01%)
occurrences (all)	1	0	10
Gastrointestinal infection			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	1	1	1
Gastrointestinal viral infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Genital herpes			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	3	0	4
Gingivitis			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	1	1	0
Helicobacter infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Herpes oesophagitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Herpes simplex			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	2	1	2

Herpes virus infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	4	0	1
Herpes zoster			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	1	1	2
Hordeolum			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	0	0	6
Impetigo			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	2
Influenza			
subjects affected / exposed	9 / 179 (5.03%)	2 / 71 (2.82%)	16 / 398 (4.02%)
occurrences (all)	11	2	19
Labyrinthitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Laryngitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	2	0	4
Localised infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Mucosal infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	38 / 179 (21.23%)	15 / 71 (21.13%)	81 / 398 (20.35%)
occurrences (all)	66	21	150
Oesophageal candidiasis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Omphalitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0

Onychomycosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Oral candidiasis			
subjects affected / exposed	3 / 179 (1.68%)	1 / 71 (1.41%)	16 / 398 (4.02%)
occurrences (all)	3	1	17
Oral fungal infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	1	0	4
Oral herpes			
subjects affected / exposed	4 / 179 (2.23%)	0 / 71 (0.00%)	7 / 398 (1.76%)
occurrences (all)	5	0	16
Oral infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Orchitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Oropharyngeal candidiasis			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Oropharyngitis fungal			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Osteomyelitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Otitis externa			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	6 / 398 (1.51%)
occurrences (all)	0	0	9
Otitis media			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	7 / 398 (1.76%)
occurrences (all)	0	0	9
Otitis media acute			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2

Papilloma viral infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	0	0	4
Pericarditis infective			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Periodontitis			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	2	2	1
Peritonsillar abscess			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	13 / 179 (7.26%)	4 / 71 (5.63%)	24 / 398 (6.03%)
occurrences (all)	13	6	31
Pharyngitis bacterial			
subjects affected / exposed	1 / 179 (0.56%)	1 / 71 (1.41%)	5 / 398 (1.26%)
occurrences (all)	1	1	6
Pharyngitis streptococcal			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	4 / 398 (1.01%)
occurrences (all)	1	0	4
Pharyngotonsillitis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Pilonidal cyst			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	1	0	1
Pneumonia			
subjects affected / exposed	1 / 179 (0.56%)	2 / 71 (2.82%)	5 / 398 (1.26%)
occurrences (all)	1	2	5
Post procedural infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1

Pulpitis dental			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Pyelonephritis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Pyuria			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rash pustular			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	1 / 398 (0.25%)
occurrences (all)	0	1	2
Respiratory tract infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection viral			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	14 / 398 (3.52%)
occurrences (all)	2	0	16
Sinusitis			
subjects affected / exposed	11 / 179 (6.15%)	4 / 71 (5.63%)	27 / 398 (6.78%)
occurrences (all)	15	4	37
Skin bacterial infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Skin candida			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Staphylococcal infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2

Staphylococcal skin infection subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Subcutaneous abscess subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0
Tinea cruris subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 2
Tinea infection subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Tinea manuum subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	1 / 71 (1.41%) 1	0 / 398 (0.00%) 0
Tinea pedis subjects affected / exposed occurrences (all)	4 / 179 (2.23%) 4	2 / 71 (2.82%) 2	8 / 398 (2.01%) 11
Tonsillitis subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 3	0 / 71 (0.00%) 0	4 / 398 (1.01%) 8
Tooth abscess subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	1 / 71 (1.41%) 1	8 / 398 (2.01%) 8
Tooth infection subjects affected / exposed occurrences (all)	10 / 179 (5.59%) 11	3 / 71 (4.23%) 3	8 / 398 (2.01%) 8
Toxocariasis subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Tracheitis subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	36 / 179 (20.11%) 61	12 / 71 (16.90%) 23	81 / 398 (20.35%) 133

Upper respiratory tract infection bacterial			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	0	1	2
Urinary tract infection			
subjects affected / exposed	10 / 179 (5.59%)	1 / 71 (1.41%)	15 / 398 (3.77%)
occurrences (all)	10	1	18
Vaginal infection			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	0	0	2
Vaginitis bacterial			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	2	0	0
Viral infection			
subjects affected / exposed	0 / 179 (0.00%)	2 / 71 (2.82%)	3 / 398 (0.75%)
occurrences (all)	0	2	3
Viral pharyngitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	5 / 179 (2.79%)	1 / 71 (1.41%)	16 / 398 (4.02%)
occurrences (all)	6	1	20
Vulvitis			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	3 / 398 (0.75%)
occurrences (all)	2	0	4
Vulvovaginal mycotic infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	2	0	2
Wound infection			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	2
Metabolism and nutrition disorders			

Abnormal loss of weight subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	0 / 398 (0.00%) 0
Carbohydrate intolerance subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Decreased appetite subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Dehydration subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	0 / 71 (0.00%) 0	3 / 398 (0.75%) 3
Diabetes mellitus subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	0 / 71 (0.00%) 0	8 / 398 (2.01%) 8
Glucose tolerance impaired subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Gout subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	0 / 71 (0.00%) 0	7 / 398 (1.76%) 7
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 179 (0.56%) 1	1 / 71 (1.41%) 1	2 / 398 (0.50%) 2
Hyperglycaemia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	1 / 71 (1.41%) 1	6 / 398 (1.51%) 7
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 179 (0.00%) 0	0 / 71 (0.00%) 0	1 / 398 (0.25%) 1
Hyperlipidaemia subjects affected / exposed occurrences (all)	2 / 179 (1.12%) 2	1 / 71 (1.41%) 1	4 / 398 (1.01%) 5

Hyperphosphataemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Hypertriglyceridaemia			
subjects affected / exposed	2 / 179 (1.12%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	2	0	1
Hyperuricaemia			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	4 / 398 (1.01%)
occurrences (all)	3	1	4
Hypoalbuminaemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	1	0	4
Hypomagnesaemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	2
Hypophosphataemia			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0
Lactose intolerance			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Metabolic acidosis			
subjects affected / exposed	1 / 179 (0.56%)	0 / 71 (0.00%)	0 / 398 (0.00%)
occurrences (all)	1	0	0

Obesity			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 179 (0.00%)	0 / 71 (0.00%)	1 / 398 (0.25%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus			
subjects affected / exposed	3 / 179 (1.68%)	0 / 71 (0.00%)	2 / 398 (0.50%)
occurrences (all)	3	0	2
Vitamin B12 deficiency			
subjects affected / exposed	0 / 179 (0.00%)	1 / 71 (1.41%)	0 / 398 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	2 / 179 (1.12%)	1 / 71 (1.41%)	2 / 398 (0.50%)
occurrences (all)	2	1	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2012	Safety reporting language was updated to be compliant with a requirement in the current version of the European Union Clinical Trial Directive. Language regarding topical therapy was clarified to specify that topical therapy containing urea was not permitted through week 52.
17 October 2013	Clarified safety follow-up and hepatotoxicity criteria. Added guidance regarding additional safety follow-up visit/end of study visit and corresponding changes to study duration.
26 March 2014	Added the Columbia-Suicide Severity Rating Scale, and Patient Health Questionnaire-8 depression scale assessments. Changed the timing of the planned interim analyses from after approximately 80% of subjects had reached week 132 to performed as deemed necessary.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported