



Clinical trial results:

A Long-term Assessment of the Safety and Efficacy of AMG 827 Subcutaneous Treatment in Subjects With Psoriasis

Summary

EudraCT number	2009-016163-12
Trial protocol	DK
Global end of trial date	19 October 2015

Results information

Result version number	v1 (current)
This version publication date	22 September 2016
First version publication date	22 September 2016

Trial information

Trial identification

Sponsor protocol code	20090403
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01101100
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	19 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	19 October 2015
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Safety Objective: To evaluate the safety of long-term exposure with brodalumab in subjects with moderate to severe plaque psoriasis

Efficacy Objectives:

To evaluate the efficacy of brodalumab as measured by the following:

- proportion of subjects with a static physician's global assessment (sPGA) of clear (0) or clear/almost clear (0 or 1)
- percent improvement in Psoriasis Area and Severity Index (PASI)
- proportion of subjects with a 50% improvement in PASI (PASI 50), PASI 75, PASI 90, and PASI 100
- body surface area (BSA) involvement

Protection of trial subjects:

This study was conducted in accordance with the principles of the Food and Drug Administration (FDA) and International Conference on 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	13 April 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Canada: 79
Country: Number of subjects enrolled	Denmark: 7
Country: Number of subjects enrolled	France: 32
Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	181
EEA total number of subjects	39

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)	173
From 65 to 84 years	8
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study (20090403) is an open-label extension of the double-blind Study 20090062 in subjects with moderate to severe plaque psoriasis. The study was conducted at 23 centers in Australia, Canada, Denmark, France, and the United States (US).

Pre-assignment

Screening details:

Subjects who completed Study 20090062 \geq 4 weeks previously underwent a screening visit prior to the baseline visit of Study 20090403. All subjects received brodalumab in this study.

The study was stopped early for administrative reasons at week 360, therefore, none of the subjects were considered to have completed the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo in 20090062

Arm description:

Participants who received placebo in parent study 20090062 received brodalumab subcutaneously (SC) at baseline and weeks 1 and 2, and then every 2 weeks (Q2W) thereafter for up to 360 weeks.

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

Dosage and administration details:

Initially, all subjects received brodalumab 210 mg. After Protocol Amendment 2, the dose of brodalumab was reduced to 140 mg in subjects who weighed \leq 100 kg. After Protocol Amendment 3, subjects who had an inadequate response during treatment with brodalumab 140 mg could have their dose increased to 210 mg. Subjects who did not have their dose reduced as part of Protocol Amendment 2 continued to receive brodalumab 210 mg.

Arm title	70 mg Q2W in 20090062
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Arm description:

Participants who received 70 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

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

Dosage and administration details:

Initially, all subjects received brodalumab 210 mg. After Protocol Amendment 2, the dose of brodalumab was reduced to 140 mg in subjects who weighed \leq 100 kg. After Protocol Amendment 3, subjects who had an inadequate response during treatment with brodalumab 140 mg could have their dose increased to 210 mg. Subjects who did not have their dose reduced as part of Protocol Amendment 2 continued to receive brodalumab 210 mg.

Arm title	140 mg Q2W in 20090062
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Arm description:

Participants who received 140 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

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

Dosage and administration details:

Initially, all subjects received brodalumab 210 mg. After Protocol Amendment 2, the dose of brodalumab was reduced to 140 mg in subjects who weighed ≤ 100 kg. After Protocol Amendment 3, subjects who had an inadequate response during treatment with brodalumab 140 mg could have their dose increased to 210 mg. Subjects who did not have their dose reduced as part of Protocol Amendment 2 continued to receive brodalumab 210 mg.

Arm title	210 mg Q2W in 20090062
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Arm description:

Participants who received 210 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

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

Dosage and administration details:

Initially, all subjects received brodalumab 210 mg. After Protocol Amendment 2, the dose of brodalumab was reduced to 140 mg in subjects who weighed ≤ 100 kg. After Protocol Amendment 3, subjects who had an inadequate response during treatment with brodalumab 140 mg could have their dose increased to 210 mg. Subjects who did not have their dose reduced as part of Protocol Amendment 2 continued to receive brodalumab 210 mg.

Arm title	280 mg Q4W in 20090062
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Arm description:

Participants who received 280 mg Q4W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

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

Dosage and administration details:

Initially, all subjects received brodalumab 210 mg. After Protocol Amendment 2, the dose of brodalumab was reduced to 140 mg in subjects who weighed ≤ 100 kg. After Protocol Amendment 3, subjects who had an inadequate response during treatment with brodalumab 140 mg could have their dose increased to 210 mg. Subjects who did not have their dose reduced as part of Protocol Amendment 2 continued to receive brodalumab 210 mg.

Number of subjects in period 1	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062
Started	33	36	37
Completed	0	0	0
Not completed	33	36	37
Consent withdrawn by subject	2	3	6
Administrative decision	20	29	26
Other	3	2	1
Death	-	-	-
Pregnancy	1	1	-
Adverse event	5	1	3
Lost to follow-up	2	-	1

Number of subjects in period 1	210 mg Q2W in 20090062	280 mg Q4W in 20090062
Started	35	40
Completed	0	0
Not completed	35	40
Consent withdrawn by subject	5	3
Administrative decision	21	30
Other	3	3
Death	-	1
Pregnancy	2	-
Adverse event	4	3
Lost to follow-up	-	-

Baseline characteristics

Reporting groups

Reporting group title	Placebo in 20090062
Reporting group description:	
Participants who received placebo in parent study 20090062 received brodalumab subcutaneously (SC) at baseline and weeks 1 and 2, and then every 2 weeks (Q2W) thereafter for up to 360 weeks.	
Reporting group title	70 mg Q2W in 20090062
Reporting group description:	
Participants who received 70 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	
Reporting group title	140 mg Q2W in 20090062
Reporting group description:	
Participants who received 140 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	
Reporting group title	210 mg Q2W in 20090062
Reporting group description:	
Participants who received 210 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	
Reporting group title	280 mg Q4W in 20090062
Reporting group description:	
Participants who received 280 mg Q4W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	

Reporting group values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062
Number of subjects	33	36	37
Age Categorical			
Units: Subjects			
< 65 years	30	35	36
≥ 65 years	3	1	1
Age Continuous			
Age data are reported at parent study baseline			
Units: years			
arithmetic mean	43.1	42.1	43.5
standard deviation	± 14.8	± 11.1	± 11.6
Gender Categorical			
Units: Subjects			
Female	13	16	11
Male	20	20	26
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	1	0
Black (or African American)	2	0	1
Hispanic or Latino	2	1	1
Other	0	0	0
White or Caucasian	29	33	35

Reporting group values	210 mg Q2W in 20090062	280 mg Q4W in 20090062	Total
Number of subjects	35	40	181

Age Categorical			
Units: Subjects			
< 65 years	34	38	173
≥ 65 years	1	2	8
Age Continuous			
Age data are reported at parent study baseline			
Units: years			
arithmetic mean	42.1	43	
standard deviation	± 12.2	± 12.1	-
Gender Categorical			
Units: Subjects			
Female	13	11	64
Male	22	29	117
Race			
Units: Subjects			
American Indian or Alaska Native	1	1	3
Asian	1	3	5
Black (or African American)	0	1	4
Hispanic or Latino	2	0	6
Other	0	1	1
White or Caucasian	31	34	162

End points

End points reporting groups

Reporting group title	Placebo in 20090062
Reporting group description: Participants who received placebo in parent study 20090062 received brodalumab subcutaneously (SC) at baseline and weeks 1 and 2, and then every 2 weeks (Q2W) thereafter for up to 360 weeks.	
Reporting group title	70 mg Q2W in 20090062
Reporting group description: Participants who received 70 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	
Reporting group title	140 mg Q2W in 20090062
Reporting group description: Participants who received 140 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	
Reporting group title	210 mg Q2W in 20090062
Reporting group description: Participants who received 210 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	
Reporting group title	280 mg Q4W in 20090062
Reporting group description: Participants who received 280 mg Q4W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.	

Primary: Number of Participants with Adverse Events

End point title	Number of Participants with Adverse Events ^[1]
End point description:	
End point type	Primary
End point timeframe: 360 weeks	
Notes: [1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point. Justification: No formal statistical tests were performed	

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: participants				
Any adverse event	33	35	36	35
Adverse event grade ≥ 2	32	35	35	35
Adverse event grade ≥ 3	6	7	7	13
Serious adverse events	6	3	5	8
Leading to discontinuation of study drug	6	2	5	5
Leading to discontinuation from study	5	1	3	4
Life-threatening adverse events	1	0	1	1
Fatal adverse events	0	0	0	0
Treatment-related adverse events (TRAE)	11	13	15	12

Treatment-related serious adverse events	1	1	4	2
TRAE leading to discontinuation of study drug	1	1	4	2
TRAE leading to discontinuation from study	1	0	2	1
Treatment-related life-threatening AEs	1	0	1	0
Treatment-related fatal AEs	0	0	0	0

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: participants				
Any adverse event	38			
Adverse event grade ≥ 2	37			
Adverse event grade ≥ 3	8			
Serious adverse events	7			
Leading to discontinuation of study drug	3			
Leading to discontinuation from study	3			
Life-threatening adverse events	0			
Fatal adverse events	1			
Treatment-related adverse events (TRAE)	10			
Treatment-related serious adverse events	0			
TRAE leading to discontinuation of study drug	1			
TRAE leading to discontinuation from study	1			
Treatment-related life-threatening AEs	0			
Treatment-related fatal AEs	0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Static Physician's Global Assessment of Clear or Almost Clear

End point title	Percentage of Participants with a Static Physician's Global Assessment of Clear or Almost Clear ^[2]
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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 analysis was performed using the full analysis set (all subjects who received at least 1 dose of brodalumab in study 20090403). N indicates the number of subjects with available data at each time point.

End point type	Primary
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End point timeframe:

Weeks 2, 12, 48, 96, 168, 216, and 264

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	42.4 (25.5 to 60.8)	64.7 (46.5 to 80.3)	77.8 (60.8 to 89.9)	71.9 (53.3 to 86.3)
Week 12 (N = 33, 34, 37, 35, 36)	90.9 (75.7 to 98.1)	94.1 (80.3 to 99.3)	89.2 (74.6 to 97)	85.7 (69.7 to 95.2)
Week 48 (N = 30, 33, 35, 31, 36)	90 (73.5 to 97.9)	78.8 (61.1 to 91)	91.4 (76.9 to 98.2)	83.9 (66.3 to 94.5)
Week 96 (N = 26, 33, 32, 29, 33)	80.8 (60.6 to 93.4)	75.8 (57.7 to 88.9)	75 (56.6 to 88.5)	79.3 (60.3 to 92)
Week 168 (N = 23, 31, 29, 28, 30)	82.6 (61.2 to 95)	64.5 (45.4 to 80.8)	86.2 (68.3 to 96.1)	78.6 (59 to 91.7)
Week 216 (N = 21, 30, 28, 23, 29)	81 (58.1 to 94.6)	76.7 (57.7 to 90.1)	89.3 (71.8 to 97.7)	82.6 (61.2 to 95)
Week 264 (N = 16, 25, 21, 19, 26)	68.8 (41.3 to 89)	60 (38.7 to 78.9)	47.6 (25.7 to 70.2)	68.4 (43.4 to 87.4)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	57.9 (40.8 to 73.7)			
Week 12 (N = 33, 34, 37, 35, 36)	91.7 (77.5 to 98.2)			
Week 48 (N = 30, 33, 35, 31, 36)	80.6 (64 to 91.8)			
Week 96 (N = 26, 33, 32, 29, 33)	69.7 (51.3 to 84.4)			
Week 168 (N = 23, 31, 29, 28, 30)	90 (73.5 to 97.9)			
Week 216 (N = 21, 30, 28, 23, 29)	82.8 (64.2 to 94.2)			
Week 264 (N = 16, 25, 21, 19, 26)	65.4 (44.3 to 82.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a Static Physician's Global Assessment of

Clear

End point title	Percentage of Participants with a Static Physician's Global Assessment of Clear ^[3]
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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). This analysis was performed using the full analysis set; N indicates the number of subjects with available data at each time point.

End point type	Primary
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End point timeframe:

Weeks 2, 12, 48, 96, 168, 216, and 264

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	0 (0 to 10.6)	20.6 (8.7 to 37.9)	25 (12.1 to 42.2)	46.9 (29.1 to 65.3)
Week 12 (N = 33, 34, 37, 35, 36)	63.6 (45.1 to 79.6)	70.6 (52.5 to 84.9)	54.1 (36.9 to 70.5)	68.6 (50.7 to 83.1)
Week 48 (N = 30, 33, 35, 31, 36)	70 (50.6 to 85.3)	57.6 (39.2 to 74.5)	57.1 (39.4 to 73.7)	58.1 (39.1 to 75.5)
Week 96 (N = 26, 33, 32, 29, 33)	42.3 (23.4 to 63.1)	42.4 (25.5 to 60.8)	53.1 (34.7 to 70.9)	62.1 (42.3 to 79.3)
Week 168 (N = 23, 31, 29, 28, 30)	60.9 (38.5 to 80.3)	51.6 (33.1 to 69.8)	55.2 (35.7 to 73.6)	60.7 (40.6 to 78.5)
Week 216 (N = 21, 30, 28, 23, 29)	57.1 (34 to 78.2)	66.7 (47.2 to 82.7)	60.7 (40.6 to 78.5)	73.9 (51.6 to 89.8)
Week 264 (N = 16, 25, 21, 19, 26)	56.3 (29.9 to 80.2)	44 (24.4 to 65.1)	38.1 (18.1 to 61.6)	31.6 (12.6 to 56.6)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	18.4 (7.7 to 34.3)			
Week 12 (N = 33, 34, 37, 35, 36)	58.3 (40.8 to 74.5)			
Week 48 (N = 30, 33, 35, 31, 36)	69.4 (51.9 to 83.7)			
Week 96 (N = 26, 33, 32, 29, 33)	60.6 (42.1 to 77.1)			
Week 168 (N = 23, 31, 29, 28, 30)	73.3 (54.1 to 87.7)			
Week 216 (N = 21, 30, 28, 23, 29)	62.1 (42.3 to 79.3)			

Week 264 (N = 16, 25, 21, 19, 26)	46.2 (26.6 to 66.6)			
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Statistical analyses

No statistical analyses for this end point

Primary: Percent Improvement from 20090062 Baseline in Psoriasis Area and Severity Index (PASI)

End point title	Percent Improvement from 20090062 Baseline in Psoriasis Area and Severity Index (PASI) ^[4]
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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.

End point type	Primary
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End point timeframe:

Parent Study 20090062 baseline and weeks 2, 12, 48, 96, 168, 216 and 264

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 2 (N = 33, 34, 36, 32, 38)	66.8 (± 26.8)	78.4 (± 19.1)	85.2 (± 15.8)	87.5 (± 20.6)
Week 12 (N = 33, 34, 37, 35, 36)	95.4 (± 7.9)	95.7 (± 11.7)	94.5 (± 11.9)	95.2 (± 10)
Week 48 (N = 30, 33, 35, 31, 36)	95.7 (± 9.6)	93.1 (± 14.6)	96.5 (± 7.2)	92.8 (± 11)
Week 96 (N = 26, 33, 32, 29, 33)	94.5 (± 11.1)	90.7 (± 16.2)	91.8 (± 15.5)	90.6 (± 16.9)
Week 168 (N = 23, 31, 29, 28, 30)	93.5 (± 14.4)	92.5 (± 12.8)	94 (± 12.7)	90.1 (± 21)
Week 216 (N = 21, 30, 28, 23, 29)	88.6 (± 32)	93 (± 15.2)	93.2 (± 13.7)	95.8 (± 8.3)
Week 264 (N = 16, 25, 20, 19, 26)	92.8 (± 10.8)	87.7 (± 21.6)	79.8 (± 32)	79.4 (± 39.5)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 2 (N = 33, 34, 36, 32, 38)	75.7 (± 24.1)			
Week 12 (N = 33, 34, 37, 35, 36)	96.1 (± 6.8)			
Week 48 (N = 30, 33, 35, 31, 36)	94.9 (± 13.1)			
Week 96 (N = 26, 33, 32, 29, 33)	91.5 (± 21)			

Week 168 (N = 23, 31, 29, 28, 30)	98 (± 4.2)			
Week 216 (N = 21, 30, 28, 23, 29)	94.4 (± 10)			
Week 264 (N = 16, 25, 20, 19, 26)	88.4 (± 19.5)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a 50% or Greater Improvement from 20090062 Baseline in PASI Score (PASI 50)

End point title	Percentage of Participants with a 50% or Greater Improvement from 20090062 Baseline in PASI Score (PASI 50) ^[5]
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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.

End point type	Primary
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End point timeframe:

Parent Study 20090062 baseline and weeks 2, 12, 48, 96, 168, 216 and 264

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	75.8 (57.7 to 88.9)	88.2 (72.5 to 96.7)	97.2 (85.5 to 99.9)	93.8 (79.2 to 99.2)
Week 12 (N = 33, 34, 37, 35, 36)	100 (89.4 to 100)	97.1 (84.7 to 99.9)	97.3 (85.8 to 99.9)	100 (90 to 100)
Week 48 (N = 30, 33, 35, 31, 36)	100 (88.4 to 100)	97 (84.2 to 99.9)	100 (90 to 100)	100 (88.8 to 100)
Week 96 (N = 26, 33, 32, 29, 33)	96.2 (80.4 to 99.9)	97 (84.2 to 99.9)	93.8 (79.2 to 99.2)	96.6 (82.2 to 99.9)
Week 168 (N = 23, 31, 29, 28, 30)	95.7 (78.1 to 99.9)	96.8 (83.3 to 99.9)	96.6 (82.2 to 99.9)	92.9 (76.5 to 99.1)
Week 216 (N = 21, 30, 28, 23, 29)	95.2 (76.2 to 99.9)	93.3 (77.9 to 99.2)	96.4 (81.7 to 99.9)	100 (85.2 to 100)
Week 264 (N = 16, 25, 20, 19, 26)	100 (79.4 to 100)	92 (74 to 99)	85 (62.1 to 96.8)	89.5 (66.9 to 98.7)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				

number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	81.6 (65.7 to 92.3)			
Week 12 (N = 33, 34, 37, 35, 36)	100 (90.3 to 100)			
Week 48 (N = 30, 33, 35, 31, 36)	97.2 (85.5 to 99.9)			
Week 96 (N = 26, 33, 32, 29, 33)	97 (84.2 to 99.9)			
Week 168 (N = 23, 31, 29, 28, 30)	100 (88.4 to 100)			
Week 216 (N = 21, 30, 28, 23, 29)	100 (88.1 to 100)			
Week 264 (N = 16, 25, 20, 19, 26)	96.2 (80.4 to 99.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a 75% or Greater Improvement from 20090062 Baseline in PASI Score (PASI 75)

End point title	Percentage of Participants with a 75% or Greater Improvement from 20090062 Baseline in PASI Score (PASI 75) ^[6]
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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.

End point type	Primary
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End point timeframe:

Parent Study 20090062 baseline and weeks 2, 12, 48, 96, 164, 212 and 264

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	48.5 (30.8 to 66.5)	61.8 (43.6 to 77.8)	77.8 (60.8 to 89.9)	84.4 (67.2 to 94.7)
Week 12 (N = 33, 34, 37, 35, 36)	100 (89.4 to 100)	94.1 (80.3 to 99.3)	94.6 (81.8 to 99.3)	94.3 (80.8 to 99.3)
Week 48 (N = 30, 33, 35, 31, 36)	96.7 (82.8 to 99.9)	90.9 (75.7 to 98.1)	97.1 (85.1 to 99.9)	87.1 (70.2 to 96.4)
Week 96 (N = 26, 33, 32, 29, 33)	96.2 (80.4 to 99.9)	93.9 (79.8 to 99.3)	87.5 (71 to 96.5)	79.3 (60.3 to 92)
Week 168 (N = 23, 31, 29, 28, 30)	91.3 (72 to 98.9)	90.3 (74.2 to 98)	96.6 (82.2 to 99.9)	85.7 (67.3 to 96)
Week 216 (N = 21, 30, 28, 23, 29)	90.5 (69.6 to 98.8)	93.3 (77.9 to 99.2)	89.3 (71.8 to 97.7)	95.7 (78.1 to 99.9)

Week 264 (N = 16, 25, 20, 19, 26)	93.8 (69.8 to 99.8)	92 (74 to 99)	75 (50.9 to 91.3)	73.7 (48.8 to 90.9)
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End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	68.4 (51.3 to 82.5)			
Week 12 (N = 33, 34, 37, 35, 36)	94.4 (81.3 to 99.3)			
Week 48 (N = 30, 33, 35, 31, 36)	94.4 (81.3 to 99.3)			
Week 96 (N = 26, 33, 32, 29, 33)	90.9 (75.7 to 98.1)			
Week 168 (N = 23, 31, 29, 28, 30)	100 (88.4 to 100)			
Week 216 (N = 21, 30, 28, 23, 29)	93.1 (77.2 to 99.2)			
Week 264 (N = 16, 25, 20, 19, 26)	84.6 (65.1 to 95.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a 90% or Greater Improvement from 20090062 Baseline in PASI Score (PASI 90)

End point title	Percentage of Participants with a 90% or Greater Improvement from 20090062 Baseline in PASI Score (PASI 90) ^[7]
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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.

End point type	Primary
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End point timeframe:

Parent Study 20090062 baseline and weeks 2, 12, 48, 96, 166, 216 and 264

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				

Week 2 (N = 33, 34, 36, 32, 38)	15.2 (5.1 to 31.9)	32.4 (17.4 to 50.5)	50 (32.9 to 67.1)	59.4 (40.6 to 76.3)
Week 12 (N = 33, 34, 37, 35, 36)	78.8 (61.1 to 91)	88.2 (72.5 to 96.7)	86.5 (71.2 to 95.5)	85.7 (69.7 to 95.2)
Week 48 (N = 30, 33, 35, 31, 36)	86.7 (69.3 to 96.2)	84.8 (68.1 to 94.9)	85.7 (69.7 to 95.2)	71 (52 to 85.8)
Week 96 (N = 26, 33, 32, 29, 33)	88.5 (69.8 to 97.6)	72.7 (54.5 to 86.7)	78.1 (60 to 90.7)	75.9 (56.5 to 89.7)
Week 168 (N = 23, 31, 29, 28, 30)	78.3 (56.3 to 92.5)	74.2 (55.4 to 88.1)	75.9 (56.5 to 89.7)	78.6 (59 to 91.7)
Week 216 (N = 21, 30, 28, 23, 29)	81 (58.1 to 94.6)	83.3 (65.3 to 94.4)	75 (55.1 to 89.3)	82.6 (61.2 to 95)
Week 264 (N = 16, 25, 20, 19, 26)	68.8 (41.3 to 89)	60 (38.7 to 78.9)	55 (31.5 to 76.9)	73.7 (48.8 to 90.9)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	34.2 (19.6 to 51.4)			
Week 12 (N = 33, 34, 37, 35, 36)	86.1 (70.5 to 95.3)			
Week 48 (N = 30, 33, 35, 31, 36)	86.1 (70.5 to 95.3)			
Week 96 (N = 26, 33, 32, 29, 33)	78.8 (61.1 to 91)			
Week 168 (N = 23, 31, 29, 28, 30)	93.3 (77.9 to 99.2)			
Week 216 (N = 21, 30, 28, 23, 29)	82.8 (64.2 to 94.2)			
Week 264 (N = 16, 25, 20, 19, 26)	65.4 (44.3 to 82.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with a 100% Improvement from 20090062 Baseline in PASI Score (PASI 100)

End point title	Percentage of Participants with a 100% Improvement from 20090062 Baseline in PASI Score (PASI 100) ^[8]
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.	
End point type	Primary
End point timeframe:	
Parent Study 20090062 baseline and weeks 2, 12, 48, 96, 168, 216 and 264	

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	0 (0 to 10.6)	20.6 (8.7 to 37.9)	25 (12.1 to 42.2)	43.8 (26.4 to 62.3)
Week 12 (N = 33, 34, 37, 35, 36)	63.6 (45.1 to 79.6)	70.6 (52.5 to 84.9)	54.1 (36.9 to 70.5)	68.6 (50.7 to 83.1)
Week 48 (N = 30, 33, 35, 31, 36)	70 (50.6 to 85.3)	57.6 (39.2 to 74.5)	57.1 (39.4 to 73.7)	54.8 (36 to 72.7)
Week 96 (N = 26, 33, 32, 29, 33)	46.2 (26.6 to 66.6)	42.4 (25.5 to 60.8)	53.1 (34.7 to 70.9)	62.1 (42.3 to 79.3)
Week 168 (N = 23, 31, 29, 28, 30)	60.9 (38.5 to 80.3)	51.6 (33.1 to 69.8)	55.2 (35.7 to 73.6)	60.7 (40.6 to 78.5)
Week 216 (N = 21, 30, 28, 23, 29)	57.1 (34 to 78.2)	66.7 (47.2 to 82.7)	60.7 (40.6 to 78.5)	73.9 (51.6 to 89.8)
Week 264 (N = 16, 25, 20, 19, 26)	56.3 (29.9 to 80.2)	44 (24.4 to 65.1)	40 (19.1 to 63.9)	31.6 (12.6 to 56.6)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)				
Week 2 (N = 33, 34, 36, 32, 38)	18.4 (7.7 to 34.3)			
Week 12 (N = 33, 34, 37, 35, 36)	58.3 (40.8 to 74.5)			
Week 48 (N = 30, 33, 35, 31, 36)	69.4 (51.9 to 83.7)			
Week 96 (N = 26, 33, 32, 29, 33)	60.6 (42.1 to 77.1)			
Week 168 (N = 23, 31, 29, 28, 30)	70 (50.6 to 85.3)			
Week 216 (N = 21, 30, 28, 23, 29)	58.6 (38.9 to 76.5)			
Week 264 (N = 16, 25, 20, 19, 26)	46.2 (26.6 to 66.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Percent Improvement from 20090062 Baseline in Body Surface Area (BSA)

Involvement

End point title	Percent Improvement from 20090062 Baseline in Body Surface Area (BSA) Involvement ^[9]
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End point description:

A measurement of psoriasis involvement, given as the physician's assessment of the percentage of the participant's total body surface area (BSA) involved with psoriasis. The percent of BSA affected was estimated by assuming that the subject's palm, excluding the fingers and thumb, represented roughly 1% of the body's surface.

End point type	Primary
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End point timeframe:

Parent Study 20090062 baseline and weeks 2, 12, 48, 96, 168, 216 and 264

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No formal statistical tests were performed

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 2 (N = 33, 34, 36, 32, 38)	40.7 (± 60.2)	65.6 (± 33.2)	81.9 (± 23.3)	85.7 (± 27)
Week 12 (N = 33, 34, 37, 35, 36)	89.7 (± 22.7)	95.3 (± 12.7)	96.2 (± 7.8)	95.3 (± 10)
Week 48 (N = 30, 33, 35, 31, 36)	95.9 (± 9.9)	93.9 (± 13.9)	97.4 (± 4.4)	93.2 (± 14.4)
Week 96 (N = 26, 33, 32, 29, 33)	94.4 (± 12.6)	91.4 (± 13.8)	93.2 (± 13.6)	90.8 (± 18.2)
Week 168 (N = 23, 31, 29, 28, 30)	94.8 (± 12.9)	88.7 (± 22.7)	94.8 (± 14.3)	90.5 (± 22.7)
Week 216 (N = 21, 30, 28, 23, 29)	89.9 (± 26.2)	92.6 (± 21.7)	93.4 (± 16.6)	95.5 (± 9.4)
Week 264 (N = 16, 25, 21, 19, 26)	93.7 (± 11)	91 (± 17.2)	85.2 (± 27.5)	83.7 (± 29.7)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percent improvement				
arithmetic mean (standard deviation)				
Week 2 (N = 33, 34, 36, 32, 38)	73.9 (± 27.4)			
Week 12 (N = 33, 34, 37, 35, 36)	95.4 (± 8)			
Week 48 (N = 30, 33, 35, 31, 36)	96.9 (± 10.2)			
Week 96 (N = 26, 33, 32, 29, 33)	92.2 (± 23.6)			
Week 168 (N = 23, 31, 29, 28, 30)	98.8 (± 2.3)			
Week 216 (N = 21, 30, 28, 23, 29)	97.5 (± 4.1)			
Week 264 (N = 16, 25, 21, 19, 26)	87.9 (± 36.9)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants with a Dermatology Life Quality Index (DLQI) Response
End point description:	
<p>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).</p> <p>A DLQI response is defined as achieving at least a 5-point improvement from baseline in parent study 20090062 or 0 (best score).</p>	
End point type	Secondary
End point timeframe:	
Parent Study 20090062 baseline and weeks 12, 48, 96, 168, 216 and 264	

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: percentage of participants				
number (confidence interval 95%)				
Week 12 (N = 33, 34, 37, 33, 37)	90.9 (75.7 to 98.1)	88.2 (72.5 to 96.7)	91.9 (78.1 to 98.3)	97 (84.2 to 99.9)
Week 48 (N = 30, 32, 33, 31, 36)	93.3 (77.9 to 99.2)	90.6 (75 to 98)	93.9 (79.8 to 99.3)	90.3 (74.2 to 98)
Week 96 (N = 25, 32, 32, 29, 33)	80 (59.3 to 93.2)	84.4 (67.2 to 94.7)	78.1 (60 to 90.7)	89.7 (72.6 to 97.8)
Week 168 (N = 23, 31, 27, 28, 30)	95.7 (78.1 to 99.9)	93.5 (78.6 to 99.2)	88.9 (70.8 to 97.6)	89.3 (71.8 to 97.7)
Week 216 (N = 21, 30, 28, 21, 28)	90.5 (69.6 to 98.8)	96.6 (82.2 to 99.9)	92.9 (76.5 to 99.1)	95.2 (76.2 to 99.9)
Week 264 (N = 11, 19, 15, 13, 21)	90.9 (58.7 to 99.8)	66.7 (41 to 86.7)	86.7 (59.5 to 98.3)	76.9 (46.2 to 95)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: percentage of participants				
number (confidence interval 95%)				
Week 12 (N = 33, 34, 37, 33, 37)	100 (90.5 to 100)			
Week 48 (N = 30, 32, 33, 31, 36)	91.7 (77.5 to 98.2)			
Week 96 (N = 25, 32, 32, 29, 33)	93.9 (79.8 to 99.3)			
Week 168 (N = 23, 31, 27, 28, 30)	93.3 (77.9 to 99.2)			
Week 216 (N = 21, 30, 28, 21, 28)	96.4 (81.7 to 99.9)			

Week 264 (N = 11, 19, 15, 13, 21)	90.5 (69.6 to 98.8)			
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Statistical analyses

No statistical analyses for this end point

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

End point title	Medical Outcomes Short Form-36 (SF-36) Mental and Physical Component Scores
End point description:	
<p>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.</p>	
End point type	Secondary
End point timeframe:	
Weeks 12, 48, 96, 168, 216 and 264	

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: units on a scale				
arithmetic mean (standard deviation)				
Mental Health: Week 12 (N = 33, 34, 37, 33, 37)	49.9 (± 12.4)	51.5 (± 11)	51.4 (± 9.2)	51 (± 9.1)
Mental Health: Week 48 (N = 30, 32, 34, 31, 35)	50.4 (± 10.1)	51.8 (± 10.2)	52.8 (± 6.9)	52.6 (± 11.4)
Mental Health: Week 96 (N = 25, 32, 32, 29, 32)	47.7 (± 12.3)	50.3 (± 11.1)	52.4 (± 8.2)	52.7 (± 8.9)
Mental Health: Week 168 (N = 22, 31, 28, 28, 30)	52.8 (± 7.8)	51.1 (± 10.1)	50.5 (± 9.2)	50.1 (± 11.8)
Mental Health: Week 216 (N = 20, 30, 28, 22, 28)	54.3 (± 8.6)	52.7 (± 8.7)	52.2 (± 9)	54.4 (± 9.4)
Mental Health: Week 264 (N = 11, 19, 15, 13, 21)	58.4 (± 7.8)	52.8 (± 8.3)	58 (± 3.4)	56.2 (± 5.5)
Physical Health: Week 12 (N = 33, 34, 37, 33, 37)	54 (± 8.4)	53.2 (± 6.8)	55 (± 5.9)	51.2 (± 7.8)
Physical Health: Week 48 (N = 30, 32, 34, 31, 35)	52.5 (± 8.5)	52.7 (± 9.2)	54.9 (± 5.6)	50.4 (± 10.3)
Physical Health: Week 96 (N = 25, 32, 32, 29, 32)	52.6 (± 9.1)	52.7 (± 8.1)	52.7 (± 8.8)	49.7 (± 10.1)
Physical Health: Week 168 (N = 22, 31, 28, 28, 30)	53.2 (± 5.5)	52.5 (± 8.2)	53.1 (± 7.8)	48.6 (± 12)

Physical Health: Week 216 (N = 20, 30, 28, 22, 28)	53.8 (± 4.6)	52.6 (± 6.2)	51.8 (± 7.6)	48.6 (± 11.7)
Physical Health: Week 264 (N = 11, 19, 15, 13, 21)	48.1 (± 7.3)	52.9 (± 6.3)	52 (± 7.9)	45.2 (± 13.3)

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: units on a scale				
arithmetic mean (standard deviation)				
Mental Health: Week 12 (N = 33, 34, 37, 33, 37)	51.5 (± 7.6)			
Mental Health: Week 48 (N = 30, 32, 34, 31, 35)	50.5 (± 9.3)			
Mental Health: Week 96 (N = 25, 32, 32, 29, 32)	50.9 (± 9.4)			
Mental Health: Week 168 (N = 22, 31, 28, 28, 30)	48.8 (± 10.1)			
Mental Health: Week 216 (N = 20, 30, 28, 22, 28)	51.5 (± 9.6)			
Mental Health: Week 264 (N = 11, 19, 15, 13, 21)	54 (± 7.6)			
Physical Health: Week 12 (N = 33, 34, 37, 33, 37)	54.4 (± 7.1)			
Physical Health: Week 48 (N = 30, 32, 34, 31, 35)	53.4 (± 7.2)			
Physical Health: Week 96 (N = 25, 32, 32, 29, 32)	53.3 (± 9)			
Physical Health: Week 168 (N = 22, 31, 28, 28, 30)	52.6 (± 8.4)			
Physical Health: Week 216 (N = 20, 30, 28, 22, 28)	51.2 (± 7.7)			
Physical Health: Week 264 (N = 11, 19, 15, 13, 21)	47.8 (± 10.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Developed Antibodies to Brodalumab

End point title	Number of Participants who Developed Antibodies to Brodalumab
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End point description:

Binding antibodies to brodalumab were detected using an anti-brodalumab immunoassay. Positive samples in the immunoassay were further analyzed for the presence of neutralizing anti-brodalumab antibodies using a bioassay. The number of participants who were binding antibody or neutralizing antibody positive post-baseline with a negative or no result at baseline is reported. Transient indicates a negative result at the subject's last time point tested within the study period.

End point type	Secondary
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End point timeframe:

360 weeks

End point values	Placebo in 20090062	70 mg Q2W in 20090062	140 mg Q2W in 20090062	210 mg Q2W in 20090062
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	33	36	37	35
Units: participants				
Binding antibody positive	3	6	4	4
Binding antibody positive - transient	2	6	4	4
Neutralizing antibody positive	0	0	0	0

End point values	280 mg Q4W in 20090062			
Subject group type	Reporting group			
Number of subjects analysed	40			
Units: participants				
Binding antibody positive	8			
Binding antibody positive - transient	8			
Neutralizing antibody positive	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

360 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	Placebo in 20090062
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Reporting group description:

Participants who received placebo in parent study 20090062 received brodalumab subcutaneously (SC) at baseline and weeks 1 and 2, and then every 2 weeks (Q2W) thereafter for up to 360 weeks.

Reporting group title	Brodalumab 70 mg Q2W in 20090062
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Reporting group description:

Participants who received 70 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

Reporting group title	Brodalumab 210 mg Q2W in 20090062
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Reporting group description:

Participants who received 210 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

Reporting group title	Brodalumab 280 mg Q4W in 20090062
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Reporting group description:

Participants who received 280 mg Q4W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

Reporting group title	Brodalumab 140 mg Q2W in 20090062
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Reporting group description:

Participants who received 140 mg Q2W brodalumab in parent study 20090062 received brodalumab SC at baseline and weeks 1 and 2, and then Q2W thereafter for up to 360 weeks.

Serious adverse events	Placebo in 20090062	Brodalumab 70 mg Q2W in 20090062	Brodalumab 210 mg Q2W in 20090062
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 33 (18.18%)	3 / 36 (8.33%)	8 / 35 (22.86%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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 adenocarcinoma			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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
Parathyroid tumour benign			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Pituitary tumour benign			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (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
Prostate cancer			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Femoral artery occlusion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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

Atrial fibrillation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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 failure congestive			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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
Myocardial infarction			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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			
Cervical radiculopathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
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			
Duodenal ulcer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis eosinophilic			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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

Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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
Skin and subcutaneous tissue disorders			
Pustular psoriasis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic skin eruption			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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			
Nephrolithiasis			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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
Osteoarthritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
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			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Hepatitis C			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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
Necrotising fasciitis streptococcal			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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
Pyelonephritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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

Pyelonephritis acute			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (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	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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
Urosepsis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (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

Serious adverse events	Brodalumab 280 mg Q4W in 20090062	Brodalumab 140 mg Q2W in 20090062	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 40 (17.50%)	5 / 37 (13.51%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour benign			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm rupture			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femoral artery occlusion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocardial infarction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cervical radiculopathy			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis eosinophilic			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			

subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Pustular psoriasis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis C			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising fasciitis streptococcal			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo in 20090062	Brodalumab 70 mg Q2W in 20090062	Brodalumab 210 mg Q2W in 20090062
Total subjects affected by non-serious adverse events			
subjects affected / exposed	33 / 33 (100.00%)	35 / 36 (97.22%)	33 / 35 (94.29%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Basal cell carcinoma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Fibroadenoma of breast			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Haemangioma of skin			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Melanocytic naevus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Neuroma			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Seborrhoeic keratosis			

subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Skin papilloma subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Squamous cell carcinoma of skin subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Thyroid neoplasm subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Vascular disorders			
Erythromelalgia subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Hot flush subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	1 / 36 (2.78%) 1	1 / 35 (2.86%) 2
Hypertension subjects affected / exposed occurrences (all)	4 / 33 (12.12%) 4	3 / 36 (8.33%) 4	4 / 35 (11.43%) 4
Hypotension subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Vascular pain subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 2	1 / 35 (2.86%) 1
Surgical and medical procedures			
Breast prosthesis implantation subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Hernia repair subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Intraocular lens implant			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Rectal polypectomy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin neoplasm excision			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Toe amputation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Tooth extraction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Wisdom teeth removal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cyst			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Fatigue			
subjects affected / exposed	1 / 33 (3.03%)	5 / 36 (13.89%)	2 / 35 (5.71%)
occurrences (all)	1	5	3
Gait disturbance			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Hyperthermia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	2
Inflammation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Injection site bruising			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Injection site erythema			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	3	1	2
Injection site oedema			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	2 / 35 (5.71%)
occurrences (all)	0	2	8
Injection site pruritus			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Injection site swelling			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Injection site urticaria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Local swelling			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Malaise			

subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	2 / 36 (5.56%) 4	0 / 35 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 2	0 / 35 (0.00%) 0
Polyp subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Pyrexia subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Xerosis subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	2 / 36 (5.56%) 2	0 / 35 (0.00%) 0
Seasonal allergy subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	2 / 36 (5.56%) 2	2 / 35 (5.71%) 2
Social circumstances Alcohol use subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Breast cyst			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Breast mass			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Endometriosis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	4	0	0
Erectile dysfunction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Metrorrhagia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ovarian cyst			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Prostatitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Sexual dysfunction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Vulva cyst			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Respiratory, thoracic and mediastinal disorders			
Allergic cough			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Allergic respiratory symptom			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Allergic sinusitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Asthma			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Bronchial disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	4 / 35 (11.43%)
occurrences (all)	0	2	4
Dry throat			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Emphysema			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Epistaxis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	1
Nasal congestion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Oropharyngeal pain			
subjects affected / exposed	2 / 33 (6.06%)	4 / 36 (11.11%)	1 / 35 (2.86%)
occurrences (all)	2	4	1
Productive cough			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	3 / 33 (9.09%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Sinus congestion			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	3	2
Sleep apnoea syndrome			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Throat irritation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Anxiety			
subjects affected / exposed	2 / 33 (6.06%)	3 / 36 (8.33%)	5 / 35 (14.29%)
occurrences (all)	2	3	5
Attention deficit/hyperactivity disorder			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Bipolar disorder			

subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	3	0	0
Depressed mood			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	2 / 33 (6.06%)	2 / 36 (5.56%)	2 / 35 (5.71%)
occurrences (all)	3	2	2
Irritability			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Libido decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nervousness			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Panic attack			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Sleep disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0

Gallbladder disorder subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Gallbladder pain subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Hepatic steatosis subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 2	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Investigations			
Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Blood glucose increased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	2 / 35 (5.71%) 2
Blood pressure increased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 1
Blood testosterone decreased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 1
Blood urine present subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Blood zinc decreased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Lymphocyte count increased			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Monocyte count decreased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Smear cervix abnormal			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vitamin D decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Weight increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Ankle fracture			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	1	0	2
Arthropod bite			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Arthropod sting			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Back injury			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Burns second degree			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cartilage injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Chest injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Contrast media reaction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	1 / 33 (3.03%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	1	2	1
Epicondylitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Facial bones fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Foot fracture			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Foreign body in eye			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hand fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Head injury			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Heat exhaustion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Joint dislocation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	2	1	1
Laceration			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	1	1	3
Ligament rupture			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	1	1	1
Ligament sprain			
subjects affected / exposed	0 / 33 (0.00%)	3 / 36 (8.33%)	0 / 35 (0.00%)
occurrences (all)	0	3	0
Limb injury			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Lower limb fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Meniscus injury			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Muscle rupture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	4 / 33 (12.12%)	2 / 36 (5.56%)	4 / 35 (11.43%)
occurrences (all)	6	2	6
Periorbital contusion			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Post procedural complication			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Post procedural swelling			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Post-traumatic pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Procedural nausea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	3 / 33 (9.09%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	5	0	1
Rib fracture			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Scratch			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Soft tissue injury			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Sunburn			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tendon rupture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Thermal burn			

subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 2
Tooth fracture subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	1 / 35 (2.86%) 1
Wound subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Congenital, familial and genetic disorders Rathke's cleft cyst subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	2 / 33 (6.06%) 3	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Cardiomyopathy subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Cardiovascular insufficiency subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Ischaemic cardiomyopathy subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Nervous system disorders Aura subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Balance disorder			

subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	3 / 35 (8.57%)
occurrences (all)	0	1	4
Cervicobrachial syndrome			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Cluster headache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	1 / 33 (3.03%)	5 / 36 (13.89%)	6 / 35 (17.14%)
occurrences (all)	1	19	8
Hypoaesthesia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Intercostal neuralgia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Migraine			

subjects affected / exposed	2 / 33 (6.06%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	3	2	1
Motor dysfunction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Myoclonus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Nerve compression			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	0 / 33 (0.00%)	3 / 36 (8.33%)	0 / 35 (0.00%)
occurrences (all)	0	5	0
Neuropathy peripheral			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	3	1
Sinus headache			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	7	1
Tension headache			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
VIIth nerve paralysis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	3 / 35 (8.57%)
occurrences (all)	0	1	3
Iron deficiency anaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Neutropenia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Ear congestion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ear discomfort			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Ear pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
External ear inflammation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Eye disorders			

Blepharitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Cataract			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Chalazion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Episcleritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Eye irritation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eyelid vascular disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Hypermetropia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Iridocyclitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Iritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1

Meibomianitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Ocular hyperaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Uveitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Visual acuity reduced			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	3 / 33 (9.09%)	3 / 36 (8.33%)	1 / 35 (2.86%)
occurrences (all)	3	3	2
Abdominal pain upper			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Abnormal faeces			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Anal fissure			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Aphthous stomatitis			
subjects affected / exposed	2 / 33 (6.06%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	2	2	2
Change of bowel habit			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Constipation			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	3 / 35 (8.57%)
occurrences (all)	2	1	3
Dental caries			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	1 / 33 (3.03%)	4 / 36 (11.11%)	0 / 35 (0.00%)
occurrences (all)	1	12	0
Diverticulum intestinal			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Faeces discoloured			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastritis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 33 (6.06%)	3 / 36 (8.33%)	2 / 35 (5.71%)
occurrences (all)	3	3	2
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Haemorrhoids			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Inguinal hernia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Intestinal polyp			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Large intestine polyp			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	3 / 35 (8.57%)
occurrences (all)	2	0	3
Oesophageal spasm			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Oesophagitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Oral mucosal eruption			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Palatal oedema			

subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Poor dental condition			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Rectal polyp			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tooth impacted			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Toothache			
subjects affected / exposed	0 / 33 (0.00%)	4 / 36 (11.11%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Vomiting			
subjects affected / exposed	1 / 33 (3.03%)	3 / 36 (8.33%)	0 / 35 (0.00%)
occurrences (all)	1	5	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Alopecia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dermal cyst			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dermatitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	4 / 35 (11.43%)
occurrences (all)	1	0	4

Dermatitis contact			
subjects affected / exposed	2 / 33 (6.06%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	2	3	0
Dry skin			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	1	1	1
Dyshidrotic eczema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Eczema asteatotic			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Guttate psoriasis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hand dermatitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Ingrowing nail			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Intertrigo			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Keratolysis exfoliativa acquired			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Lichen planus			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Mechanical urticaria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Miliaria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Nail psoriasis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	2
Onycholysis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 33 (3.03%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	1	5	1
Pruritus generalised			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Psoriasis			
subjects affected / exposed	5 / 33 (15.15%)	3 / 36 (8.33%)	3 / 35 (8.57%)
occurrences (all)	5	5	3
Pustular psoriasis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Rash pruritic			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0

Skin disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Skin fissures			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Solar urticaria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Urticaria			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	2	1	0
Urticaria contact			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Bilirubinuria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Bladder diverticulum			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Bladder spasm			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Haematuria			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Nephrolithiasis			
subjects affected / exposed	1 / 33 (3.03%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	2	2	1
Pollakiuria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Proteinuria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Renal colic			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Renal cyst			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Renal failure			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hypogonadism			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hypothyroidism			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	2	0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 33 (15.15%)	8 / 36 (22.22%)	8 / 35 (22.86%)
occurrences (all)	5	18	12
Arthritis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	1	1	0
Back pain			
subjects affected / exposed	2 / 33 (6.06%)	7 / 36 (19.44%)	3 / 35 (8.57%)
occurrences (all)	2	8	4
Bone pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Bursitis			
subjects affected / exposed	1 / 33 (3.03%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	1	2	0
Coccydynia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Compartment syndrome			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Costochondritis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Dactylitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Dupuytren's contracture			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Exostosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Fibromyalgia			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Gouty arthritis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Intervertebral disc protrusion			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	1 / 33 (3.03%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	1	2	0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Muscle atrophy			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	2	1	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Myalgia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	4	1
Myositis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	3 / 35 (8.57%)
occurrences (all)	0	2	3
Osteoarthritis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	1	2
Osteonecrosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Osteoporosis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 33 (0.00%)	5 / 36 (13.89%)	2 / 35 (5.71%)
occurrences (all)	0	7	2
Plantar fasciitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Polyarthrititis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Psoriatic arthropathy			
subjects affected / exposed	4 / 33 (12.12%)	1 / 36 (2.78%)	6 / 35 (17.14%)
occurrences (all)	6	1	7
Rheumatic disorder			

subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Rheumatoid arthritis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Rotator cuff syndrome			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	2
Synovitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Temporomandibular joint syndrome			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Tendon pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Tendonitis			
subjects affected / exposed	2 / 33 (6.06%)	4 / 36 (11.11%)	2 / 35 (5.71%)
occurrences (all)	2	4	3
Tenosynovitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Tenosynovitis stenosans			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Torticollis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Trigger finger			

subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	0 / 35 (0.00%) 0
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Abscess limb			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Bacterial disease carrier			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	1 / 33 (3.03%)	3 / 36 (8.33%)	3 / 35 (8.57%)
occurrences (all)	2	3	5
Bronchitis viral			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Candida infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	3 / 33 (9.09%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	3	0	1
Conjunctivitis			
subjects affected / exposed	1 / 33 (3.03%)	3 / 36 (8.33%)	2 / 35 (5.71%)
occurrences (all)	1	3	3
Cystitis			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	3	0	1
Diverticulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	3	2

External ear cellulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Eye infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Folliculitis			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	2	1	1
Fungal skin infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	5 / 33 (15.15%)	2 / 36 (5.56%)	2 / 35 (5.71%)
occurrences (all)	7	3	2
Gastroenteritis viral			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	1	1	1
Gastrointestinal bacterial infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Genital herpes			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Gingival abscess			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	2
Gingivitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Helicobacter infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1

Herpes simplex			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Herpes virus infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Hordeolum			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	2
Influenza			
subjects affected / exposed	6 / 33 (18.18%)	7 / 36 (19.44%)	4 / 35 (11.43%)
occurrences (all)	9	10	4
Laryngitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Latent tuberculosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			
subjects affected / exposed	12 / 33 (36.36%)	12 / 36 (33.33%)	10 / 35 (28.57%)
occurrences (all)	22	25	16
Nipple infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Onychomycosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Oral candidiasis			
subjects affected / exposed	2 / 33 (6.06%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	2	1	5
Oral fungal infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	2	1	1
Oral infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Otitis externa			
subjects affected / exposed	1 / 33 (3.03%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	1	1	3
Otitis media			
subjects affected / exposed	2 / 33 (6.06%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	2	0	0
Paronychia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Perineal abscess			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Pertussis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Pharyngitis			
subjects affected / exposed	2 / 33 (6.06%)	3 / 36 (8.33%)	5 / 35 (14.29%)
occurrences (all)	2	3	5
Pharyngitis streptococcal			
subjects affected / exposed	3 / 33 (9.09%)	2 / 36 (5.56%)	4 / 35 (11.43%)
occurrences (all)	3	2	5

Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Respiratory tract infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	3 / 33 (9.09%)	3 / 36 (8.33%)	2 / 35 (5.71%)
occurrences (all)	3	3	3
Sinusitis			
subjects affected / exposed	3 / 33 (9.09%)	5 / 36 (13.89%)	5 / 35 (14.29%)
occurrences (all)	3	5	6
Skin bacterial infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Staphylococcal scalded skin syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	4	0
Tinea pedis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Tinea versicolour			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Tonsillitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Tooth abscess			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Tooth infection			

subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	2	0
Tracheitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	5	0
Upper respiratory tract infection			
subjects affected / exposed	7 / 33 (21.21%)	10 / 36 (27.78%)	9 / 35 (25.71%)
occurrences (all)	10	24	15
Urethritis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 33 (3.03%)	3 / 36 (8.33%)	1 / 35 (2.86%)
occurrences (all)	2	5	1
Vaginal infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Viral infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Viral labyrinthitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	0	0	1
Viral pharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	1 / 35 (2.86%)
occurrences (all)	1	0	1
Viral rash			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Viral upper respiratory tract infection			
subjects affected / exposed	2 / 33 (6.06%)	3 / 36 (8.33%)	3 / 35 (8.57%)
occurrences (all)	2	6	3
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			

subjects affected / exposed	2 / 33 (6.06%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	2	3	0
Wound infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	1	1
Gout			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Hypercholesterolaemia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	2	1
Hyperglycaemia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Hypochloraemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Hypokalaemia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	1	0
Hyponatraemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	1	0	0
Insulin resistance			
subjects affected / exposed	0 / 33 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0
Vitamin B12 deficiency subjects affected / exposed occurrences (all)	0 / 33 (0.00%) 0	0 / 36 (0.00%) 0	1 / 35 (2.86%) 1
Vitamin D deficiency subjects affected / exposed occurrences (all)	1 / 33 (3.03%) 1	1 / 36 (2.78%) 1	0 / 35 (0.00%) 0

Non-serious adverse events	Brodalumab 280 mg Q4W in 20090062	Brodalumab 140 mg Q2W in 20090062	
Total subjects affected by non-serious adverse events subjects affected / exposed	37 / 40 (92.50%)	36 / 37 (97.30%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 2	1 / 37 (2.70%) 1	
Basal cell carcinoma subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Fibroadenoma of breast subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 37 (2.70%) 1	
Haemangioma of skin subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 37 (2.70%) 1	
Melanocytic naevus subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Neuroma subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Seborrhoeic keratosis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Skin papilloma			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Thyroid neoplasm			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Erythromelalgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	2 / 40 (5.00%)	5 / 37 (13.51%)	
occurrences (all)	3	6	
Hypotension			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Vascular pain			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
Breast prosthesis implantation			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hernia repair			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Intraocular lens implant			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Rectal polypectomy			

subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Skin neoplasm excision			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Toe amputation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tooth extraction			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Wisdom teeth removal			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 40 (0.00%)	3 / 37 (8.11%)	
occurrences (all)	0	4	
Chest pain			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Cyst			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	1	2	
Gait disturbance			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Hyperthermia			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Inflammation		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Influenza like illness		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Injection site bruising		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	3	0
Injection site erythema		
subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)
occurrences (all)	4	4
Injection site oedema		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Injection site pain		
subjects affected / exposed	2 / 40 (5.00%)	2 / 37 (5.41%)
occurrences (all)	2	2
Injection site pruritus		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	2
Injection site swelling		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Injection site urticaria		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Local swelling		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Malaise		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Oedema peripheral		

subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Pain			
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Peripheral swelling			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Polyp			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Xerosis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Seasonal allergy			
subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)	
occurrences (all)	1	3	
Social circumstances			
Alcohol use			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Breast cyst			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Breast mass			

subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Dysfunctional uterine bleeding			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Endometriosis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Erectile dysfunction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Metrorrhagia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Ovarian cyst			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Prostatitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Sexual dysfunction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Vaginal haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Vulva cyst			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Allergic respiratory symptom			

subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Allergic sinusitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Asthma		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Bronchial disorder		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Cough		
subjects affected / exposed	1 / 40 (2.50%)	3 / 37 (8.11%)
occurrences (all)	2	3
Dry throat		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dyspnoea		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Emphysema		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Epistaxis		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Nasal congestion		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Oropharyngeal pain		
subjects affected / exposed	7 / 40 (17.50%)	4 / 37 (10.81%)
occurrences (all)	11	7
Productive cough		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Respiratory tract congestion		

subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Rhinitis allergic			
subjects affected / exposed	1 / 40 (2.50%)	3 / 37 (8.11%)	
occurrences (all)	1	5	
Rhinorrhoea			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Sinus congestion			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Sleep apnoea syndrome			
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Throat irritation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Upper-airway cough syndrome			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Anxiety			
subjects affected / exposed	2 / 40 (5.00%)	3 / 37 (8.11%)	
occurrences (all)	2	4	
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Bipolar disorder			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Confusional state			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Depressed mood			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Insomnia			
subjects affected / exposed	1 / 40 (2.50%)	3 / 37 (8.11%)	
occurrences (all)	1	3	
Irritability			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Libido decreased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Nervousness			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Panic attack			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Cholelithiasis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Gallbladder disorder			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	

Gallbladder pain subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 37 (2.70%) 1	
Hepatic steatosis subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	1 / 37 (2.70%) 1	
Investigations			
Blood cholesterol increased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 37 (2.70%) 1	
Blood glucose increased subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Blood pressure increased subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Blood testosterone decreased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Blood urine present subjects affected / exposed occurrences (all)	2 / 40 (5.00%) 2	0 / 37 (0.00%) 0	
Blood zinc decreased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Haemoglobin decreased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Lymphocyte count increased subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Monocyte count decreased			

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Smear cervix abnormal			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Vitamin D decreased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Ankle fracture			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Arthropod bite			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	2	
Arthropod sting			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Back injury			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Burns second degree			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Cartilage injury			

subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Chest injury		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Concussion		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Contrast media reaction		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Contusion		
subjects affected / exposed	4 / 40 (10.00%)	3 / 37 (8.11%)
occurrences (all)	7	4
Epicondylitis		
subjects affected / exposed	1 / 40 (2.50%)	3 / 37 (8.11%)
occurrences (all)	1	3
Facial bones fracture		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Fall		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Foot fracture		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Foreign body in eye		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Hand fracture		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Head injury		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Heat exhaustion		

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Joint dislocation		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Joint injury		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Laceration		
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)
occurrences (all)	2	1
Ligament rupture		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Ligament sprain		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Limb injury		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Lower limb fracture		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Meniscus injury		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Muscle rupture		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Muscle strain		
subjects affected / exposed	2 / 40 (5.00%)	4 / 37 (10.81%)
occurrences (all)	2	6
Periorbital contusion		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Post procedural complication		

subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Post procedural swelling		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Post-traumatic pain		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Procedural nausea		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Procedural pain		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Rib fracture		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Scratch		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Skin abrasion		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Soft tissue injury		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Sunburn		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Tendon rupture		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Thermal burn		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Tooth fracture		

subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 37 (2.70%) 1	
Wound subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	2 / 37 (5.41%) 2	
Congenital, familial and genetic disorders Rathke's cleft cyst subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Cardiac disorders Angina pectoris subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Cardiomyopathy subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Cardiovascular insufficiency subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Ischaemic cardiomyopathy subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Palpitations subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Nervous system disorders Aura subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Balance disorder subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Carpal tunnel syndrome			

subjects affected / exposed	2 / 40 (5.00%)	3 / 37 (8.11%)
occurrences (all)	2	3
Cervicobrachial syndrome		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Cluster headache		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Disturbance in attention		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dizziness		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	2	0
Dysaesthesia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dysgeusia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Headache		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Hypoaesthesia		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	2
Intercostal neuralgia		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Lethargy		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Migraine		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Motor dysfunction		

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Myoclonus			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Nerve compression			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Neuralgia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Paraesthesia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 40 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Sinus headache			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tension headache			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
VIIth nerve paralysis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	

Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Neutropenia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Ear and labyrinth disorders			
Cerumen impaction subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	1 / 37 (2.70%) 1	
Ear congestion subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Ear discomfort subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Ear pain subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	1 / 37 (2.70%) 2	
External ear inflammation subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Otorrhoea subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	0 / 37 (0.00%) 0	
Vertigo subjects affected / exposed occurrences (all)	1 / 40 (2.50%) 1	1 / 37 (2.70%) 1	
Eye disorders			
Blepharitis subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
Cataract			

subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Chalazion		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dry eye		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Episcleritis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Eye haemorrhage		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Eye irritation		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Eyelid vascular disorder		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Hypermetropia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Iridocyclitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Iritis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Lacrimation increased		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Meibomianitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Ocular hyperaemia		

subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Ulcerative keratitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Uveitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Visual acuity reduced			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Visual impairment			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Abdominal distension			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Abdominal pain			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Abdominal pain upper			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Abnormal faeces			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Anal fissure			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Aphthous stomatitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	

Change of bowel habit		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Constipation		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Dental caries		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Diarrhoea		
subjects affected / exposed	1 / 40 (2.50%)	3 / 37 (8.11%)
occurrences (all)	1	3
Diverticulum intestinal		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dyspepsia		
subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)
occurrences (all)	1	2
Dysphagia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Faeces discoloured		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Flatulence		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Food poisoning		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Gastritis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Gastrooesophageal reflux disease		
subjects affected / exposed	3 / 40 (7.50%)	3 / 37 (8.11%)
occurrences (all)	3	3

Haemorrhoidal haemorrhage		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Haemorrhoids		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	3	0
Inguinal hernia		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Intestinal polyp		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Large intestine polyp		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Nausea		
subjects affected / exposed	4 / 40 (10.00%)	2 / 37 (5.41%)
occurrences (all)	5	2
Oesophageal spasm		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Oesophagitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Oral mucosal eruption		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Oral pain		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Palatal oedema		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Poor dental condition		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	2	1

Rectal polyp			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Tooth impacted			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Alopecia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Blister			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Dermal cyst			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Dermatitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Dry skin			

subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	2	0
Dyshidrotic eczema		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Ecchymosis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Eczema		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Eczema asteatotic		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Erythema		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Guttate psoriasis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Hand dermatitis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Ingrowing nail		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Intertrigo		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Keratolysis exfoliativa acquired		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Lichen planus		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Mechanical urticaria		

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Miliaria		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Nail psoriasis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Onycholysis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Pruritus		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Pruritus generalised		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Psoriasis		
subjects affected / exposed	4 / 40 (10.00%)	4 / 37 (10.81%)
occurrences (all)	4	4
Pustular psoriasis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Rash		
subjects affected / exposed	0 / 40 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	2
Rash pruritic		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Seborrhoeic dermatitis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Skin disorder		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Skin exfoliation		

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Skin fissures			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	2	
Skin lesion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Skin ulcer			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Solar urticaria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Urticaria			
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)	
occurrences (all)	4	1	
Urticaria contact			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Bilirubinuria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Bladder diverticulum			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Bladder spasm			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	2 / 40 (5.00%)	3 / 37 (8.11%)	
occurrences (all)	3	4	

Pollakiuria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Renal colic			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Renal cyst			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Renal failure			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Urinary incontinence			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hypogonadism			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Hypothyroidism			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 40 (22.50%)	7 / 37 (18.92%)	
occurrences (all)	12	10	
Arthritis			

subjects affected / exposed	0 / 40 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	2
Back pain		
subjects affected / exposed	7 / 40 (17.50%)	7 / 37 (18.92%)
occurrences (all)	8	9
Bone pain		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Bursitis		
subjects affected / exposed	2 / 40 (5.00%)	2 / 37 (5.41%)
occurrences (all)	2	2
Coccydynia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Compartment syndrome		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Costochondritis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dactylitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Dupuytren's contracture		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Exostosis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Fibromyalgia		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Flank pain		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Gouty arthritis		

subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Intervertebral disc degeneration		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Intervertebral disc disorder		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Intervertebral disc protrusion		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Joint swelling		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Lumbar spinal stenosis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Muscle atrophy		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Muscle spasms		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	2
Musculoskeletal chest pain		
subjects affected / exposed	0 / 40 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	2
Musculoskeletal discomfort		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	2	0
Musculoskeletal pain		
subjects affected / exposed	3 / 40 (7.50%)	2 / 37 (5.41%)
occurrences (all)	3	2
Musculoskeletal stiffness		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Myalgia		

subjects affected / exposed	0 / 40 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	3
Myositis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Neck pain		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	2
Osteoarthritis		
subjects affected / exposed	4 / 40 (10.00%)	2 / 37 (5.41%)
occurrences (all)	4	2
Osteonecrosis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Osteoporosis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Pain in extremity		
subjects affected / exposed	5 / 40 (12.50%)	4 / 37 (10.81%)
occurrences (all)	8	4
Plantar fasciitis		
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)
occurrences (all)	3	0
Polyarthritis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Psoriatic arthropathy		
subjects affected / exposed	1 / 40 (2.50%)	6 / 37 (16.22%)
occurrences (all)	1	6
Rheumatic disorder		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Rheumatoid arthritis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Rotator cuff syndrome		

subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Synovial cyst			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Synovitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Temporomandibular joint syndrome			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tendon pain			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tendonitis			
subjects affected / exposed	3 / 40 (7.50%)	1 / 37 (2.70%)	
occurrences (all)	8	1	
Tenosynovitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tenosynovitis stenosans			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Torticollis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Trigger finger			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Infections and infestations			
Abscess			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	

Abscess limb		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Bacterial disease carrier		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Bronchitis		
subjects affected / exposed	3 / 40 (7.50%)	5 / 37 (13.51%)
occurrences (all)	4	5
Bronchitis viral		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Candida infection		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Cellulitis		
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)
occurrences (all)	3	1
Conjunctivitis		
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)
occurrences (all)	2	1
Cystitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Diverticulitis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Ear infection		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	2	1
External ear cellulitis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Eye infection		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0

Folliculitis		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	2
Fungal skin infection		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Furuncle		
subjects affected / exposed	0 / 40 (0.00%)	2 / 37 (5.41%)
occurrences (all)	0	2
Gastroenteritis		
subjects affected / exposed	9 / 40 (22.50%)	6 / 37 (16.22%)
occurrences (all)	9	6
Gastroenteritis viral		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Gastrointestinal bacterial infection		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Genital herpes		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Gingival abscess		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Gingivitis		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Helicobacter infection		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Herpes simplex		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Herpes virus infection		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1

Herpes zoster		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Hordeolum		
subjects affected / exposed	1 / 40 (2.50%)	3 / 37 (8.11%)
occurrences (all)	1	3
Influenza		
subjects affected / exposed	6 / 40 (15.00%)	5 / 37 (13.51%)
occurrences (all)	7	5
Laryngitis		
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)
occurrences (all)	5	1
Latent tuberculosis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Localised infection		
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)
occurrences (all)	2	1
Lower respiratory tract infection		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	11 / 40 (27.50%)	8 / 37 (21.62%)
occurrences (all)	31	19
Nipple infection		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Onychomycosis		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Oral candidiasis		
subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)
occurrences (all)	1	7
Oral fungal infection		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0

Oral herpes		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Oral infection		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Otitis externa		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Otitis media		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Paronychia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Perineal abscess		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Periodontitis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Pertussis		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Pharyngitis		
subjects affected / exposed	2 / 40 (5.00%)	1 / 37 (2.70%)
occurrences (all)	3	1
Pharyngitis streptococcal		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Pneumonia		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Respiratory tract infection		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0

Rhinitis			
subjects affected / exposed	1 / 40 (2.50%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	5 / 40 (12.50%)	3 / 37 (8.11%)	
occurrences (all)	9	3	
Skin bacterial infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Staphylococcal infection			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Staphylococcal scalded skin syndrome			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tinea pedis			
subjects affected / exposed	0 / 40 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	3	
Tinea versicolour			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	2 / 40 (5.00%)	3 / 37 (8.11%)	
occurrences (all)	2	3	
Tooth infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			

subjects affected / exposed	10 / 40 (25.00%)	7 / 37 (18.92%)	
occurrences (all)	20	16	
Urethritis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 40 (2.50%)	4 / 37 (10.81%)	
occurrences (all)	1	4	
Vaginal infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Viral infection			
subjects affected / exposed	2 / 40 (5.00%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Viral labyrinthitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Viral pharyngitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Viral rash			
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Vulvovaginal mycotic infection			
subjects affected / exposed	2 / 40 (5.00%)	0 / 37 (0.00%)	
occurrences (all)	8	0	
Wound infection			
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			

Dehydration		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Diabetes mellitus		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Gout		
subjects affected / exposed	1 / 40 (2.50%)	0 / 37 (0.00%)
occurrences (all)	1	0
Hypercholesterolaemia		
subjects affected / exposed	0 / 40 (0.00%)	3 / 37 (8.11%)
occurrences (all)	0	3
Hyperglycaemia		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Hyperuricaemia		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Hypochloraemia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Hypokalaemia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Hyponatraemia		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0
Insulin resistance		
subjects affected / exposed	0 / 40 (0.00%)	1 / 37 (2.70%)
occurrences (all)	0	1
Type 2 diabetes mellitus		
subjects affected / exposed	1 / 40 (2.50%)	1 / 37 (2.70%)
occurrences (all)	1	1
Vitamin B12 deficiency		
subjects affected / exposed	0 / 40 (0.00%)	0 / 37 (0.00%)
occurrences (all)	0	0

Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 40 (0.00%) 0	0 / 37 (0.00%) 0	
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More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2010	The protocol was amended pursuant to a recommendation from the Data Review Team that CBCs be monitored at every study visit. This recommendation stemmed from a serious adverse event of grade-3 neutropenia reported in a single subject in study 20090062, the phase 2 study in subjects with psoriasis that this trial extends. Conservative rules for dosing in response to laboratory monitoring were also added to safeguard subjects. Updated safety information, including a description of the neutropenic event and other laboratory abnormalities, were incorporated. Other administrative details were changed, including the key sponsor contacts and their contact information. Clarification was provided regarding testing hemoglobin A1c in type 2 diabetics. Typographical errors were changed throughout. Additional language was added to clarify the length of study.
24 January 2011	The protocol was amended based on results from the parent study (20090062). In that dose-ranging study, the results indicated that 140 mg every other week provided near-maximal PASI 75 response for subjects ≤ 100 kg. Response in subjects > 100 kg was more variable, and 140 mg did not appear to provide near maximal PASI 75 response. Accordingly, Amendment 2 decreases dose to 140 mg every other week in subjects who are ≤ 100 kg when the amendment was enacted; subjects who were > 100 kg when the amendment was enacted continued at 210 mg AMG 827 every other week. Other changes included: <ul style="list-style-type: none">• Background information was updated;• Pharmacokinetic sample collection was added;• Allowable and prohibited medications were clarified;• Reporting procedure for serious adverse events was clarified;• Typographical errors were fixed and changes for clarity were made throughout.
21 May 2012	Recognizing that some subjects may have an inadequate response with the 140 mg dose, Amendment 3 allows subjects to reinstitute the 210 mg dose in response to objective criteria. The rules regarding concomitant therapy for control of psoriasis were updated as a result of the allowance for dose increase from 140 mg to 210 mg. Visit procedures for unscheduled visits to assess inadequate response were added. The study was also updated to extend the period of contraception for women after the last dose of study drug from 40 days to 8 weeks based on the duration for 95% of the patients to have approximately 3% of the last dose of AMG 827 (210 mg) remaining. In compliance with a requirement contained in the current version of the European Union Clinical Trial Directive, the safety reporting language in Section 9.2.2 "Reporting Procedures for Serious Adverse Events" has been updated. <ul style="list-style-type: none">• The reporting timeline for the Investigator to report a serious adverse event to Amgen upon knowledge of the event has been changed to within 24 hours (removed within 1 business day).• Removed language that limited the types of serious adverse events the Investigator was to report to Amgen after the end of study (removed reporting of related serious adverse events only). Minor changes include correction of typographical errors, reformatting in Section 6 for clarity, and the addition of the generic name for AMG 827 (brodalumab).
16 October 2013	In order to gain additional safety and efficacy data, the study duration has been extended by approximately 2 years. The protocol was also revised to: <ul style="list-style-type: none">• Provide clarity regarding the safety follow-up in Section 7.• Update the IP dosing window in Section 6.1.1.2 "Administration and Schedule"• Provide additional guidance regarding subjects that discontinue IP and continue in the study in Section 8• Reflect the current interim analysis plan in Section 10.4 "Interim Analysis and Early Stopping Guidelines"• Reflect the current International Committee of Medical Journal Editors criteria for authorship in Section 12.5

26 March 2014	Based on identification of suicidal behavior and suicidal ideation as a potential risk and after discussion with regulatory agencies, the Columbia Suicide Severity Rating Score and the Patient Health Questionnaire-8 were added as instruments to monitor subject safety (ie, stopping rules). The information for the current Investigator's Brochure was updated in Section 13. Other minor editorial corrections and clarifications were made.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported