



Clinical trial results: A Phase III Safety and Efficacy Study to Compare Immune Responses following Injection with Either Two Doses of HEPLISAV™ or Three Doses of Engerix-B®

Summary

EudraCT number	2006-006743-31
Trial protocol	DE
Global end of trial date	03 October 2008

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022

Trial information

Trial identification

Sponsor protocol code	DV2-HBV-10
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00435812
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Dynavax Technologies Corporation
Sponsor organisation address	2100 Powell Street, Suite 720, Emeryville, United States, California 94608
Public contact	Robert Janssen, Dynavax Technologies Corporation, 01 510-665-0414 x:1414, rjanssen@dynavax.com
Scientific contact	Robert Janssen, Dynavax Technologies Corporation, 01 510-665-0414 x:1414, rjanssen@dynavax.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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 November 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 March 2008
Global end of trial reached?	Yes
Global end of trial date	03 October 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective of this trial is to compare the proportion of subjects who exhibit seroprotective immune response (SPR - anti-HBsAg antibodies [anti-HBsAg] ≥ 10 mIU/ml by AUSAB® assay) when measured at Week 12 following vaccination with HEPLISAV at 0 and 1 month to the proportion of subjects who exhibit SPRs when measured at Week 28 following vaccination with Engerix-B at 0, 1 and 6 months.

Protection of trial subjects:

This study was conducted in accordance with the protocol, good clinical practice (GCP) as defined in the International Conference on Harmonisation (ICH) guidelines, country-specific laws and regulations governing clinical studies of investigational products, and the Declaration of Helsinki (1989).

Subjects could withdraw their consent to participate at any time without prejudice. Also, the investigator could withdraw a subject from further treatment if, in the investigator's clinical judgment, it was in the best interest of the subject or if the subject was unable to comply with protocol requirements.

For subjects who were discontinued from the study due to adverse events (AEs), the AE was monitored until resolution or, if the event was determined to be chronic it was monitored until it was stable. If the event remained unresolved at the conclusion of the study, a clinical assessment was made by the investigator and medical monitor to determine whether continued follow-up of the event was warranted. Subjects who were not seroprotected at Week 28 were offered an optional additional injection of Engerix-B and were provided with the anti-HBsAg test results following the additional injection. The optional additional vaccination and test results were outside of protocol procedures and were not captured in the database.

In the event the Sponsor stopped the study prior to completion, subjects were to be offered Engerix-B.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 December 2006
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	Canada: 1489
Country: Number of subjects enrolled	Germany: 939
Worldwide total number of subjects	2428
EEA total number of subjects	939

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)	13
Adults (18-64 years)	2415
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

11-55 yrs recruited in Canada, 18-55 yrs recruited in Germany (age adjustment in 1st Amendment). Canada recruitment period: 12-Dec-2006 to 11-July-2007. Germany recruitment period 08-Feb-2007 to 11-July-2007.

2400 subjects planned (1018 ISS-HBsAg: 1800; Engerix-B: 600); 2428 subjects enrolled and analyzed (1018 ISS-HBsAg: 1820; Engerix-B: 608)

Pre-assignment

Screening details:

Medical history, medical evaluation, vital signs, serum pregnancy, urine pregnancy prior to injection, Anti-HBsAg, Hepatitis screen, ANA and anti-ds DNA screens were all performed in the period of -28 to -3 days prior to the first study injection (at Day 0)

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject

Blinding implementation details:

The subjects and the study personnel who evaluated them were blinded to treatment assignment. Independent pharmacists or nurses who had no other study responsibilities were not blinded so they could prepare and/or administer the study injections. In addition, an unblinded study monitor with no other study responsibilities performed drug accountability.

SAEs were evaluated by the medical monitor, who remained blinded to treatment assignment.

Arms

Are arms mutually exclusive?	Yes
Arm title	1018 ISS-HBsAg group

Arm description:

Subjects in the 1018 ISS-HBsAg group received active vaccine (Hepilisav-B) at Weeks 0 and 4 and saline placebo at Week 24

Arm type	Experimental
Investigational medicinal product name	1018 ISS-HBsAg
Investigational medicinal product code	
Other name	HEPLISAV, Hepilisav-B
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

The test product (1018 ISS-HBsAg) was 20 mcg HBsAg with 3000 mcg 1018 immunostimulatory sequence (ISS) adjuvant. Subjects received a single intramuscular injection (total injection volume 0.5 mL) into the right or left deltoid muscle at Weeks 0 and 4 (placebo at Week 24). The arm used for injection was alternated with each injection.

Arm title	Engerix-B group
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Arm description:

3-dose regimen of Engerix-B (Weeks 0, 4 and 24)

Arm type	Active comparator
Investigational medicinal product name	Engerix-B
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Engerix-B (20 mcg HBsAg combined with 500 mcg alum adjuvant/mL; GlaxoSmithKline Biologicals) administered as a single intramuscular injection (1.0 mL) into the deltoid muscle at Weeks 0, 4, and 24. The arm used for injection was alternated with each injection.

Number of subjects in period 1	1018 ISS-HBsAg group	Engerix-B group
Started	1820	608
Completed	1757	590
Not completed	63	18
Subject Non-Compliance	3	2
Consent withdrawn by subject	18	2
Adverse event, non-fatal	2	2
Other	8	2
Lost to follow-up	30	10
Protocol deviation	2	-

Baseline characteristics

Reporting groups

Reporting group title	1018 ISS-HBsAg group
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Reporting group description:

Subjects in the 1018 ISS-HBsAg group received active vaccine (Heplisav-B) at Weeks 0 and 4 and saline placebo at Week 24

Reporting group title	Engerix-B group
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Reporting group description:

3-dose regimen of Engerix-B (Weeks 0, 4 and 24)

Reporting group values	1018 ISS-HBsAg group	Engerix-B group	Total
Number of subjects	1820	608	2428
Age categorical			
The effect of age on immunogenicity was evaluated in 4 age strata: Subjects 18 to 55 years of age Subjects 18-39 years of age Subjects 40-55 years of age Subjects 11 to 17 years of age Safety analysis populations: Subjects 11-39 years of age, and subjects 40-55 years of age			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
11-17 years	11	2	13
18-39 years	818	275	1093
40-55 years	991	331	1322
11-39	0	0	0
Age continuous			
Age mean (SD) by treatment group			
Units: years			
arithmetic mean	39.7	39.8	
standard deviation	± 9.56	± 9.11	-
Gender categorical			
Male or female			
Units: Subjects			
Female	959	346	1305
Male	861	262	1123

Subject analysis sets

Subject analysis set title	1018 ISS-HBsAg PP
Subject analysis set type	Per protocol

Subject analysis set description:

The primary immunogenicity analysis was based on the PP population. The PP analysis population comprised all subjects who met eligibility criteria, did not violate the protocol in a substantial manner, received all protocol-specified study injections, had their primary serology and all injections within the specified day ranges as defined in Section 8.5 of the SAP, and had serology at their primary endpoint (Week 12 for 1018 ISS-HBsAg group).

Subject analysis set title	Engerix-B PP
Subject analysis set type	Per protocol

Subject analysis set description:

The primary immunogenicity analysis was based on the PP population. The PP analysis population comprised all subjects who met eligibility criteria, did not violate the protocol in a substantial manner, received all protocol-specified study injections, had their primary serology and all injections within the specified day ranges as defined in Section 8.5 of the SAP, and had serology at their primary endpoint (Week 28 for Engerix-B group).

Subject analysis set title	1018 ISS-HBsAg Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Enrolled subjects who received at least 1 study injection and had any post-baseline safety data.

Subject analysis set title	Engerix-B Safety
Subject analysis set type	Safety analysis

Subject analysis set description:

Enrolled subjects who received at least 1 study injection and had any post-baseline safety data

Reporting group values	1018 ISS-HBsAg PP	Engerix-B PP	1018 ISS-HBsAg Safety
Number of subjects	1520	523	1820
Age categorical			
<p>The effect of age on immunogenicity was evaluated in 4 age strata: Subjects 18 to 55 years of age Subjects 18-39 years of age Subjects 40-55 years of age Subjects 11 to 17 years of age Safety analysis populations: Subjects 11-39 years of age, and subjects 40-55 years of age</p>			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
11-17 years	10	2	0
18-39 years	654	222	0
40-55 years	856	299	991
11-39	0	0	829

Age continuous			
Age mean (SD) by treatment group			
Units: years			
arithmetic mean	40.1	40.4	39.9
standard deviation	± 9.46	± 8.94	± 9.36
Gender categorical			
Male or female			
Units: Subjects			
Female	815	304	959
Male	705	219	861

Reporting group values	Engerix-B Safety		
Number of subjects	608		
Age categorical			
The effect of age on immunogenicity was evaluated in 4 age strata: Subjects 18 to 55 years of age Subjects 18-39 years of age Subjects 40-55 years of age Subjects 11 to 17 years of age Safety analysis populations: Subjects 11-39 years of age, and subjects 40-55 years of age			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	0		
85 years and over	0		
11-17 years	0		
18-39 years	0		
40-55 years	331		
11-39	277		
Age continuous			
Age mean (SD) by treatment group			
Units: years			
arithmetic mean	39.8		
standard deviation	± 9.01		
Gender categorical			
Male or female			
Units: Subjects			
Female	346		
Male	262		

End points

End points reporting groups

Reporting group title	1018 ISS-HBsAg group
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Reporting group description:

Subjects in the 1018 ISS-HBsAg group received active vaccine (Hepilisav-B) at Weeks 0 and 4 and saline placebo at Week 24

Reporting group title	Engerix-B group
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Reporting group description:

3-dose regimen of Engerix-B (Weeks 0, 4 and 24)

Subject analysis set title	1018 ISS-HBsAg PP
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Subject analysis set type	Per protocol
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Subject analysis set description:

The primary immunogenicity analysis was based on the PP population. The PP analysis population comprised all subjects who met eligibility criteria, did not violate the protocol in a substantial manner, received all protocol-specified study injections, had their primary serology and all injections within the specified day ranges as defined in Section 8.5 of the SAP, and had serology at their primary endpoint (Week 12 for 1018 ISS-HBsAg group).

Subject analysis set title	Engerix-B PP
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Subject analysis set type	Per protocol
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Subject analysis set description:

The primary immunogenicity analysis was based on the PP population. The PP analysis population comprised all subjects who met eligibility criteria, did not violate the protocol in a substantial manner, received all protocol-specified study injections, had their primary serology and all injections within the specified day ranges as defined in Section 8.5 of the SAP, and had serology at their primary endpoint (Week 28 for Engerix-B group).

Subject analysis set title	1018 ISS-HBsAg Safety
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Enrolled subjects who received at least 1 study injection and had any post-baseline safety data.

Subject analysis set title	Engerix-B Safety
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Enrolled subjects who received at least 1 study injection and had any post-baseline safety data

Primary: Primary Immunogenicity Analysis: SPR after the final active injection

End point title	Primary Immunogenicity Analysis: SPR after the final active injection
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End point description:

SPR at 12 weeks post last active injection

End point type	Primary
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End point timeframe:

Week 12 for 1018 ISS-HBsAg group, and Week 28 for Engerix-B group.

End point values	1018 ISS-HBsAg PP	Engerix-B PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1520	523		
Units: percent				
number (not applicable)	95.02	81.36		

Statistical analyses

Statistical analysis title	Primary immunogenicity analysis
Statistical analysis description: The primary immunogenicity analysis determined the difference in the SPR between Engerix-B at Week 28 and 1018 ISS-HBsAg at Week 12 with a 2 sided 95% CI on the difference (Engerix-B minus 1018 ISS-HBsAg) in SPR. If the upper limit of this CI is below the pre-specified non-inferiority criterion (+10%), 1018 ISS-HBsAg was non-inferior to Engerix-B in SPR.	
Comparison groups	1018 ISS-HBsAg PP v Engerix-B PP
Number of subjects included in analysis	2043
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.05
Method	t-test, 2-sided

Secondary: Secondary Immunogenicity Analysis: SPR measured 4 weeks after the first injection (onset of response)

End point title	Secondary Immunogenicity Analysis: SPR measured 4 weeks after the first injection (onset of response)
End point description:	
End point type	Secondary
End point timeframe: 4 weeks after the first injection for both treatment groups	

End point values	1018 ISS-HBsAg PP	Engerix-B PP		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1510	521		
Units: percent				
number (not applicable)	23.54	4.06		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety: Solicited post-injection reactions

End point title	Safety: Solicited post-injection reactions
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End point description:

End point type Other pre-specified

End point timeframe:

Days 0-6 following each injection (Wks 0, 4 and 24)

End point values	1018 ISS- HBsAg Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1820	608		
Units: percent				
number (not applicable)	52.0	48.4		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety: Change in ANA levels from baseline

End point title Safety: Change in ANA levels from baseline

End point description:

End point type Other pre-specified

End point timeframe:

Baseline to Week 28

End point values	1018 ISS- HBsAg Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1820	608		
Units: percent				
number (not applicable)				
1 dilution increase	1.7	1.3		
2 dilution increase	0.5	1.0		
3 dilution increase	0.1	0		
4 dilution increase	0	0		
>4 dilution increase	0	0		
At least 2 dilution increase	0.6	1.0		

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Safety: Change in Anti-ds DNA levels from baseline

End point title	Safety: Change in Anti-ds DNA levels from baseline
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End point description:

End point type	Other pre-specified
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End point timeframe:

Baseline to Week 28

End point values	1018 ISS- HBsAg Safety	Engerix-B Safety		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	1820	608		
Units: percent				
number (not applicable)				
Negative to negative	94.8	94.6		
Negative to positive	0.5	0.5		
Positive to negative	0.3	0.5		
Positive to positive	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Any AE that began on or after the day of the first study injection, or any AE that began before the day of the first study injection and worsened on or after the day of the first study injection, and are referred to simply as AEs

Adverse event reporting additional description:

All AEs described in this section were treatment emergent, defined according to the timeframe above. Note that AEs are referred to as unsolicited adverse experiences in the CSR.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.0
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Reporting groups

Reporting group title	1018 ISS-HBsAg
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Reporting group description:

Subjects receiving the experimental vaccine

Reporting group title	Engerix-B
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Reporting group description:

Subjects received active comparator vaccine

Serious adverse events	1018 ISS-HBsAg	Engerix-B	
Total subjects affected by serious adverse events			
subjects affected / exposed	28 / 1820 (1.54%)	13 / 608 (2.14%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Papillary thyroid cancer			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Meningioma surgery			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anti-neutrophil cytoplasmic antibody positive vasculitis			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
menorrhagia			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wegener's Granulomatosis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium tremens			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dislocation of joint prosthesis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Meniscus lesion			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sternal fracture			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebral ischaemia			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (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			
Renal failure			

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bursitis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Tonsillitis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adnexitis			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	1018 ISS-HBsAg	Engerix-B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1098 / 1820 (60.33%)	376 / 608 (61.84%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Skin papilloma			
subjects affected / exposed	10 / 1820 (0.55%)	3 / 608 (0.49%)	
occurrences (all)	10	3	
Breast cancer			
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)	
occurrences (all)	2	0	
Benign breast neoplasm			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Benign neoplasm of adrenal gland			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Nasal neoplasm			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Melanocytic naevus			
subjects affected / exposed	2 / 1820 (0.11%)	3 / 608 (0.49%)	
occurrences (all)	2	3	
Basal cell carcinoma			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Haemangioma of skin			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Vascular disorders			

Hypertension		
subjects affected / exposed	38 / 1820 (2.09%)	17 / 608 (2.80%)
occurrences (all)	38	17
Circulatory collapse		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Phlebitis		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Hypotension		
subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
Thrombosis		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Venous insufficiency		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Deep vein thrombosis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Haematoma		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Peripheral vascular disorder		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Varicose vein		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Flushing		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Raynaud's phenomenon		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1

Surgical and medical procedures			
Meningioma surgery			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Wart excision			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Inguinal hernia repair			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Wisdom teeth removal			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	21 / 1820 (1.15%)	11 / 608 (1.81%)	
occurrences (all)	21	11	
Fatigue			
subjects affected / exposed	24 / 1820 (1.32%)	4 / 608 (0.66%)	
occurrences (all)	24	4	
Influenza like illness			
subjects affected / exposed	11 / 1820 (0.60%)	3 / 608 (0.49%)	
occurrences (all)	11	3	
Oedema peripheral			
subjects affected / exposed	9 / 1820 (0.49%)	1 / 608 (0.16%)	
occurrences (all)	9	1	
Chills			
subjects affected / exposed	3 / 1820 (0.16%)	2 / 608 (0.33%)	
occurrences (all)	3	2	
Malaise			
subjects affected / exposed	5 / 1820 (0.27%)	6 / 608 (0.99%)	
occurrences (all)	5	6	
Pain			
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)	
occurrences (all)	3	1	
Chest discomfort			

subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Polyp		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Asthenia		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Axillary pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Chest pain		
subjects affected / exposed	4 / 1820 (0.22%)	1 / 608 (0.16%)
occurrences (all)	4	1
Cyst		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
Feeling cold		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Hangover		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
local swelling		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Thirst		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Feeling abnormal		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
lower extremity mass		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Vessel puncture site haematoma		

subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1
Vessel puncture site reaction subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1
Injection site bruising subjects affected / exposed occurrences (all)	11 / 1820 (0.60%) 11	2 / 608 (0.33%) 2
Injection site discomfort subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	0 / 608 (0.00%) 0
Injection site pruritus subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	1 / 608 (0.16%) 1
Facial pain subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0
Injection site haematoma subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0
Injection site warmth subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0
Injection site reaction subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1
Peripheral coldness subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1
Anti-neutrophil cytoplasmic antibody		

positive vasculitis subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Contrast media allergy subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Immune system disorders			
Seasonal allergy subjects affected / exposed occurrences (all)	6 / 1820 (0.33%) 6	3 / 608 (0.49%) 3	
Allergy to arthropod bite subjects affected / exposed occurrences (all)	2 / 1820 (0.11%) 2	0 / 608 (0.00%) 0	
Hypersensitivity subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	2 / 608 (0.33%) 2	
Food allergy subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	1 / 608 (0.16%) 1	
house dust allergy subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Allergy to plants subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Reproductive system and breast disorders			
Dysmenorrhoea subjects affected / exposed occurrences (all)	21 / 1820 (1.15%) 21	8 / 608 (1.32%) 8	
Menstrual disorder subjects affected / exposed occurrences (all)	5 / 1820 (0.27%) 5	2 / 608 (0.33%) 2	
Amenorrhoea subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Breast cyst			

subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Breast pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Breast swelling		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Dyspareunia		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Menopausal disorder		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Menorrhagia		
subjects affected / exposed	6 / 1820 (0.33%)	2 / 608 (0.33%)
occurrences (all)	6	2
Ovarian cyst		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Pelvic pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Postmenopausal haemorrhage		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Prostatitis		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Vulvovaginal pruritus		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Metrorrhagia		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Vaginal haemorrhage		

subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
Vulva cyst		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Vulvovaginal dryness		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Erectile dysfunction		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Breast discomfort		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Hot flush		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Menopausal symptoms		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Premenstrual syndrome		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Sexual dysfunction		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Vaginal discharge		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Vulvovaginal discomfort		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Balanitis		
subjects affected / exposed	0 / 1820 (0.00%)	2 / 608 (0.33%)
occurrences (all)	0	2
Respiratory, thoracic and mediastinal		

disorders		
Pharyngolaryngeal pain		
subjects affected / exposed	80 / 1820 (4.40%)	25 / 608 (4.11%)
occurrences (all)	80	25
Cough		
subjects affected / exposed	57 / 1820 (3.13%)	17 / 608 (2.80%)
occurrences (all)	57	17
Nasal congestion		
subjects affected / exposed	31 / 1820 (1.70%)	4 / 608 (0.66%)
occurrences (all)	31	4
Sinus headache		
subjects affected / exposed	14 / 1820 (0.77%)	3 / 608 (0.49%)
occurrences (all)	14	3
Rhinorrhoea		
subjects affected / exposed	8 / 1820 (0.44%)	0 / 608 (0.00%)
occurrences (all)	8	0
Asthma		
subjects affected / exposed	9 / 1820 (0.49%)	2 / 608 (0.33%)
occurrences (all)	9	2
Rhinitis allergic		
subjects affected / exposed	5 / 1820 (0.27%)	0 / 608 (0.00%)
occurrences (all)	5	0
Respiratory tract congestion		
subjects affected / exposed	5 / 1820 (0.27%)	0 / 608 (0.00%)
occurrences (all)	5	0
Dyspnoea		
subjects affected / exposed	4 / 1820 (0.22%)	2 / 608 (0.33%)
occurrences (all)	4	2
Epistaxis		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Pharyngitis		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Dry throat		

subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
Hypoxia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Nasal dryness		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Nasal polyps		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Pneumothorax		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Postnasal drip		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Sleep apnoea syndrome		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Sneezing		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Upper respiratory tract congestion		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Vocal cord disorder		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Wheezing		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Nasal discomfort		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Pleuritic pain		

subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Sinus congestion subjects affected / exposed occurrences (all)	9 / 1820 (0.49%) 9	4 / 608 (0.66%) 4	
Pulmonary embolism subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	0 / 608 (0.00%) 0	
Adenoidal hypertrophy subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Bronchial hyperreactivity subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Bronchitis chronic subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Dysphonia subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Pleurisy subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Wegener's Granulomatosis subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Pleural effusion subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Psychiatric disorders Sleep disorder			

subjects affected / exposed	21 / 1820 (1.15%)	10 / 608 (1.64%)
occurrences (all)	21	10
Stress		
subjects affected / exposed	4 / 1820 (0.22%)	1 / 608 (0.16%)
occurrences (all)	4	1
Mood swings		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Nightmare		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Restlessness		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Delirium tremens		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Nervousness		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Panic disorder		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Anxiety disorder		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Generalised anxiety disorder		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Attention deficit hyperactivity disorder		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Investigations		
Antinuclear antibody increased		

subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)	
occurrences (all)	2	1	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Bleeding time prolonged			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Hepatitis C positive			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	14 / 1820 (0.77%)	7 / 608 (1.15%)	
occurrences (all)	14	7	
Contusion			
subjects affected / exposed	10 / 1820 (0.55%)	3 / 608 (0.49%)	
occurrences (all)	10	3	
Muscle strain			
subjects affected / exposed	13 / 1820 (0.71%)	5 / 608 (0.82%)	
occurrences (all)	13	5	
Post procedural complication			
subjects affected / exposed	14 / 1820 (0.77%)	7 / 608 (1.15%)	
occurrences (all)	14	7	
Skin laceration			

subjects affected / exposed	8 / 1820 (0.44%)	6 / 608 (0.99%)
occurrences (all)	8	6
Soft tissue injury		
subjects affected / exposed	5 / 1820 (0.27%)	2 / 608 (0.33%)
occurrences (all)	5	2
Epicondylitis		
subjects affected / exposed	6 / 1820 (0.33%)	6 / 608 (0.99%)
occurrences (all)	6	6
Foot fracture		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
meniscus lesion		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Thermal burn		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Wound		
subjects affected / exposed	5 / 1820 (0.27%)	0 / 608 (0.00%)
occurrences (all)	5	0
Arthropod bite		
subjects affected / exposed	5 / 1820 (0.27%)	3 / 608 (0.49%)
occurrences (all)	5	3
Arthropod sting		
subjects affected / exposed	1 / 1820 (0.05%)	3 / 608 (0.49%)
occurrences (all)	1	3
Back injury		
subjects affected / exposed	5 / 1820 (0.27%)	3 / 608 (0.49%)
occurrences (all)	5	3
Clavicle fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Dislocation of joint prosthesis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Incision site pain		

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Limb injury		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Multiple injuries		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Muscle rupture		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Patella fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Procedural pain		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Rib fracture		
subjects affected / exposed	5 / 1820 (0.27%)	0 / 608 (0.00%)
occurrences (all)	5	0
Road traffic accident		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Sternal fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tendon rupture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Ulna fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Brachial plexus injury		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Burns first degree		

subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Femur fracture		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Heat stroke		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Neck injury		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Sunburn		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Tibia fracture		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Upper limb fracture		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Whiplash injury		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Ligament rupture		
subjects affected / exposed	4 / 1820 (0.22%)	0 / 608 (0.00%)
occurrences (all)	4	0
Eye injury		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
Jaw fracture		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Animal scratch		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Ankle fracture		

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Facial bones fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Fall		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Fractured coccyx		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Head injury		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Heart injury		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Overdose		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Pelvic fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Periorbital haematoma		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Post-traumatic pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Radius fracture		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Skeletal injury		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tooth fracture		

subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Wound complication subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	1 / 608 (0.16%) 1	
Concussion subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Thoracic vertebral fracture subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Congenital, familial and genetic disorders			
Gilbert's syndrome subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Cardiac disorders			
Arrhythmia subjects affected / exposed occurrences (all)	8 / 1820 (0.44%) 8	4 / 608 (0.66%) 4	
Angina pectoris subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	0 / 608 (0.00%) 0	
Cardiac disorder subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Supraventricular tachycardia subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	206 / 1820 (11.32%) 206	62 / 608 (10.20%) 62	
Dizziness subjects affected / exposed occurrences (all)	20 / 1820 (1.10%) 20	7 / 608 (1.15%) 7	
Migraine			

subjects affected / exposed	18 / 1820 (0.99%)	8 / 608 (1.32%)
occurrences (all)	18	8
Paraesthesia		
subjects affected / exposed	3 / 1820 (0.16%)	2 / 608 (0.33%)
occurrences (all)	3	2
Hypoaesthesia		
subjects affected / exposed	2 / 1820 (0.11%)	3 / 608 (0.49%)
occurrences (all)	2	3
Sciatica		
subjects affected / exposed	2 / 1820 (0.11%)	3 / 608 (0.49%)
occurrences (all)	2	3
Syncope		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Cervical root pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Loss of consciousness		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Nerve compression		
subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
nerve root compression		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Trigeminal neuralgia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Balance disorder		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Carpal tunnel syndrome		
subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
Lethargy		

subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Depression		
subjects affected / exposed	21 / 1820 (1.15%)	4 / 608 (0.66%)
occurrences (all)	21	4
Anxiety		
subjects affected / exposed	9 / 1820 (0.49%)	4 / 608 (0.66%)
occurrences (all)	9	4
Amnesia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Dysphasia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Facial spasm		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Guillain-Barre syndrome		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Post-traumatic headache		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Restless legs syndrome		
subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
Tension headache		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tremor		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tunnel vision		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
facial palsy		

subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Hyperreflexia subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	4 / 1820 (0.22%) 4	1 / 608 (0.16%) 1	
Lymphadenopathy subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	1 / 608 (0.16%) 1	
Leukopenia subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Splenomegaly subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	14 / 1820 (0.77%) 14	3 / 608 (0.49%) 3	
Otitis media subjects affected / exposed occurrences (all)	14 / 1820 (0.77%) 14	6 / 608 (0.99%) 6	
Otitis externa subjects affected / exposed occurrences (all)	5 / 1820 (0.27%) 5	0 / 608 (0.00%) 0	
Ear discomfort subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	1 / 608 (0.16%) 1	
Deafness subjects affected / exposed occurrences (all)	2 / 1820 (0.11%) 2	0 / 608 (0.00%) 0	
Labyrinthitis			

subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Tinnitus			
subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	1 / 608 (0.16%) 1	
Vertigo			
subjects affected / exposed occurrences (all)	2 / 1820 (0.11%) 2	0 / 608 (0.00%) 0	
Ear congestion			
subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Motion sickness			
subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	2 / 608 (0.33%) 2	
Vertigo positional			
subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Eye disorders			
Conjunctivitis			
subjects affected / exposed occurrences (all)	13 / 1820 (0.71%) 13	4 / 608 (0.66%) 4	
Dry eye			
subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Eyelid oedema			
subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Hordeolum			
subjects affected / exposed occurrences (all)	2 / 1820 (0.11%) 2	0 / 608 (0.00%) 0	
Lacrimation increased			
subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	1 / 608 (0.16%) 1	
Presbyopia			
subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	

Vision blurred		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
Blepharitis		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Blepharospasm		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Blindness		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Conjunctivitis allergic		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Corneal lesion		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Eye inflammation		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Eye irritation		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Glaucoma		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Macular degeneration		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Eye swelling		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Asthenopia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0

Conjunctivitis infective subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	1 / 608 (0.16%) 1	
Eye discharge subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Iritis subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Ocular hyperaemia subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	1 / 608 (0.16%) 1	
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	43 / 1820 (2.36%) 43	14 / 608 (2.30%) 14	
Tooth disorder subjects affected / exposed occurrences (all)	39 / 1820 (2.14%) 39	17 / 608 (2.80%) 17	
Abdominal pain subjects affected / exposed occurrences (all)	33 / 1820 (1.81%) 33	12 / 608 (1.97%) 12	
Nausea subjects affected / exposed occurrences (all)	32 / 1820 (1.76%) 32	20 / 608 (3.29%) 20	
Vomiting subjects affected / exposed occurrences (all)	14 / 1820 (0.77%) 14	10 / 608 (1.64%) 10	
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	15 / 1820 (0.82%) 15	7 / 608 (1.15%) 7	
Dyspepsia subjects affected / exposed occurrences (all)	14 / 1820 (0.77%) 14	6 / 608 (0.99%) 6	
Abdominal discomfort			

subjects affected / exposed	6 / 1820 (0.33%)	6 / 608 (0.99%)
occurrences (all)	6	6
Gingival disorder		
subjects affected / exposed	10 / 1820 (0.55%)	4 / 608 (0.66%)
occurrences (all)	10	4
Constipation		
subjects affected / exposed	4 / 1820 (0.22%)	4 / 608 (0.66%)
occurrences (all)	4	4
Flatulence		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Dysphagia		
subjects affected / exposed	4 / 1820 (0.22%)	1 / 608 (0.16%)
occurrences (all)	4	1
Food poisoning		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Gastrointestinal disorder		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Gingival pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Haemorrhoids		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
sensitivity of teeth		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Stomatitis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tongue coated		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Anal fissure		

subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
aphthous stomatitis		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
Gastritis		
subjects affected / exposed	6 / 1820 (0.33%)	1 / 608 (0.16%)
occurrences (all)	6	1
Oral pain		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Abdominal distension		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Cheilosis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Inguinal hernia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Lip swelling		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Proctalgia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tooth deposit		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Pancreatitis		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Rectal haemorrhage		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Hepatobiliary disorders		

Cholecystitis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Cholelithiasis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Hepatitis			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Biliary colic			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Cholecystitis acute			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	12 / 1820 (0.66%)	2 / 608 (0.33%)	
occurrences (all)	12	2	
Rash			
subjects affected / exposed	12 / 1820 (0.66%)	3 / 608 (0.49%)	
occurrences (all)	12	3	
Urticaria			
subjects affected / exposed	8 / 1820 (0.44%)	0 / 608 (0.00%)	
occurrences (all)	8	0	
Dermatitis			
subjects affected / exposed	12 / 1820 (0.66%)	0 / 608 (0.00%)	
occurrences (all)	12	0	
Hyperhidrosis			
subjects affected / exposed	4 / 1820 (0.22%)	1 / 608 (0.16%)	
occurrences (all)	4	1	
Dermatitis allergic			

subjects affected / exposed	5 / 1820 (0.27%)	1 / 608 (0.16%)
occurrences (all)	5	1
Photosensitivity reaction		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Rash maculo-papular		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Rosacea		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Acrodermatitis		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Actinic keratosis		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Anhidrosis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Eczema		
subjects affected / exposed	6 / 1820 (0.33%)	3 / 608 (0.49%)
occurrences (all)	6	3
Erythema		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Hyperkeratosis		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Lichen planus		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Nail bed bleeding		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Rash macular		

subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Rash papular		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Rash pruritic		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Seborrhoeic dermatitis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Swelling face		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Urticaria thermal		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Dermal cyst		
subjects affected / exposed	0 / 1820 (0.00%)	2 / 608 (0.33%)
occurrences (all)	0	2
Dermatitis contact		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Skin lesion		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Pruritus		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Acne cystic		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Alopecia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Dry skin		

subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Ecchymosis subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Heat rash subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Ingrowing nail subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Skin fissures subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Skin ulcer subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Drug eruption subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Hypoaesthesia facial subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Neurodermatitis subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Renal and urinary disorders			
Cystitis subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	4 / 608 (0.66%) 4	
Dysuria subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	2 / 608 (0.33%) 2	
Nephrolithiasis subjects affected / exposed occurrences (all)	2 / 1820 (0.11%) 2	1 / 608 (0.16%) 1	

Pollakiuria			
subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)	
occurrences (all)	1	2	
Renal colic			
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)	
occurrences (all)	1	1	
Cystitis noninfective			
subjects affected / exposed	0 / 1820 (0.00%)	2 / 608 (0.33%)	
occurrences (all)	0	2	
Polyuria			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Urogenital disorder			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Calculus urinary			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)	
occurrences (all)	1	1	
Haematuria			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Ureteric stenosis			
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	
Endocrine disorders			
Goitre			
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism			
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)	
occurrences (all)	3	0	
Hypothyroidism			

subjects affected / exposed occurrences (all)	3 / 1820 (0.16%) 3	1 / 608 (0.16%) 1	
Thyroid disorder subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Basedow's disease subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	1 / 608 (0.16%) 1	
Thyroiditis subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Musculoskeletal and connective tissue disorders			
Back pain subjects affected / exposed occurrences (all)	93 / 1820 (5.11%) 93	31 / 608 (5.10%) 31	
Arthralgia subjects affected / exposed occurrences (all)	43 / 1820 (2.36%) 43	18 / 608 (2.96%) 18	
Pain in extremity subjects affected / exposed occurrences (all)	28 / 1820 (1.54%) 28	7 / 608 (1.15%) 7	
Myalgia subjects affected / exposed occurrences (all)	20 / 1820 (1.10%) 20	7 / 608 (1.15%) 7	
Neck pain subjects affected / exposed occurrences (all)	24 / 1820 (1.32%) 24	8 / 608 (1.32%) 8	
Musculoskeletal pain subjects affected / exposed occurrences (all)	23 / 1820 (1.26%) 23	8 / 608 (1.32%) 8	
Bursitis subjects affected / exposed occurrences (all)	10 / 1820 (0.55%) 10	2 / 608 (0.33%) 2	
Muscle spasms			

subjects affected / exposed	9 / 1820 (0.49%)	4 / 608 (0.66%)
occurrences (all)	9	4
Musculoskeletal chest pain		
subjects affected / exposed	10 / 1820 (0.55%)	1 / 608 (0.16%)
occurrences (all)	10	1
Musculoskeletal stiffness		
subjects affected / exposed	6 / 1820 (0.33%)	3 / 608 (0.49%)
occurrences (all)	6	3
Joint swelling		
subjects affected / exposed	7 / 1820 (0.38%)	1 / 608 (0.16%)
occurrences (all)	7	1
Tendonitis		
subjects affected / exposed	11 / 1820 (0.60%)	2 / 608 (0.33%)
occurrences (all)	11	2
Musculoskeletal discomfort		
subjects affected / exposed	5 / 1820 (0.27%)	0 / 608 (0.00%)
occurrences (all)	5	0
Osteoarthritis		
subjects affected / exposed	7 / 1820 (0.38%)	0 / 608 (0.00%)
occurrences (all)	7	0
Spinal osteoarthritis		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Arthritis		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
Bone pain		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Coccydynia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Gouty arthritis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Groin pain		

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Intervertebral disc degeneration		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Muscular weakness		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Osteopenia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Pain in jaw		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Rheumatoid arthritis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Sensation of heaviness		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Torticollis		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Intervertebral disc protrusion		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Plantar fasciitis		
subjects affected / exposed	0 / 1820 (0.00%)	3 / 608 (0.49%)
occurrences (all)	0	3
Temporomandibular joint syndrome		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Tenosynovitis		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Cervical spinal stenosis		

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Chondropathy		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Costochondritis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Exostosis		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Flank pain		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Joint range of motion decreased		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Pseudarthrosis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Synovial cyst		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Systemic lupus erythematosus		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Toe deformity		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Fibromyalgia		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Joint stiffness		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Mixed connective tissue disease		

subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
myopathy steroid subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Neck mass subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Scleroderma subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	304 / 1820 (16.70%) 304	100 / 608 (16.45%) 100	
Sinusitis subjects affected / exposed occurrences (all)	59 / 1820 (3.24%) 59	22 / 608 (3.62%) 22	
Gastrointestinal infection subjects affected / exposed occurrences (all)	31 / 1820 (1.70%) 31	7 / 608 (1.15%) 7	
Urinary tract infection subjects affected / exposed occurrences (all)	29 / 1820 (1.59%) 29	13 / 608 (2.14%) 13	
Bronchitis subjects affected / exposed occurrences (all)	46 / 1820 (2.53%) 46	13 / 608 (2.14%) 13	
Upper respiratory tract infection subjects affected / exposed occurrences (all)	34 / 1820 (1.87%) 34	19 / 608 (3.13%) 19	
Vaginal infection subjects affected / exposed occurrences (all)	23 / 1820 (1.26%) 23	4 / 608 (0.66%) 4	
Pharyngitis			

subjects affected / exposed occurrences (all)	23 / 1820 (1.26%) 23	8 / 608 (1.32%) 8
Rhinitis		
subjects affected / exposed occurrences (all)	19 / 1820 (1.04%) 19	7 / 608 (1.15%) 7
Tooth infection		
subjects affected / exposed occurrences (all)	17 / 1820 (0.93%) 17	2 / 608 (0.33%) 2
Herpes virus infection		
subjects affected / exposed occurrences (all)	13 / 1820 (0.71%) 13	1 / 608 (0.16%) 1
Influenza		
subjects affected / exposed occurrences (all)	11 / 1820 (0.60%) 11	4 / 608 (0.66%) 4
Lower respiratory tract infection		
subjects affected / exposed occurrences (all)	9 / 1820 (0.49%) 9	4 / 608 (0.66%) 4
Tonsillitis		
subjects affected / exposed occurrences (all)	11 / 1820 (0.60%) 11	4 / 608 (0.66%) 4
Ear infection		
subjects affected / exposed occurrences (all)	7 / 1820 (0.38%) 7	4 / 608 (0.66%) 4
Fungal infection		
subjects affected / exposed occurrences (all)	12 / 1820 (0.66%) 12	4 / 608 (0.66%) 4
Pneumonia		
subjects affected / exposed occurrences (all)	7 / 1820 (0.38%) 7	3 / 608 (0.49%) 3
Laryngitis		
subjects affected / exposed occurrences (all)	4 / 1820 (0.22%) 4	2 / 608 (0.33%) 2
Respiratory tract infection		
subjects affected / exposed occurrences (all)	11 / 1820 (0.60%) 11	1 / 608 (0.16%) 1
Eye infection		

subjects affected / exposed	5 / 1820 (0.27%)	1 / 608 (0.16%)
occurrences (all)	5	1
Localised infection		
subjects affected / exposed	5 / 1820 (0.27%)	2 / 608 (0.33%)
occurrences (all)	5	2
Abscess limb		
subjects affected / exposed	1 / 1820 (0.05%)	1 / 608 (0.16%)
occurrences (all)	1	1
Anal infection		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Arthritis infective		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Balanitis candida		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Cellulitis		
subjects affected / exposed	8 / 1820 (0.44%)	1 / 608 (0.16%)
occurrences (all)	8	1
Cystitis		
subjects affected / exposed	9 / 1820 (0.49%)	5 / 608 (0.82%)
occurrences (all)	9	5
Erysipelas		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Eyelid infection		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Folliculitis		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Furuncle		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
gingival infection		

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Herpes zoster		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Pyelonephritis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Rash pustular		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Skin infection		
subjects affected / exposed	2 / 1820 (0.11%)	1 / 608 (0.16%)
occurrences (all)	2	1
Subcutaneous abscess		
subjects affected / exposed	3 / 1820 (0.16%)	1 / 608 (0.16%)
occurrences (all)	3	1
Tinea pedis		
subjects affected / exposed	1 / 1820 (0.05%)	2 / 608 (0.33%)
occurrences (all)	1	2
Viral infection		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
adnexitis		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Chronic sinusitis		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Clostridial infection		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Groin abscess		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Impetigo		

subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Pilonidal cyst		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Wound infection		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Hand fracture		
subjects affected / exposed	2 / 1820 (0.11%)	2 / 608 (0.33%)
occurrences (all)	2	2
Onychomycosis		
subjects affected / exposed	4 / 1820 (0.22%)	0 / 608 (0.00%)
occurrences (all)	4	0
Anogenital warts		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Oral candidiasis		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Kidney infection		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Scarlet fever		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Acute tonsillitis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Borrelia infection		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Chlamydial infection		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Erythema migrans		

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Gingival abscess		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Infected cyst		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Infected insect bite		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Mastitis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Meningitis bacterial		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Paronychia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Peritonsillar abscess		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Pyoderma		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Sinusitis fungal		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Streptococcal infection		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Tracheobronchitis		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Urosepsis		

subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
West Nile viral infection subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Genital herpes subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Infected skin ulcer subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Liver abscess subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Septic shock subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Tinea cruris subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	2 / 608 (0.33%) 2	
Tracheitis subjects affected / exposed occurrences (all)	0 / 1820 (0.00%) 0	1 / 608 (0.16%) 1	
Metabolism and nutrition disorders			
Dyslipidaemia subjects affected / exposed occurrences (all)	5 / 1820 (0.27%) 5	3 / 608 (0.49%) 3	
Diabetes mellitus subjects affected / exposed occurrences (all)	1 / 1820 (0.05%) 1	0 / 608 (0.00%) 0	
Diabetes mellitus non-insulin- dependent subjects affected / exposed occurrences (all)	2 / 1820 (0.11%) 2	1 / 608 (0.16%) 1	
Glucose tolerance impaired			

subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Gout		
subjects affected / exposed	3 / 1820 (0.16%)	0 / 608 (0.00%)
occurrences (all)	3	0
Iron deficiency		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Hypercholesterolaemia		
subjects affected / exposed	3 / 1820 (0.16%)	2 / 608 (0.33%)
occurrences (all)	3	2
Hypertriglyceridaemia		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Polydipsia		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Hyperuricaemia		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Vitamin B12 deficiency		
subjects affected / exposed	2 / 1820 (0.11%)	0 / 608 (0.00%)
occurrences (all)	2	0
Anorexia		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Underweight		
subjects affected / exposed	1 / 1820 (0.05%)	0 / 608 (0.00%)
occurrences (all)	1	0
Impaired fasting glucose		
subjects affected / exposed	0 / 1820 (0.00%)	2 / 608 (0.33%)
occurrences (all)	0	2
Overweight		
subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)
occurrences (all)	0	1
Vitamin C deficiency		

subjects affected / exposed	0 / 1820 (0.00%)	1 / 608 (0.16%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 February 2007	Amendment 1 <ul style="list-style-type: none">• Differentiated efficacy and safety objectives and defined a safety endpoint• Provided guidance on administration and follow-up for additional dosing with Engerix-B• Increased the sample size• Adjusted the age range to 18 - 55 years for the United States and Germany• Clarified the statistical tests for the efficacy description
29 May 2007	Amendment 2: <ul style="list-style-type: none">• Added a EudraCT number• Removed the United States as a participating country• Provided additional details regarding stopping rules and the handling of confidential subject information
04 February 2008	Amendment 3: <ul style="list-style-type: none">• Increased the sample size• Updated and clarified the statistical considerations, comparisons, and determination of sample size• Clarified the severity grading of AEs
08 May 2008	Amendment 4: <ul style="list-style-type: none">• Changed the anti-HBsAg testing assay from AUSAB AxSYM to the Hep B Eci assay
03 October 2008	Amendment 5: <ul style="list-style-type: none">• Updated and clarified the objectives, statistical considerations, comparisons, and determination of sample size• Defined the end of the trial as the database lock for the study, which was selected due to the delay resulting from the change in the anti-HBsAg assay

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported