Clinical trial results:
Efficacy and safety of Eslicarbazepine Acetate (BIA 2 093) as adjunctive therapy for refractory partial seizures in children: a double-blind, randomised, placebo-controlled, parallel-group, multicentre clinical trial

Summary

EudraCT number	2007-001887-55
Trial protocol	PT HU CZ AT FR SK IT ES GB DE
Global end of trial date	24 August 2017

Results information

Result version number	v3 (current)
This version publication date	11 March 2018
First version publication date	07 August 2015
Version creation reason	
Summary attachment (see zip file)	BIA-2093-305_Synopsis_part I-II (BIA-2093-305_Synopsis_part I-II.pdf) BIA-2093-305_Synopsis_part III-V (BIA-2093-305_Synopsis_part III-V.pdf) BIA-2093-305_Synopsis Part III- V final (BIA-2093-305 Part III- V final _Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	BIA-2093-305

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00988156
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BIAL - Portela & CA, S.A.
Sponsor organisation address	À Av. Siderurgia Nacional, Coronado, Portugal, 4745-457
Public contact	André Garrido, BIAL - Portela & Cª, S.A., 00351 229866100, andre.garrido@bial.com
Scientific contact	Helena Gama, BIAL - Portela & Cª, S.A., 00351 229866100, helena.gama@bial.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000696-PIP02-10
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No	Yes

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 February 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2012
Global end of trial reached?	Yes
Global end of trial date	24 August 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary: The primary objective of the study is to assess the efficacy of Eslicarbazepine Acetate as adjunctive therapy in children and adolescents with refractory partial seizures.
The primary analysis variables for the assessment of efficacy will be:
1. the responder rate, defined as the proportion of patients with at least a 50% decrease in the standardised seizure frequency
2. the relative reduction in the standardised seizure frequency

Protection of trial subjects:

The trial was conducted in accordance with the International Conference on Harmonisation (ICH), Good Clinical Practices (GCP), Good Manufacturing Practice (GMP), the ethical principles of the Declaration of Helsinki and with applicable local regulations. This trial was conducted by qualified persons who respected the rights and welfare of the subjects and after the review and approval of the protocol by an EC. Adverse events were collected throughout the trial and subject was followed by 4 weeks after last treatment visit in the double blind phase and 4 weeks after last treatment visit in the open blind phase.

Background therapy:

Concomitant AED therapy (1 or 2 AEDs).

Evidence for comparator: -

Actual start date of recruitment	07 December 2007
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	Austria: 3
Country: Number of subjects enrolled	Bosnia and Herzegovina: 4
Country: Number of subjects enrolled	Czech Republic: 31
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Hungary: 38
Country: Number of subjects enrolled	Italy: 12

Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Philippines: 17
Country: Number of subjects enrolled	Poland: 22
Country: Number of subjects enrolled	Portugal: 8
Country: Number of subjects enrolled	Romania: 4
Country: Number of subjects enrolled	Russian Federation: 20
Country: Number of subjects enrolled	Serbia: 37
Country: Number of subjects enrolled	Slovakia: 15
Country: Number of subjects enrolled	Ukraine: 63
Worldwide total number of subjects	304
EEA total number of subjects	160

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)	207
Adolescents (12-17 years)	96
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The patient recruitment period will last approximately 66 months. The actual overall study duration or patient recruitment period may vary.

Pre-assignment

Screening details:

Subjects who met all the inclusion criteria and none of the exclusion criteria. 370 subjects were enrolled to the trial and 66 subjects were screening failures including 5 IMP recalls and 41 randomised subjects were IMP recall.

Pre-assignment period milestones

Number of subjects started	370[1]
Number of subjects completed	263

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Adverse event, non-fatal: 2
Reason: Number of subjects	Consent withdrawn by subject: 3
Reason: Number of subjects	Physician decision: 1
Reason: Number of subjects	Ineligibility: 44
Reason: Number of subjects	Treatment with > 2 conc. AEDs at the same time: 5
Reason: Number of subjects	IMP recall: 46
Reason: Number of subjects	Sponsor decision: 6

Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects reported to have started the pre-assignment period is the number of enrolled subjects; The worldwide number of subjects enrolled in the trial is number of randomised subjects.

Period 1

Period 1 title	PART I: DOUBLE-BLIND TREATMENT
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Part I - Placebo

Arm description:

Patients aged 2–6 years will receive the study treatment as 50 mg/mL placebo oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg placebo tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily.

Titration period:
First 2 weeks: 10 mg/kg/day;
Next 4 weeks: 20 mg/kg/day (maximum 1200 mg/day) (if no AE occurred), 10 mg/kg/day (if AE occurred);
Maintenance period:
Next 12 weeks: 20 mg/kg/day (if acceptable tolerability), 30 mg/kg/day (maximum 1200 mg/day) (if unsatisfactory response), 10 mg/kg/day (if during the previous period will receive this dose)
Tapering-off \follow-up period:
After the 12-week maintenance period, the study treatment will be tapered off in 10 mg/kg/day steps every 2 weeks, followed by a 4 week observational follow-up period.

Arm title	Part I - ESL

Arm description:

Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.

Arm type	Active comparator
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily.

Titration period:
First 2 weeks: 10 mg/kg/day;
Next 4 weeks: 20 mg/kg/day (maximum 1200 mg/day) (if no AE occurred), 10 mg/kg/day (if AE occurred);
Maintenance period:
Next 12 weeks: 20 mg/kg/day (if acceptable tolerability), 30 mg/kg/day (maximum 1200 mg/day) (if unsatisfactory response), 10 mg/kg/day (if during the previous period will receive this dose)
Tapering-off \follow-up period:
After the 12-week maintenance period, the study treatment will be tapered off in 10 mg/kg/day steps every 2 weeks, followed by a 4 week observational follow-up period.

Number of subjects in period 1[2]	Part I - Placebo	Part I - ESL
Started	129	134
Completed	118	120
Not completed	11	14
Adverse event, serious fatal	1	1
Consent withdrawn by subject	5	5
Physician decision	2	2
Adverse event, non-fatal	1	2
Other reason	1	-
Adverse event, serious non-fatal	-	2

Not serious AE and lack of efficacy	-	1
Treatment with > 2 conc. AEDs at the same time	-	1
Lack of efficacy	1	-

Notes:

[2] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline period does not include 41 subjects with IMP recall.

Period 2

Period 2 title	PART II: OPEN-LABEL EXTENSION PERIOD
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part II - ESL

Arm description:

Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.

Arm type	Active comparator
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily.
The starting dose will be 10 mg/kg/day or 800 mg/day for patients with high body weight. The daily dose will be titrated by the investigator according to clinical response in the dose range from 10 mg/kg/day to 30 mg/kg/day (or 800 mg/day to maximum 1200 mg/day for patients with high body weight). Down-titration will be allowed during Part II according to clinical response or in case of intolerable AEs.

Number of subjects in period 2[3]	Part II - ESL
Started	226
Completed	163
Not completed	63
Consent withdrawn by subject	16
Physician decision	3
Adverse event, non-fatal	6
At the specific request of the sponsor	2

Other reason	3
Adverse event, serious non-fatal	3
Lack of efficacy	30

Notes:

[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Number of subjects 238 completed double blind part and 12 of them did not start open label part.

Period 3

Period 3 title	PART III-V: OPEN-LABEL EXTENSION PERIOD
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Part III - V - ESL

Arm description:

Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.

Arm type	Active comparator
Investigational medicinal product name	Eslicarbazepine acetate
Investigational medicinal product code	BIA 2093
Other name	Zebinix
Pharmaceutical forms	Tablet, Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Part III starting dose will be the same dose of Eslicarbazepine Acetate that patient was receiving at the end of the Part II, unless investigator decides to titrate this dose to achieve further reduction in seizure frequency or due to the occurrence of any intolerable AEs. Eslicarbazepine Acetate dose titration schema during this study extension (Part III) will be the same defined for study Part II. The daily dose will be titrated by the investigator according to clinical response in the dose range from 10 mg/kg/day to 30 mg/kg/day (or 800 mg/day to maximum 1200 mg/day for patients with high body weight). The maximum Eslicarbazepine Acetate dosage will be 1200 mg once daily. Down-titration will be allowed during Part III according to clinical response or in case of intolerable AEs.
The same dosage will be applied in the Part IV and Part V as in the Part III.

Number of subjects in period 3[4]	Part III - V - ESL
Started	152
Completed	14
Not completed	138
Adverse event, serious fatal	2
Consent withdrawn by subject	13
Physician decision	1

Switched to Zebinix	3
Discontinued after Part III	13
At the specific request of the sponsor	82
Other reason	4
Lost to follow-up	4
Discontinued after Part IV	6
Lack of efficacy	10

Notes:

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

Justification: Number of subjects 183 completed Part II and 31 of them did not start Part III-V.

Baseline characteristics

Reporting groups	
Reporting group title	Part I - Placebo
Reporting group description:	
Patients aged 2–6 years will receive the study treatment as 50 mg/mL placebo oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg placebo tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.	
Reporting group title	Part I - ESL
Reporting group description:	
Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.	

Reporting group values	Part I - Placebo	Part I - ESL	Total
Number of subjects	129	134	263
Age Categorical			
Age Categorical Characteristic			
Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days – 23months)	0	0	0
Children (2-11 years)	84	82	166
Adolescents (12-17 year)	45	51	96
From 18 - 64 years	0	1	1
From 65 – 84 years	0	0	0
Over 85 years	0	0	0
Age Continuous			
Age Continuous Characteristic			
Units: Years			
arithmetic mean	9.5	9.9	
standard deviation	± 3.85	± 4.22	-
Gender Categorical			
Gender Categorical Characteristic			
Units: Subjects			
Female	67	70	137
Male	62	64	126

End points

End points reporting groups

Reporting group title	Part I - Placebo
Reporting group description:	
Patients aged 2–6 years will receive the study treatment as 50 mg/mL placebo oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg placebo tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.	
Reporting group title	Part I - ESL
Reporting group description:	
Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.	
Reporting group title	Part II - ESL
Reporting group description:	
Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.	
Reporting group title	Part III - V - ESL
Reporting group description:	
Patients aged 2–6 years will receive the study treatment as 50 mg/mL Eslicarbazepine Acetate oral suspension. Patients aged 7 or over will receive the study treatment in the form of 200 mg Eslicarbazepine Acetate tablets. The study treatment should be administered once daily, preferably at the same time of the day. The maximum absolute dosage will be 1200 mg once daily. Subjects without IMP recall.	
Subject analysis set title	Part I - Placebo x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least one dose of double-blind study treatment excluding those stratum I patients who were randomised before the IMP recall	
Subject analysis set title	Part I - ESL x Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All patients who received at least one dose of double-blind study treatment excluding those stratum I patients who were randomised before the IMP recall	
Subject analysis set title	Part I - Placebo x Intent-to-treat Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised, treated with at least one dose of study medication after randomisation, and with at least one post-baseline seizure frequency assessment excluding those stratum I patients who were randomised before the IMP recall	
Subject analysis set title	Part I - ESL x Intent-to-treat Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All patients randomised, treated with at least one dose of study medication after randomisation, and with at least one post-baseline seizure frequency assessment excluding those stratum I patients who were randomised before the IMP recall	
Subject analysis set title	Part I - Placebo x Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All patients of the ITT without any major protocol deviations	
Subject analysis set title	Part I - ESL x Per Protocol Set

Subject analysis set type	Per protocol

Subject analysis set description:

All patients of the ITT without any major protocol deviations

Subject analysis set title	Part II - ESL x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients entering Part II who received at least one dose of Eslicarbazepine Acetate during the open-label extension period excluding stratum I patients randomised before the IMP recall irrespective of treatment with suspension or tablets in Part II

Subject analysis set title	Part II - ESL x Intent-to-treat Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients entering Part II, treated with at least one dose of Eslicarbazepine Acetate during the open-label extension period, and with at least one seizure frequency assessment during the extension period excluding stratum I patients randomised before the IMP recall irrespective of treatment with suspension or tablets in Part II

Subject analysis set title	Part III-V - ESL x Safety Set
Subject analysis set type	Safety analysis

Subject analysis set description:

All patients entering Part III – V, treated with at least one dose of Eslicarbazepine Acetate during the open-label extension period (Part III – V)

Subject analysis set title	Part III-V - ESL x Intent-to-treat Set
Subject analysis set type	Intention-to-treat

Subject analysis set description:

All patients entering Part III – V, treated with at least one dose of Eslicarbazepine Acetate during the open-label extension period (Part III – V), and with at least one seizure frequency assessment during the extension period (Part III – V)

Primary: Responder rate in the Part I

End point title	Responder rate in the Part I

End point description:

Responder rate defined as the number of patients with at least a 50% decrease in the standardised 4-week seizure frequency from the baseline period to the 12-week maintenance period

End point type	Primary

End point timeframe:

Baseline up to Visit 7 in the Part I

End point values	Part I - Placebo x Intent-to-treat Set	Part I - ESL x Intent-to-treat Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	129	134		
Units: Participants				
number (not applicable)				
Participants	40	41		

Statistical analyses

Statistical analysis title	Cochran—Mantel—Haenszel—test strat. by age stratum

Statistical analysis description:

The responder rate during the 12-week maintenance period were analysed by a Cochran-Mantel-Haenszel (CMH) test with age stratum as stratification factor.

Comparison groups	Part I - ESL x Intent-to-treat Set v Part I - Placebo x Intent-to-treat Set
Number of subjects included in analysis	263
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.9017
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.63

Primary: Relative Reduction From Baseline in Seizure Frequency in the Part I

End point title	Relative Reduction From Baseline in Seizure Frequency in the Part I

End point description:

Relative reduction in the standardised 4-week seizure frequency from the baseline period to the 12-week maintenance period

End point type	Primary

End point timeframe:

Baseline up to Visit 7 in the Part I

End point values	Part I - Placebo x Intent-to-treat Set	Part I - ESL x Intent-to-treat Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	129	134		
Units: Seizures				
least squares mean (standard error)				
Seizures	-8.6 (± 5.93)	-18.100000000		

Statistical analyses

Statistical analysis title	ANCOVA model for comparison

Statistical analysis description:

ANCOVA model with treatment and stratum group as fixed effects and baseline seizure frequency as a covariate.

Comparison groups	Part I - Placebo x Intent-to-treat Set v Part I - ESL x Intent-

	to-treat Set
Number of subjects included in analysis	263
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.249
Method	ANCOVA
Parameter estimate	LS mean
Point estimate	9.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.71
upper limit	25.77
Variability estimate	Standard error of the mean
Dispersion value	8.25

Primary: Relative Change From Baseline in Seizure Frequency in the Part I

End point title	Relative Change From Baseline in Seizure Frequency in the Part I[1]

End point description:

Relative change in the standardised 4-week seizure frequency from the baseline period to the 12-week maintenance period

End point type	Primary

End point timeframe:

Baseline up to Visit 7 in the Part I

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 statistical analyses have been performed for this primary end point.

End point values	Part I - Placebo x Intent-to-treat Set	Part I - ESL x Intent-to-treat Set		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	129	134		
Units: Seizures				
arithmetic mean (standard deviation)				
Seizures	-9.6 (± 70.1500000000)	-19.2 (± 64.1000000000)		

Statistical analyses

No statistical analyses for this end point

Primary: Responder rate in the Part II

End point title	Responder rate in the Part II[2]

End point description:

Responder rate defined as the number of patients with at least a 50% decrease in the standardised 4-

week seizure frequency

End point type	Primary

End point timeframe:

Baseline till the end of Part II

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 statistical analyses have been performed for this primary end point.

End point values	Part II - ESL x Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	225			
Units: Participants				
number (not applicable)				
Participants	105			

Statistical analyses

No statistical analyses for this end point

Primary: Relative Change From Baseline in Seizure Frequency in the Part II

End point title	Relative Change From Baseline in Seizure Frequency in the Part II[3]

End point description:

Relative change in the standardised 4-week seizure frequency

End point type	Primary

End point timeframe:

Baseline till the end of Part II

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 statistical analyses have been performed for this primary end point.

End point values	Part II - ESL x Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	225			
Units: Seizures				
arithmetic mean (standard deviation)				
Seizures	-33.9 (± 58.65)			

Statistical analyses

No statistical analyses for this end point

Primary: Responder rate in the Part III-V

End point title	Responder rate in the Part III-V[4]

End point description:

Responder rate defined as the number of patients with at least a 50% decrease in the standardised 4-week seizure frequency

End point type	Primary

End point timeframe:

Baseline till the end of Part III-V

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 statistical analyses have been performed for this primary end point.

End point values	Part III-V - ESL x Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	148			
Units: Participants				
number (not applicable)				
Participants	104			

Statistical analyses

No statistical analyses for this end point

Primary: Relative Change From Baseline in Seizure Frequency in the Part III

End point title	Relative Change From Baseline in Seizure Frequency in the Part III[5]

End point description:

Relative change in the standardised 4-week seizure frequency

End point type	Primary

End point timeframe:

Baseline till the end of Part III

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 statistical analyses have been performed for this primary end point.

End point values	Part III-V - ESL x Intent-to-treat Set			
Subject group type	Subject analysis set			
Number of subjects analysed	148			
Units: Seizures				
arithmetic mean (standard deviation)				
Seizures	-59.3 (± 50.37)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first study treatment up to 28 days after the last dose of study medication in the corresponding part.

Adverse event reporting additional description:

Part I: up to the date of visit FU1 for patients continuing if the visit occurs within these 28 days
Part II: up to 28 days after the last dose of IMP for patients discontinuing treatment during Part II or the date of Visit OL6 for patients continuing with treatment in Part III of the study
Part III-V: up to 28 days after the last dose of IMP

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Part I - Placebo x Safety Set

Reporting group description:

Subjects in the Safety Set treated with placebo during Part I

Reporting group title	Part I - ESL x Safety Set

Reporting group description:

Subjects in the Safety Set treated with ESL during Part I

Reporting group title	Part II - ESL x Safety Set

Reporting group description:

Subjects in the Safety Set treated with ESL during Part II

Reporting group title	Part III-V - ESL x Safety Set

Reporting group description:

Subjects in the Safety Set treated with ESL during Part III - V

Serious adverse events	Part I - Placebo x Safety Set	Part I - ESL x Safety Set	Part II - ESL x Safety Set
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 129 (6.98%)	15 / 134 (11.19%)	23 / 226 (10.18%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Medical device change			

subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (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
General disorders and administration site conditions			
Device malfunction			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug withdrawal syndrome			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (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
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Epistaxis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Conduct disorder			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (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
Concussion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Head injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Joint dislocation			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain oedema			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (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
Convulsion			
subjects affected / exposed	2 / 129 (1.55%)	2 / 134 (1.49%)	6 / 226 (2.65%)
occurrences causally related to treatment / all	1 / 2	0 / 2	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dysarthria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Grand mal convulsion			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			

subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (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
Hypotonia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nystagmus			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures with secondary generalisation			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 129 (0.00%)	3 / 134 (2.24%)	2 / 226 (0.88%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Ear and labyrinth disorders			
Otosalpingitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Eye disorders			
Diplopia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal hernia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Coeliac disease			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (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
Colitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash vesicular			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
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 purpura			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
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			
Abdominal wall abscess			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Abscess neck			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Bronchopneumonia			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dengue fever			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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

Gastroenteritis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Infectious mononucleosis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (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
Lobar pneumonia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung abscess			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (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
Pharyngitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	3 / 129 (2.33%)	1 / 134 (0.75%)	4 / 226 (1.77%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicella			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part III-V - ESL x Safety Set		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 152 (12.50%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Medical device change			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Device malfunction			

subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Drug withdrawal syndrome				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Irritability				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asphyxia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Conduct disorder				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Aspartate aminotransferase increased				

subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Brain herniation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Brain oedema			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Dysarthria			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Grand mal convulsion			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hydrocephalus			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nystagmus			

subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Partial seizures with secondary generalisation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Ear and labyrinth disorders			
Otosalpingitis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal hernia			

subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coeliac disease				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Rash vesicular				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urticaria				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular purpura				

subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteochondrosis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abdominal wall abscess			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abscess neck			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Dengue fever			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Infectious mononucleosis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lobar pneumonia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lung abscess			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pharyngitis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 152 (2.63%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part I - Placebo x Safety Set	Part I - ESL x Safety Set	Part II - ESL x Safety Set
Total subjects affected by non-serious adverse events			
subjects affected / exposed	92 / 129 (71.32%)	108 / 134 (80.60%)	172 / 226 (76.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oral papilloma			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Pyogenic granuloma			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Sebaceous adenoma			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Skin papilloma			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	2	0	0
Hypertension			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Phlebitis			

subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Systolic hypertension			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Brain operation			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Plastic surgery to the face			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Suture insertion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Tenotomy			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Tooth extraction			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	3 / 226 (1.33%)
occurrences (all)	0	2	3
Chest pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Device malfunction			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Face oedema			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	3 / 129 (2.33%)	5 / 134 (3.73%)	6 / 226 (2.65%)
occurrences (all)	3	7	6
Feeling hot			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Gait disturbance			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	4 / 226 (1.77%)
occurrences (all)	0	2	4
Hyperthermia			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	2 / 226 (0.88%)
occurrences (all)	1	2	2
Irritability			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	4 / 226 (1.77%)
occurrences (all)	1	2	4
Malaise			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	2	2
Oedema			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	7 / 129 (5.43%)	10 / 134 (7.46%)	20 / 226 (8.85%)
occurrences (all)	13	14	27
Sluggishness			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Thirst			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			

Allergy to arthropod bite			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Drug hypersensitivity			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Hypersensitivity			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	3 / 226 (1.33%)
occurrences (all)	0	1	3
Immunodeficiency			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Seasonal allergy			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences (all)	0	2	2
Social circumstances			
Learning disability			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Epididymal cyst			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Labia enlarged			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Menstruation irregular			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Pelvic pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Polycystic ovaries			

subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Vaginal discharge			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 129 (0.00%)	3 / 134 (2.24%)	1 / 226 (0.44%)
occurrences (all)	0	6	3
Bronchospasm			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	4 / 129 (3.10%)	2 / 134 (1.49%)	6 / 226 (2.65%)
occurrences (all)	4	3	8
Epistaxis			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	3 / 226 (1.33%)
occurrences (all)	1	1	3
Laryngospasm			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	3	3
Nasal discomfort			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Nasal obstruction			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Nasal septum deviation			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 129 (0.78%)	3 / 134 (2.24%)	4 / 226 (1.77%)
occurrences (all)	1	3	5
Respiratory disorder			

subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	2 / 226 (0.88%)
occurrences (all)	0	3	2
Rhinitis allergic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	2 / 129 (1.55%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	3	0	3
Tonsillar hypertrophy			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Tonsillar inflammation			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Vasomotor rhinitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	3 / 226 (1.33%)
occurrences (all)	1	2	3
Affect lability			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Agitation			
subjects affected / exposed	1 / 129 (0.78%)	5 / 134 (3.73%)	1 / 226 (0.44%)
occurrences (all)	1	5	1
Anxiety			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Apathy			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Attention deficit/Hyperactivity disorder			

subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Bradyphrenia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Bruxism			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Disorientation			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Dyslogia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Dysthymic disorder			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Emotional distress			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Encopresis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Inappropriate affect			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	2	0
Initial insomnia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Insomnia			

subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences (all)	1	4	1
Listless			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Mood altered			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Mood swings			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences (all)	0	2	1
Nervousness			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Panic attack			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Restlessness			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	1	2	0
Sleep disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Sleep talking			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Somatoform disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Biliary dyskinesia			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	1	0	2

Hepatic cyst			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Blood bicarbonate decreased			
subjects affected / exposed	2 / 129 (1.55%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	2	0	0
Blood calcium decreased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 129 (1.55%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences (all)	2	2	1
Blood glucose decreased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	2 / 226 (0.88%)
occurrences (all)	1	2	2

Blood triglycerides increased			
subjects affected / exposed	2 / 129 (1.55%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	2	0	1
Body temperature increased			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	1	1	0
Breath sounds abnormal			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Ecg p wave inverted			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Electrocardiogram pr shortened			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram pr prolongation			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Electrocardiogram qrs complex prolonged			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Electrocardiogram repolarisation abnormality			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Eosinophil count increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	7 / 226 (3.10%)
occurrences (all)	1	1	7
Haemoglobin decreased			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Platelet count decreased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Platelet count increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Positive rombergism			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	3 / 226 (1.33%)
occurrences (all)	1	1	4
Rheumatoid factor increased			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Thyroxine decreased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Thyroxine increased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Transaminases increased			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	2
Weight decreased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	2 / 129 (1.55%)	5 / 134 (3.73%)	3 / 226 (1.33%)
occurrences (all)	2	5	3
White blood cell count increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural			

complications			
Arthropod bite			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Clavicle fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Concussion			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Contusion			
subjects affected / exposed	1 / 129 (0.78%)	3 / 134 (2.24%)	0 / 226 (0.00%)
occurrences (all)	1	3	0
Drug toxicity			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Excoriation			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	3 / 226 (1.33%)
occurrences (all)	2	1	3
Face injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	3
Fall			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	3 / 226 (1.33%)
occurrences (all)	1	0	7
Foot fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Forearm fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Hand fracture			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	1	1	0
Head injury			

subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	4 / 226 (1.77%)
occurrences (all)	1	2	4
Injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Joint injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Laceration			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences (all)	0	2	1
Lip injury			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Overdose			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Poisoning			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Radius fracture			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Skin injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Soft tissue injury			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Thermal burn			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Tibia fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Tooth injury			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Toxicity to various agents			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Traumatic haematoma			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Upper limb fracture			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Wound			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Wrist fracture			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Phimosis			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Bradyarrhythmia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Bundle branch block right			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	2	1
Tricuspid valve incompetence			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Wolff-parkinson-white syndrome			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 129 (0.78%)	3 / 134 (2.24%)	2 / 226 (0.88%)
occurrences (all)	1	4	2
Balance disorder			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Cerebellar ataxia			
subjects affected / exposed	1 / 129 (0.78%)	3 / 134 (2.24%)	3 / 226 (1.33%)
occurrences (all)	1	3	3
Cerebrovascular disorder			

subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Circadian rhythm sleep disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Convulsion			
subjects affected / exposed	13 / 129 (10.08%)	11 / 134 (8.21%)	29 / 226 (12.83%)
occurrences (all)	18	15	47
Coordination abnormal			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Depressed level of consciousness			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	2 / 129 (1.55%)	5 / 134 (3.73%)	6 / 226 (2.65%)
occurrences (all)	2	5	10
Epilepsy			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	1	0	2
Head titubation			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	8 / 129 (6.20%)	18 / 134 (13.43%)	20 / 226 (8.85%)
occurrences (all)	14	22	26
Hypotonia			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	2 / 226 (0.88%)
occurrences (all)	1	1	2
Intention tremor			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	1	1	1
Intracranial haematoma			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Memory impairment			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Mental impairment			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Migraine			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Nystagmus			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	3 / 226 (1.33%)
occurrences (all)	0	1	3
Paraesthesia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Partial seizures with secondary generalisation			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Poor quality sleep			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Postictal headache			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Postictal state			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Psychomotor hyperactivity			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	1	1	1

Somnolence			
subjects affected / exposed	6 / 129 (4.65%)	15 / 134 (11.19%)	20 / 226 (8.85%)
occurrences (all)	8	16	25
Speech disorder			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Status epilepticus			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Tremor			
subjects affected / exposed	2 / 129 (1.55%)	2 / 134 (1.49%)	3 / 226 (1.33%)
occurrences (all)	2	2	3
Unresponsive to stimuli			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	1	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Leukopenia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Lymphadenopathy			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	0 / 226 (0.00%)
occurrences (all)	0	2	0
Neutropenia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Pancytopenia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Thrombocytopenia			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Tympanic membrane perforation			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 129 (0.00%)	5 / 134 (3.73%)	5 / 226 (2.21%)
occurrences (all)	0	11	9
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Astigmatism			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Chalazion			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	2 / 129 (1.55%)	8 / 134 (5.97%)	12 / 226 (5.31%)
occurrences (all)	2	12	14
Eye pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Eye swelling			

subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Lacrimation increased			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Optic atrophy			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Visual impairment			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	4 / 129 (3.10%)	3 / 134 (2.24%)	6 / 226 (2.65%)
occurrences (all)	7	4	8
Abdominal pain upper			
subjects affected / exposed	0 / 129 (0.00%)	4 / 134 (2.99%)	3 / 226 (1.33%)
occurrences (all)	0	4	4
Aphthous stomatitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Constipation			
subjects affected / exposed	2 / 129 (1.55%)	3 / 134 (2.24%)	1 / 226 (0.44%)
occurrences (all)	2	3	6
Dental caries			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	3 / 129 (2.33%)	1 / 134 (0.75%)	4 / 226 (1.77%)
occurrences (all)	3	1	4

Dyspepsia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Enterocolitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Food poisoning			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	1	1	0
Frequent bowel movements			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Gastritis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Gastroduodenitis			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	1	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Gingival bleeding			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	2	0	0

Irritable bowel syndrome			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Lip dry			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Mouth ulceration			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	1 / 129 (0.78%)	7 / 134 (5.22%)	5 / 226 (2.21%)
occurrences (all)	1	9	7
Odynophagia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Pancreatic disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Periodontitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Peritonitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Rectal fissure			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	3 / 226 (1.33%)
occurrences (all)	0	1	3

Stomatitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Tooth disorder			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	1	1	0
Vomiting			
subjects affected / exposed	8 / 129 (6.20%)	8 / 134 (5.97%)	21 / 226 (9.29%)
occurrences (all)	9	11	32
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	1
Alopecia			
subjects affected / exposed	2 / 129 (1.55%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	2	0	1
Dermatitis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	2 / 129 (1.55%)	2 / 134 (1.49%)	2 / 226 (0.88%)
occurrences (all)	3	2	2
Dermatitis atopic			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	10
Dermatitis contact			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	2 / 226 (0.88%)
occurrences (all)	0	1	2
Dermatitis diaper			

subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Heat rash			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Ingrowing nail			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Onychomadesis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Papule			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Pityriasis rosea			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Rash			
subjects affected / exposed	4 / 129 (3.10%)	2 / 134 (1.49%)	3 / 226 (1.33%)
occurrences (all)	5	2	3
Rash erythematous			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Skin exfoliation			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Solar dermatitis			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Urticaria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Enuresis			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	0 / 226 (0.00%)
occurrences (all)	0	2	0
Haematuria			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Incontinence			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Leukocyturia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Nephropathy			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Nocturia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Renal failure acute			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0

Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	2 / 226 (0.88%)
occurrences (all)	0	1	2
Hypothalamo-pituitary disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	2 / 226 (0.88%)
occurrences (all)	0	2	2
Precocious puberty			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Ankle deformity			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	0 / 226 (0.00%)
occurrences (all)	1	2	0
Arthritis reactive			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Back pain			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	1	0	3
Chest wall mass			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Elbow deformity			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Foot deformity			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Groin pain			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Haemarthrosis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Myalgia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	2	1	1
Rhabdomyolysis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Acute sinusitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	2	0	0
Acute tonsillitis			
subjects affected / exposed	1 / 129 (0.78%)	1 / 134 (0.75%)	6 / 226 (2.65%)
occurrences (all)	1	2	7
Appendicitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	7 / 129 (5.43%)	5 / 134 (3.73%)	8 / 226 (3.54%)
occurrences (all)	7	5	10

Bronchopneumonia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Bullous impetigo			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Conjunctivitis bacterial			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	2	0
Cystitis			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	0 / 226 (0.00%)
occurrences (all)	1	2	0
Ear infection			
subjects affected / exposed	3 / 129 (2.33%)	0 / 134 (0.00%)	6 / 226 (2.65%)
occurrences (all)	4	0	6
Febrile infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Fungal skin infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Furuncle			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 129 (0.78%)	3 / 134 (2.24%)	8 / 226 (3.54%)
occurrences (all)	1	4	9
Gastroenteritis viral			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	2 / 226 (0.88%)
occurrences (all)	0	1	2
Gastrointestinal viral infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Helicobacter infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0

Herpes simplex			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Hordeolum			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Impetigo			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Infected bites			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	1 / 129 (0.78%)	4 / 134 (2.99%)	6 / 226 (2.65%)
occurrences (all)	2	9	14
Laryngitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	2 / 226 (0.88%)
occurrences (all)	0	0	2
Lower respiratory tract infection			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Mastitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	15 / 129 (11.63%)	15 / 134 (11.19%)	31 / 226 (13.72%)
occurrences (all)	23	22	43
Onychomycosis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	1 / 226 (0.44%)
occurrences (all)	0	2	1

Otitis externa			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	2 / 226 (0.88%)
occurrences (all)	1	2	2
Otitis media acute			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Parasitic gastroenteritis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Paronychia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	9 / 129 (6.98%)	9 / 134 (6.72%)	10 / 226 (4.42%)
occurrences (all)	9	10	14
Pharyngotonsillitis			
subjects affected / exposed	1 / 129 (0.78%)	2 / 134 (1.49%)	3 / 226 (1.33%)
occurrences (all)	1	2	3
Pneumonia			
subjects affected / exposed	2 / 129 (1.55%)	1 / 134 (0.75%)	2 / 226 (0.88%)
occurrences (all)	2	1	2
Pulmonary tuberculosis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Pulpitis dental			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	7 / 129 (5.43%)	7 / 134 (5.22%)	13 / 226 (5.75%)
occurrences (all)	7	10	28
Respiratory tract infection viral			
subjects affected / exposed	3 / 129 (2.33%)	2 / 134 (1.49%)	6 / 226 (2.65%)
occurrences (all)	3	3	14

Rhinitis			
subjects affected / exposed	7 / 129 (5.43%)	4 / 134 (2.99%)	5 / 226 (2.21%)
occurrences (all)	7	5	7
Sinusitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Subcutaneous abscess			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Tinea infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
subjects affected / exposed	4 / 129 (3.10%)	2 / 134 (1.49%)	4 / 226 (1.77%)
occurrences (all)	4	2	5
Tracheitis			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Tracheobronchitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	5 / 129 (3.88%)	6 / 134 (4.48%)	10 / 226 (4.42%)
occurrences (all)	8	8	18
Urinary tract infection			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	4 / 226 (1.77%)
occurrences (all)	1	0	4
Urinary tract infection bacterial			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Varicella			
subjects affected / exposed	2 / 129 (1.55%)	2 / 134 (1.49%)	2 / 226 (0.88%)
occurrences (all)	2	2	2
Viral infection			
subjects affected / exposed	6 / 129 (4.65%)	5 / 134 (3.73%)	12 / 226 (5.31%)
occurrences (all)	7	5	13

Viral pharyngitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Viral rash			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Viral upper respiratory tract infection			
subjects affected / exposed	3 / 129 (2.33%)	5 / 134 (3.73%)	7 / 226 (3.10%)
occurrences (all)	6	6	9
Vulvitis			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	0 / 129 (0.00%)	2 / 134 (1.49%)	0 / 226 (0.00%)
occurrences (all)	0	2	0
Decreased appetite			
subjects affected / exposed	1 / 129 (0.78%)	6 / 134 (4.48%)	2 / 226 (0.88%)
occurrences (all)	1	8	2
Dehydration			
subjects affected / exposed	1 / 129 (0.78%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	1	0	0
Electrolyte imbalance			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Feeding disorder			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Hyperphagia			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Hypoalbuminaemia			

subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	0 / 226 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	1 / 226 (0.44%)
occurrences (all)	0	1	1
Iron deficiency			
subjects affected / exposed	0 / 129 (0.00%)	1 / 134 (0.75%)	0 / 226 (0.00%)
occurrences (all)	0	1	0
Obesity			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1
Weight gain poor			
subjects affected / exposed	0 / 129 (0.00%)	0 / 134 (0.00%)	1 / 226 (0.44%)
occurrences (all)	0	0	1

Non-serious adverse events	Part III-V - ESL x Safety Set		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	97 / 152 (63.82%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Oral papilloma			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Pyogenic granuloma			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Sebaceous adenoma			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Skin papilloma			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Hypertension			

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Phlebitis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Systolic hypertension			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Surgical and medical procedures			
Adenoidectomy			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Brain operation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Plastic surgery to the face			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Suture insertion			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tenotomy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tooth extraction			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	3		
Chest pain			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Device malfunction			

subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Face oedema				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Fatigue				
subjects affected / exposed	3 / 152 (1.97%)			
occurrences (all)	5			
Feeling hot				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Gait disturbance				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Hyperthermia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Irritability				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Malaise				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Oedema				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Pain				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Pyrexia				
subjects affected / exposed	16 / 152 (10.53%)			
occurrences (all)	38			
Sluggishness				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Thirst				

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Drug hypersensitivity			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Hypersensitivity			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Immunodeficiency			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Seasonal allergy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Social circumstances			
Learning disability			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	2		
Epididymal cyst			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Labia enlarged			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Menstruation irregular			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Pelvic pain			

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Polycystic ovaries			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Vaginal discharge			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	12		
Bronchospasm			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	7 / 152 (4.61%)		
occurrences (all)	18		
Epistaxis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Laryngospasm			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Nasal discomfort			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Nasal obstruction			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Nasal septum deviation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			

subjects affected / exposed	3 / 152 (1.97%)		
occurrences (all)	7		
Respiratory disorder			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Rhinitis allergic			
subjects affected / exposed	3 / 152 (1.97%)		
occurrences (all)	4		
Rhinorrhoea			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tonsillar hypertrophy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tonsillar inflammation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Vasomotor rhinitis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Affect lability			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Agitation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Apathy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		

Attention deficit/Hyperactivity disorder				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Bradyphrenia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Bruxism				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Confusional state				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Depressed mood				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Disorientation				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dyslogia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dysthymic disorder				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Emotional distress				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Encopresis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Inappropriate affect				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Initial insomnia				

subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Insomnia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	2		
Listless			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Mood altered			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Mood swings			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Nervousness			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Obsessive-compulsive disorder			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Panic attack			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Restlessness			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Sleep disorder			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Sleep talking			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Somatoform disorder			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Hepatobiliary disorders			

Biliary dyskinesia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Hepatic cyst			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Hepatic steatosis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Blood bicarbonate decreased			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Blood calcium decreased			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	5 / 152 (3.29%)		
occurrences (all)	5		
Blood glucose decreased			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Blood thyroid stimulating hormone			

increased				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Blood triglycerides increased				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Body temperature increased				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Breath sounds abnormal				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Ecg p wave inverted				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Electrocardiogram pr shortened				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Electrocardiogram pr prolongation				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Electrocardiogram qrs complex prolonged				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Electrocardiogram qt prolonged				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Electrocardiogram repolarisation abnormality				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Eosinophil count increased				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Gamma-glutamyltransferase increased				

subjects affected / exposed	9 / 152 (5.92%)			
occurrences (all)	10			
Haemoglobin decreased				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Hepatic enzyme increased				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Platelet count decreased				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Platelet count increased				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Positive rombergism				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Rheumatoid factor increased				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Thyroxine decreased				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Thyroxine increased				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Transaminases increased				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Weight decreased				
subjects affected / exposed	4 / 152 (2.63%)			
occurrences (all)	5			
Weight increased				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
White blood cell count increased				

subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	2		
Clavicle fracture			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Concussion			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Drug toxicity			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Excoriation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Face injury			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Foot fracture			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Forearm fracture			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Hand fracture			

subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Head injury				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Injury				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Joint injury				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Laceration				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Ligament sprain				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Limb injury				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Lip injury				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Overdose				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Poisoning				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Radius fracture				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Skin injury				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Skin wound				

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Soft tissue injury			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	2		
Tibia fracture			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Tooth fracture			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tooth injury			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Toxicity to various agents			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Traumatic haematoma			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Upper limb fracture			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Wound			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Wrist fracture			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Congenital, familial and genetic disorders			
Atrial septal defect			

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Phimosis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Bradyarrhythmia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Bundle branch block right			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Sinus bradycardia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tricuspid valve incompetence			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Wolff-parkinson-white syndrome			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Balance disorder			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Cerebellar ataxia			

subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Cerebrovascular disorder				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Circadian rhythm sleep disorder				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	4			
Cognitive disorder				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Convulsion				
subjects affected / exposed	20 / 152 (13.16%)			
occurrences (all)	28			
Coordination abnormal				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Depressed level of consciousness				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Dizziness				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Epilepsy				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Head titubation				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Headache				
subjects affected / exposed	12 / 152 (7.89%)			
occurrences (all)	18			
Hypotonia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Intention tremor				

subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Intracranial haematoma				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Lethargy				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Memory impairment				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Mental impairment				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Migraine				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Nystagmus				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Paraesthesia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Partial seizures with secondary generalisation				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Poor quality sleep				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Postictal headache				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Postictal state				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			

Psychomotor hyperactivity subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Somnolence subjects affected / exposed occurrences (all)	3 / 152 (1.97%) 3			
Speech disorder subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Status epilepticus subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Syncope subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Tremor subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Unresponsive to stimuli subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	2 / 152 (1.32%) 2			
Leukopenia subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Neutropenia subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0			
Pancytopenia				

subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Thrombocytopenia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tinnitus			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Tympanic membrane perforation			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Vertigo			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Eye disorders			
Abnormal sensation in eye			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Astigmatism			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Chalazion			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Conjunctival haemorrhage			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Eye pain			

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Eye swelling			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Lacrimation increased			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Optic atrophy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Abdominal pain			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	6		
Abdominal pain upper			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Aphthous stomatitis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Constipation			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Dental caries			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		

Diarrhoea				
subjects affected / exposed	10 / 152 (6.58%)			
occurrences (all)	14			
Dyspepsia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Enteritis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Enterocolitis				
subjects affected / exposed	5 / 152 (3.29%)			
occurrences (all)	6			
Flatulence				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Food poisoning				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Frequent bowel movements				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Gastritis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Gastroduodenitis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Gingival bleeding				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			

Gingivitis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Irritable bowel syndrome				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Lip dry				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Mouth ulceration				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Nausea				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Odynophagia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Oesophagitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Oral pain				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Pancreatic disorder				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Periodontitis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Peritonitis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Rectal fissure				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			

Salivary hypersecretion				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Stomatitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Tooth disorder				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Toothache				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Vomiting				
subjects affected / exposed	10 / 152 (6.58%)			
occurrences (all)	14			
Skin and subcutaneous tissue disorders				
Acne				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Alopecia				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dermatitis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dermatitis acneiform				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dermatitis allergic				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Dermatitis atopic				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	10			
Dermatitis contact				

subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dermatitis diaper				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Dry skin				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Heat rash				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Ingrowing nail				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Onychomadesis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Papule				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Pityriasis rosea				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Pruritus				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Rash				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Rash erythematous				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Rash pruritic				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Seborrhoeic dermatitis				

subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Skin exfoliation			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Solar dermatitis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Urticaria			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Enuresis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Haematuria			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Incontinence			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	2		
Leukocyturia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Nephropathy			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Nocturia			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Renal failure acute			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		

Urinary retention subjects affected / exposed occurrences (all)	0 / 152 (0.00%) 0		
Endocrine disorders Goitre subjects affected / exposed occurrences (all) Hypothalamo-pituitary disorder subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all) Precocious puberty subjects affected / exposed occurrences (all)	 1 / 152 (0.66%) 1 1 / 152 (0.66%) 1 4 / 152 (2.63%) 4 2 / 152 (1.32%) 2		
Musculoskeletal and connective tissue disorders Ankle deformity subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Arthritis reactive subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Chest wall mass subjects affected / exposed occurrences (all) Elbow deformity subjects affected / exposed occurrences (all) Foot deformity	 1 / 152 (0.66%) 1 2 / 152 (1.32%) 2 0 / 152 (0.00%) 0 0 / 152 (0.00%) 0 0 / 152 (0.00%) 0 0 / 152 (0.00%) 0		

subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Groin pain			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Haemarthrosis			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Joint swelling			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Myalgia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Rhabdomyolysis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Infections and infestations			
Abscess limb			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Acute sinusitis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	3		
Acute tonsillitis			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Appendicitis			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		

Bronchitis				
subjects affected / exposed	13 / 152 (8.55%)			
occurrences (all)	27			
Bronchopneumonia				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Bullous impetigo				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Conjunctivitis bacterial				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Cystitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Ear infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Febrile infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Fungal skin infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Furuncle				
subjects affected / exposed	3 / 152 (1.97%)			
occurrences (all)	4			
Gastroenteritis				
subjects affected / exposed	8 / 152 (5.26%)			
occurrences (all)	10			
Gastroenteritis viral				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	3			
Gastrointestinal viral infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			

Helicobacter infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Herpes simplex				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Hordeolum				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Impetigo				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Infected bites				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Infection				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	5 / 152 (3.29%)			
occurrences (all)	7			
Laryngitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Lower respiratory tract infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Mastitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	16 / 152 (10.53%)			
occurrences (all)	31			
Onychomycosis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			

Oral herpes				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Otitis externa				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Otitis media				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Otitis media acute				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Parasitic gastroenteritis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Paronychia				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Pharyngitis				
subjects affected / exposed	9 / 152 (5.92%)			
occurrences (all)	18			
Pharyngotonsillitis				
subjects affected / exposed	5 / 152 (3.29%)			
occurrences (all)	6			
Pneumonia				
subjects affected / exposed	5 / 152 (3.29%)			
occurrences (all)	14			
Pulmonary tuberculosis				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Pulpitis dental				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Respiratory tract infection				
subjects affected / exposed	8 / 152 (5.26%)			
occurrences (all)	17			

Respiratory tract infection viral				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Rhinitis				
subjects affected / exposed	11 / 152 (7.24%)			
occurrences (all)	22			
Sinusitis				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Subcutaneous abscess				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Tinea infection				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Tonsillitis				
subjects affected / exposed	5 / 152 (3.29%)			
occurrences (all)	7			
Tracheitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	2			
Tracheobronchitis				
subjects affected / exposed	1 / 152 (0.66%)			
occurrences (all)	1			
Upper respiratory tract infection				
subjects affected / exposed	13 / 152 (8.55%)			
occurrences (all)	32			
Urinary tract infection				
subjects affected / exposed	2 / 152 (1.32%)			
occurrences (all)	2			
Urinary tract infection bacterial				
subjects affected / exposed	0 / 152 (0.00%)			
occurrences (all)	0			
Varicella				
subjects affected / exposed	3 / 152 (1.97%)			
occurrences (all)	3			

Viral infection			
subjects affected / exposed	9 / 152 (5.92%)		
occurrences (all)	11		
Viral pharyngitis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Viral rash			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Vulvitis			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Appetite disorder			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Decreased appetite			
subjects affected / exposed	2 / 152 (1.32%)		
occurrences (all)	2		
Dehydration			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Electrolyte imbalance			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Feeding disorder			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Hyperphagia			

subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	1 / 152 (0.66%)		
occurrences (all)	1		
Increased appetite			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Iron deficiency			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Obesity			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		
Weight gain poor			
subjects affected / exposed	0 / 152 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 December 2007	Global Amendment#1 The reason for this study global protocol amendment is to harmonized the requests from different Ethics Committees and/or Regulatory Authorities
29 April 2009	Global Amendment#2 The reason is to define a study extension (Part III) in order to allow patients who participated in study SCO/BIA-2093-305 to continue receiving the study medication
17 May 2010	Global Amendment#3 The reason is to define a study extension (Part IV) in order to allow patients who participated in study SCO/BIA-2093-305 to continue receiving the study medication
07 June 2010	Global Amendment#4 The reason is the recall of the oral suspension formulation of the investigational medicinal product (50 mg/mL) used in the age group of 2-6 years children for Part I and Part II.
16 September 2010	Global Amendment#4 The reason is the recall of the oral suspension formulation of the investigational medicinal product (50 mg/mL) used in the age group of 2-6 years children for Part I and Part II.
12 May 2011	Global Amendment#3 The reason is to define a study extension (Part V) in order to allow patients who participated in study SCO/BIA-2093-305 to continue receiving the study medication

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported