Clinical trial results:
A phase II multicenter clinical study evaluating long-term safety, tolerability and efficacy of 5-year treatment with deferasirox in pediatric patients with beta-thalassemia major

An extension of:

An open label, phase IIa study to evaluate the safety, tolerability, pharmacokinetics and the effects on liver iron concentration of repeated doses of 10 mg/kg/day of ICL670 administered to pediatric patients with transfusion-dependent beta-thalassemia major

Summary

EudraCT number	2015-003535-35
Trial protocol	Outside EU/EEA
Global end of trial date	12 February 2008
Results information	
Result version number	v1 (current)
This version publication date	27 July 2016
First version publication date	27 July 2016

Trial information

Trial identification	
Sponsor protocol code	CICL670A0106E1
Additional study identifiers	
ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00390858
WHO universal trial number (UTN)	-

Notes:

Sponsors	
Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, +41 613241111,

Notes:

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

Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 February 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	12 February 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the trial was to evaluate the long-term safety and tolerability profile of deferasirox (ICL670) after administration of multiple doses.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 September 2003
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	Italy: 38
Country: Number of subjects enrolled	France: 2
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	20

Adolescents (12-17 years)	20
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was performed at 4 centres in Italy and France.

Pre-assignment

Screening details:

A total of 40 subjects (20 children and 20 adolescents) were enrolled, out of which 39 completed the 1-year treatment (core study) and entered the 4-year extension study. One subject withdrew consent from extension phase of the study.

Period 1

Period 1 title	Core Study 1 year
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Deferasirox in Children (< 12 years)

Arm description:

Children of age below 12 years were orally administered with initial once daily dose of 10 milligram (mg)/kilogram (kg) of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether Liver Iron Concentration (LIC), and serum ferritin were increasing or decreasing.

Arm type	Experimental
Investigational medicinal product name	Deferasirox
Investigational medicinal product code	ICL670
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast.

Arm title	Deferasirox in Adolescents (≥ 12 years)

Arm description:

Adolescents of age equal to or above 12 years up to 17 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing.

Arm type	Experimental
Investigational medicinal product name	Deferasirox
Investigational medicinal product code	ICL670
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast.

Number of subjects in period 1	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)
Started	20	20
Completed	19	20
Not completed	1	0
Consent withdrawn by subject	1	-

Period 2

Period 2 title	Extension 4 years
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Extension Defersirox in children(<12years)

Arm description:

Children of age below 12 years were orally administered with initial once daily dose of 10 milligram (mg)/kilogram (kg) of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether Liver Iron Concentration (LIC), and serum ferritin were increasing or decreasing.

Arm type	Experimental
Investigational medicinal product name	Deferasirox
Investigational medicinal product code	ICL670
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast.

Arm title	Extension Defersirox in children(≥12years)

Arm description:

Adolescents of age equal to or above 12 years up to 17 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing

Arm type	Experimental
Investigational medicinal product name	Deferasirox
Investigational medicinal product code	ICL670
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast.

Number of subjects in period 2	Extension Defersirox in children(<12years)	Extension Defersirox in children(≥12years)
Started	19	20
Completed	11	13
Not completed	8	7
Consent withdrawn by subject	2	4
Adverse event, non-fatal	6	2
Unsatisfactory therapeutic effect	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Deferasirox in Children (< 12 years)
Reporting group description:	
Children of age below 12 years were orally administered with initial once daily dose of 10 milligram (mg)/kilogram (kg) of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether Liver Iron Concentration (LIC), and serum ferritin were increasing or decreasing.	
Reporting group title	Deferasirox in Adolescents (≥ 12 years)
Reporting group description:	
Adolescents of age equal to or above 12 years up to 17 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing.	

Reporting group values	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)	Total
Number of subjects	20	20	40
Age categorical Units: Subjects			
Children (2-11 years)	20	0	20
Adolescents (12-17 years)	0	20	20
Age Continuous Units: years			
arithmetic mean	6.7	14.1	
standard deviation	± 2.83	± 1.64	-
Gender, Male/Female Units: participants			
Female	12	11	23
Male	8	9	17
Race/Ethnicity, Customized Units: Subjects			
Caucasian	20	20	40

End points

End points reporting groups

Reporting group title	Deferasirox in Children (< 12 years)

Reporting group description:

Children of age below 12 years were orally administered with initial once daily dose of 10 milligram (mg)/kilogram (kg) of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether Liver Iron Concentration (LIC), and serum ferritin were increasing or decreasing.

Reporting group title	Deferasirox in Adolescents (≥ 12 years)

Reporting group description:

Adolescents of age equal to or above 12 years up to 17 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing.

Reporting group title	Extension Defersirox in children(<12years)

Reporting group description:

Children of age below 12 years were orally administered with initial once daily dose of 10 milligram (mg)/kilogram (kg) of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether Liver Iron Concentration (LIC), and serum ferritin were increasing or decreasing.

Reporting group title	Extension Defersirox in children(≥12years)

Reporting group description:

Adolescents of age equal to or above 12 years up to 17 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing

Primary: Number of subjects with adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation and who died

End point title	Number of subjects with adverse events (AEs), serious adverse events (SAEs), AEs leading to discontinuation and who died[1]

End point description:

AEs are defined as any unfavorable and unintended diagnosis, symptom, sign (including an abnormal laboratory finding), syndrome or disease which either occurs during study, having been absent at baseline, or, if present at baseline, appears to worsen. Serious adverse events are any untoward medical occurrences that result in death, are life threatening, require (or prolong) hospitalization, cause persistent or significant disability/incapacity, result in congenital anomalies or birth defects, or are other conditions which in judgment of investigators represent significant hazards. The analysis was performed on safety set population defined as all subjects who received at least one dose of deferasirox during the core or extension study.

End point type	Primary

End point timeframe:

Core: 1 year, Extension: 4 years

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: Only descriptive summary statistics was planned for this outcome measure.

End point values	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Subjects				
AEs	18	11		
SAEs	4	8		
AEs leading to Discontinuation	6	2		
Deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Change in liver iron concentration (LIC) from baseline of core period to end of extension period

End point title	Change in liver iron concentration (LIC) from baseline of core period to end of extension period[2]

End point description:

Change in liver iron content (LIC) as assessed by superconducting quantum interference device (SQUID) was evaluated by comparing the LIC at the start of deferasirox treatment to the LIC at the end of the extension study. LIC was expressed in milligrams of iron per gram of liver dry weight (mgFe/g dw). The analysis was performed in safety set population.

End point type	Primary

End point timeframe:

Core period: Baseline, 4, 12, 24, 36 and 48 weeks.
Extension period: 6 months for 1st and 2nd year and annually for 3rd and 4th year.

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: Only descriptive summary statistics was planned for this outcome measure.

End point values	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mg Fe/g dw				
arithmetic mean (standard deviation)				
Core Baseline LIC (n = 20, 20)	6.25 (± 2.507)	5.73 (± 2.185)		
End of Extension LIC (n=19, 20)	5.46 (± 3.192)	4.66 (± 3.533)		
Change from Baseline LIC (n=19, 20)	-0.9 (± 3.85)	-1.1 (± 3.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Body Iron Elimination (TBIE) Rate from baseline of core period to end of extension period

End point title	Total Body Iron Elimination (TBIE) Rate from baseline of core period to end of extension period

End point description:

Total body iron elimination rate (TBIE) was defined as TBIE = Kin + [Us(t0)-Us(t)]/(t-t0) where, Kin was the known iron influx rate from transfusions, calculated from time t0 to time t, Us(t) (mg(s) of iron) was the estimated TBI from LIC at time t, Us(t) = 10.6 × LIC× (body weight), where LIC was in mg(s) of iron/g of dry weight of liver and body weight in kilograms, and t0 was taken as last available date prior start of treatment with deferasirox, where LIC was measured.
The analysis was performed in safety set population.

End point type	Secondary

End point timeframe:

Baseline of Core Study to End of Extension Study (up to 5 years)

End point values	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mg/kg/Day				
arithmetic mean (standard deviation)				
Core Baseline TBIE (n=19, 20)	0.4292 (± 0.06454)	0.4083 (± 0.07158)		
End of Extension TBIE (n=11,14)	0.4939 (± 0.05175)	0.4286 (± 0.0637)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Change in serum ferritin level from baseline of core period to end of extension period

End point title	Relative Change in serum ferritin level from baseline of core period to end of extension period

End point description:

Serum levels were drawn at the baseline of the Core Study up to 18 months of the Extension Study. Relative change (%) in serum ferritin level was assessed. Relative Change was defined as 1 - (Change in ferritin level from Baseline/Baseline level) x 100. The analysis was performed in safety set population.

End point type	Secondary

End point timeframe:

Baseline of Core Study to End of Extension Study (up to 5 years)

End point values	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: percent change				
arithmetic mean (standard deviation)				

Core Baseline	2146.3 (± 1422.53)	1867.5 (± 711.37)		
Last available value	2973.7 (± 1016.39)	2707.7 (± 1107.11)		
Relative change	62.4 (± 53.47)	54.9 (± 64.64)		

Statistical analyses

No statistical analyses for this end point

Secondary: Relative Change in Serum Transferrin Level from baseline of core period to end of extension period

End point title	Relative Change in Serum Transferrin Level from baseline of core period to end of extension period

End point description:

Transferrin saturation were calculated as a variable derived from serum iron and transferrin concentrations. Relative change (%) in serum transferrin level was assessed, relative change was defined as 1 - (Change in transferrin level from Baseline/Baseline level) x 100. The analysis was performed in safety set population.

End point type	Secondary

End point timeframe:

Baseline of Core Study to End of Extension Study (up to 5 years)

End point values	Deferasirox in Children (< 12 years)	Deferasirox in Adolescents (≥ 12 years)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: percent change				
arithmetic mean (standard deviation)				
Core Baseline	1.246 (± 0.1891)	1.449 (± 0.2613)		
End of study	1.212 (± 0.198)	1.37 (± 0.2101)		
Relative change	-1.86 (± 13.5137)	-4.177 (± 11.6573)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events are monitored from date of First Subject First Visit (FSFV) until Last Subject Last Visit (LSLV). All other adverse events are monitored from First Subject First Treatment until LSLV.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Deferasirox in Adolescents (≥ 12 years)

Reporting group description:

Adolescents of age equal to or above 12 years up to 17 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing.

Reporting group title	Deferasirox in Children (< 12 years)

Reporting group description:

Children of age below 12 years were orally administered with initial once daily dose of 10 mg/kg of deferasirox 30 minutes prior to breakfast. Dose adjustments were performed (± 5 or 10 mg/kg) depending on safety parameters (e.g. renal and hematology) and whether LIC and serum ferritin were increasing or decreasing.

Serious adverse events	Deferasirox in Adolescents (≥ 12 years)	Deferasirox in Children (< 12 years)	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 20 (40.00%)	4 / 20 (20.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Transaminases increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Allergic transfusion reaction			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Splenectomy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystectomy			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillectomy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Splenomegaly			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Local swelling			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatolithiasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fluid collection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious mononucleosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Deferasirox in Adolescents (≥ 12 years)	Deferasirox in Children (< 12 years)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)	20 / 20 (100.00%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 20 (40.00%)	7 / 20 (35.00%)	
occurrences (all)	16	7	
Chest pain			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Influenza like illness			

subjects affected / exposed	1 / 20 (5.00%)	3 / 20 (15.00%)	
occurrences (all)	1	3	
Hyperpyrexia			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	3	2	
Cyst			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pyrexia			
subjects affected / exposed	16 / 20 (80.00%)	18 / 20 (90.00%)	
occurrences (all)	40	59	
Suprapubic pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy to plants			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Food allergy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Drug hypersensitivity			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	3 / 20 (15.00%)	0 / 20 (0.00%)	
occurrences (all)	6	0	
Menorrhagia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dysmenorrhoea			

subjects affected / exposed	4 / 20 (20.00%)	0 / 20 (0.00%)	
occurrences (all)	9	0	
Breast discomfort			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Menstrual disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Polymenorrhoea			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pelvic pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Ovarian cyst			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dysphonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	16 / 20 (80.00%)	18 / 20 (90.00%)	
occurrences (all)	40	70	
Asthma			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	3	
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	3 / 20 (15.00%)	4 / 20 (20.00%)	
occurrences (all)	4	6	
Nasal congestion			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pharyngolaryngeal pain			
subjects affected / exposed	9 / 20 (45.00%)	7 / 20 (35.00%)	
occurrences (all)	11	13	
Productive cough			
subjects affected / exposed	0 / 20 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Throat irritation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Depression			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	5	0	
Nervousness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Beta 2 microglobulin urine increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			

subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)		
occurrences (all)	4	1		
Blood folate decreased				
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)		
occurrences (all)	0	1		
Blood homocysteine increased				
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)		
occurrences (all)	1	0		
Creatinine renal clearance decreased				
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)		
occurrences (all)	0	1		
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)		
occurrences (all)	0	1		
Glomerular filtration rate abnormal				
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)		
occurrences (all)	0	1		
Transaminases increased				
subjects affected / exposed	2 / 20 (10.00%)	8 / 20 (40.00%)		
occurrences (all)	4	10		
Protein C decreased				
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)		
occurrences (all)	1	0		
Glucose urine present				
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)		
occurrences (all)	1	0		
Urinary casts				
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)		
occurrences (all)	0	2		
Urine protein/creatinine ratio increased				
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)		
occurrences (all)	1	0		
White blood cell count increased				
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)		
occurrences (all)	1	0		

Vitamin E decreased			
subjects affected / exposed	4 / 20 (20.00%)	2 / 20 (10.00%)	
occurrences (all)	4	2	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Chest injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eye injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Hand fracture			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	2	2	
Foreign body trauma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Joint sprain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Limb injury			
subjects affected / exposed	0 / 20 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	3	
Transfusion reaction			

subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	3	
Thermal burn			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Sunburn			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Vertebral injury			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Wound			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Congenital, familial and genetic disorders			
Talipes			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Cardiomyopathy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	4	1	
Nervous system disorders			
Aphonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Disturbance in attention			

subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	12 / 20 (60.00%)	9 / 20 (45.00%)	
occurrences (all)	36	27	
Migraine			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	2	
Somnolence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Splenomegaly			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Lymphadenopathy			
subjects affected / exposed	4 / 20 (20.00%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Ear and labyrinth disorders			
Auricular pseudocyst			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Ear pain			
subjects affected / exposed	4 / 20 (20.00%)	8 / 20 (40.00%)	
occurrences (all)	4	13	
Vertigo			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	6	1	
Hypoacusis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eye disorders			

Conjunctival haemorrhage			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Conjunctivitis			
subjects affected / exposed	4 / 20 (20.00%)	3 / 20 (15.00%)	
occurrences (all)	4	3	
Conjunctivitis allergic			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eye irritation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Eyelid oedema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Ocular icterus			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hypermetropia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Retinal degeneration			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Retinopathy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Vision blurred			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	10 / 20 (50.00%)	15 / 20 (75.00%)	
occurrences (all)	24	28	
Abdominal pain upper			
subjects affected / exposed	8 / 20 (40.00%)	1 / 20 (5.00%)	
occurrences (all)	14	1	
Cheilitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Aphthous stomatitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dental caries			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Constipation			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	4	1	
Diarrhoea			
subjects affected / exposed	9 / 20 (45.00%)	8 / 20 (40.00%)	
occurrences (all)	24	12	
Dry mouth			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Dyspepsia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Dysphagia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Flatulence			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Enteritis			

subjects affected / exposed	4 / 20 (20.00%)	3 / 20 (15.00%)	
occurrences (all)	6	3	
Gingivitis			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Gingival bleeding			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Intestinal congestion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	10 / 20 (50.00%)	2 / 20 (10.00%)	
occurrences (all)	23	2	
Odynophagia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	4 / 20 (20.00%)	2 / 20 (10.00%)	
occurrences (all)	4	2	
Vomiting			
subjects affected / exposed	9 / 20 (45.00%)	12 / 20 (60.00%)	
occurrences (all)	24	33	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Cholecystitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	

Cholelithiasis			
subjects affected / exposed	4 / 20 (20.00%)	1 / 20 (5.00%)	
occurrences (all)	4	1	
Jaundice			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Dermatitis			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Eczema			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Erythema			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Hyperkeratosis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Ingrowing nail			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pityriasis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pityriasis alba			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Psoriasis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Rash			

subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Rash pruritic			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Rash papular			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Skin discolouration			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Skin exfoliation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	2	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nephropathy toxic			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Renal colic			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	11	0	
Proteinuria			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	6	
Endocrine disorders			
Growth hormone deficiency			

subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hypogonadism			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 20 (15.00%)	5 / 20 (25.00%)	
occurrences (all)	4	5	
Groin pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Bone swelling			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	9 / 20 (45.00%)	3 / 20 (15.00%)	
occurrences (all)	20	6	
Musculoskeletal pain			
subjects affected / exposed	3 / 20 (15.00%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 20 (0.00%)	3 / 20 (15.00%)	
occurrences (all)	0	4	
Muscle spasms			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Neck mass			

subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Neck pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Torticollis			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Infections and infestations			
Acute tonsillitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Bacterial infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	5 / 20 (25.00%)	5 / 20 (25.00%)	
occurrences (all)	5	7	
Bronchopneumonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	2 / 20 (10.00%)	9 / 20 (45.00%)	
occurrences (all)	2	17	
Catheter related infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Fungal infection			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	2	
Gastroenteritis			
subjects affected / exposed	8 / 20 (40.00%)	10 / 20 (50.00%)	
occurrences (all)	11	20	

Gastroenteritis viral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Genital infection female			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Herpes simplex			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	2	
Impetigo			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	3	
Influenza			
subjects affected / exposed	11 / 20 (55.00%)	7 / 20 (35.00%)	
occurrences (all)	19	18	
Laryngitis			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	3	
Localised infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Leptospirosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Lymphangitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	2 / 20 (10.00%)	6 / 20 (30.00%)	
occurrences (all)	2	13	
Oral candidiasis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	2	

Otitis media			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Pharyngitis			
subjects affected / exposed	10 / 20 (50.00%)	12 / 20 (60.00%)	
occurrences (all)	40	24	
Pharyngotonsillitis			
subjects affected / exposed	4 / 20 (20.00%)	1 / 20 (5.00%)	
occurrences (all)	5	2	
Pyoderma			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	13 / 20 (65.00%)	17 / 20 (85.00%)	
occurrences (all)	27	70	
Sinusitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Subcutaneous abscess			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Skin infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Tinea versicolour			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Tonsillitis			
subjects affected / exposed	5 / 20 (25.00%)	3 / 20 (15.00%)	
occurrences (all)	6	4	
Tooth abscess			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	3	
Urinary tract infection			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	4	0	

Tracheitis			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	3	
Varicella			
subjects affected / exposed	1 / 20 (5.00%)	5 / 20 (25.00%)	
occurrences (all)	1	5	
Vulvitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Glucose tolerance impaired			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hyperinsulinism			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Zinc deficiency			
subjects affected / exposed	5 / 20 (25.00%)	3 / 20 (15.00%)	
occurrences (all)	5	3	
Vitamin C deficiency			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Hypozincaemia			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2006	Prolonged the duration of the extension study to 4 years in order to obtain long-term data on safety and efficacy of deferasirox treatment. Together with the core study duration this resulted in a total of 5 years exposure for enrolled subjects.
06 November 2006	• Aligned the deferasirox dosing guidelines in the protocol as specified in the EU approved deferasirox label. • Specified the frequency of data safety reviews by the independent Program Safety Board (PSB) as "within approximately every 12 – 18 months" in line with the timing of regular safety updates to the European regulatory authority, EMEA. • Clarified that for efficacy, the success criteria analysis would be based on absolute and relative changes from baseline in LIC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported