Clinical trial results:
An open-label study evaluating the Pharmacokinetics and Tolerability of vortioxetine in connection with multiple oral dosing of vortioxetine in child and adolescent patients with a DSM-IV-TRTM diagnosis of Depressive or Anxiety Disorder

Summary

EudraCT number	2010-020170-42
Trial protocol	DE
Global end of trial date	08 June 2015

Results information

Result version number	v1 (current)
This version publication date	06 July 2016
First version publication date	01 July 2015

Trial information

Trial identification

Sponsor protocol code	12708A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01491035
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	H. Lundbeck A/S
Sponsor organisation address	Ottiliavej 9, Valby, Denmark,
Public contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S , +45 36301311, lundbeckClinicalTrials@lundbeck.com
Scientific contact	LundbeckClinicalTrials@lundbeck.com, H. Lundbeck A/S , +45 36301311, lundbeckClinicalTrials@lundbeck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000455-PIP02-10
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	10 December 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 December 2014
Global end of trial reached?	Yes
Global end of trial date	08 June 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the pharmacokinetics of vortioxetine, and its metabolites in connection with multiple oral dosing in child and adolescent patients with a DSM-IV-TRTM diagnosis of a Depressive or Anxiety Disorder
- To assess safety and tolerability of vortioxetine
- Provide supportive information for dose regimen in paediatric efficacy and safety studies with vortioxetine

Protection of trial subjects:

This study was designed and conducted in accordance with the principles of the Declaration of Helsinki. E.g. assent was documented by each patient and consent by his or her legal representative and the corresponding principal investigator or designee, all of whom signed and dated the Informed Consent/Assent Form. A copy of the signed Informed consent/Assent Form was given to the patient and his or her legal representative

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 April 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 5
Country: Number of subjects enrolled	United States: 43
Worldwide total number of subjects	48
EEA total number of subjects	5

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	0

months)	
Children (2-11 years)	24
Adolescents (12-17 years)	24
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adolescents (12-17yr) and children (7-11yr) (boys and girls) for whom treatment with antidepressant therapy was warranted, as judged by the investigator, and who had a diagnosis of depressive or anxiety disorder according to DSM-IV-TR (TM) criteria

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Adolescents, 5 mg cohort

Arm description:

6 adolescents (12-17 yr). 5 mg tablets for 14 days.

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

5 mg tablets for 14 days; orally; once daily

Arm title	Adolescents, 10 mg cohort

Arm description:

6 adolescents (12-17 yr). 10 mg tablets for 14 days.

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg tablets for 14 days (initial up-titration 5 mg/day for 2 days); orally; once daily

Arm title	Adolescents, 15 mg cohort

Arm description:

6 adolescents (12-17 yr). 15 mg tablets for 14 days.

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15 mg tablets for 14 days (initial up-titration 5 mg/day for 2 days followed by 10 mg/day for 2 days);

orally; once daily

Arm title	Adolescents, 20 mg cohort
Arm description:	
6 adolescents (12-17 yr). 20 mg tablets for 14 days.	
Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
20 mg tablets for 14 days (initial up-titration 5 mg/day for 2 days followed by 10 mg/day for 2 days and 15 mg/day for 2 days); orally; once daily	
Arm title	Children, 5 mg cohort
Arm description:	
6 children (7-11 yr). 5 mg tablets for 14 days.	
Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
5 mg tablets for 14 days; orally; once daily	
Arm title	Children, 10 mg cohort
Arm description:	
6 children (7-11 yr). 10 mg tablets for 14 days.	
Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
10 mg tablets for 14 days (initial up-titration 5mg/day for two days); orally; once daily	
Arm title	Children, 15 mg cohort
Arm description:	
6 children (7-11 yr). 15 mg tablets for 14 days.	
Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
15 mg tablets for 14 days (initial up-titration 5 mg/day for 2 days followed by 10 mg/day for 2 days); orally; once daily	

Arm title	Children, 20 mg cohort

Arm description:

6 children (7-11 yr). 20 mg tablets for 14 days.

Arm type	Experimental
Investigational medicinal product name	Vortioxetine
Investigational medicinal product code	
Other name	Lu AA21004, Brintellix®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

20 mg tablets for 14 days (initial up-titration 5 mg/day for 2 days followed by 10 mg/day for 2 days and 15 mg/day for 2 days); orally; once daily

Number of subjects in period 1	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort
Started	6	6	6
Completed	5	6	6
Not completed	1	0	0
Lost to follow-up	1	-	-

Number of subjects in period 1	Adolescents, 20 mg cohort	Children, 5 mg cohort	Children, 10 mg cohort
Started	6	6	6
Completed	6	6	6
Not completed	0	0	0
Lost to follow-up	-	-	-

Number of subjects in period 1	Children, 15 mg cohort	Children, 20 mg cohort
Started	6	6
Completed	6	6
Not completed	0	0
Lost to follow-up	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Adolescents, 5 mg cohort
Reporting group description:	
6 adolescents (12-17 yr). 5 mg tablets for 14 days.	
Reporting group title	Adolescents, 10 mg cohort
Reporting group description:	
6 adolescents (12-17 yr). 10 mg tablets for 14 days.	
Reporting group title	Adolescents, 15 mg cohort
Reporting group description:	
6 adolescents (12-17 yr). 15 mg tablets for 14 days.	
Reporting group title	Adolescents, 20 mg cohort
Reporting group description:	
6 adolescents (12-17 yr). 20 mg tablets for 14 days.	
Reporting group title	Children, 5 mg cohort
Reporting group description:	
6 children (7-11 yr). 5 mg tablets for 14 days.	
Reporting group title	Children, 10 mg cohort
Reporting group description:	
6 children (7-11 yr). 10 mg tablets for 14 days.	
Reporting group title	Children, 15 mg cohort
Reporting group description:	
6 children (7-11 yr). 15 mg tablets for 14 days.	
Reporting group title	Children, 20 mg cohort
Reporting group description:	
6 children (7-11 yr). 20 mg tablets for 14 days.	

Reporting group values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort
Number of subjects	6	6	6
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	15.7	15.3	15.2
standard deviation	± 1.9	± 1.9	± 1.2

Gender categorical Units: Subjects			
Female	3	3	5
Male	3	3	1

Reporting group values	Adolescents, 20 mg cohort	Children, 5 mg cohort	Children, 10 mg cohort
Number of subjects	6	6	6
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: years			
arithmetic mean	14.8	10.3	9.7
standard deviation	± 1.9	± 1.2	± 1.2
Gender categorical Units: Subjects			
Female	4	3	3
Male	2	3	3

Reporting group values	Children, 15 mg cohort	Children, 20 mg cohort	Total
Number of subjects	6	6	48
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age continuous Units: years			
arithmetic mean	10.5	9.8	
standard deviation	± 0.8	± 1.8	-
Gender categorical Units: Subjects			
Female	2	2	25
Male	4	4	23

End points

End points reporting groups

Reporting group title	Adolescents, 5 mg cohort
Reporting group description: 6 adolescents (12-17 yr). 5 mg tablets for 14 days.	
Reporting group title	Adolescents, 10 mg cohort
Reporting group description: 6 adolescents (12-17 yr). 10 mg tablets for 14 days.	
Reporting group title	Adolescents, 15 mg cohort
Reporting group description: 6 adolescents (12-17 yr). 15 mg tablets for 14 days.	
Reporting group title	Adolescents, 20 mg cohort
Reporting group description: 6 adolescents (12-17 yr). 20 mg tablets for 14 days.	
Reporting group title	Children, 5 mg cohort
Reporting group description: 6 children (7-11 yr). 5 mg tablets for 14 days.	
Reporting group title	Children, 10 mg cohort
Reporting group description: 6 children (7-11 yr). 10 mg tablets for 14 days.	
Reporting group title	Children, 15 mg cohort
Reporting group description: 6 children (7-11 yr). 15 mg tablets for 14 days.	
Reporting group title	Children, 20 mg cohort
Reporting group description: 6 children (7-11 yr). 20 mg tablets for 14 days.	

Primary: Cmax of vortioxetine

End point title	Cmax of vortioxetine[1]
End point description: Maximum plasma concentration of vortioxetine	
End point type	Primary
End point timeframe: Day 14-20, depending on assigned dose level	

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 comparison between parameter was performed. Only descriptive statistics are presented here

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: ng/mL				
median (standard deviation)	4.3 (± 3.7)	7.8 (± 2.8)	15 (± 6.2)	16 (± 8.1)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ng/mL				
median (standard deviation)	5 (± 3.3)	14 (± 8.2)	26 (± 21)	31 (± 20)

Statistical analyses

No statistical analyses for this end point

Primary: AUC(0-24h) of vortioxetine

End point title	AUC(0-24h) of vortioxetine[2]

End point description:

Area under the vortioxetine plasma concentration

End point type	Primary

End point timeframe:

Day 14, 16, 18 or 20, depending on assigned dose level

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 comparison between parameter was performed. Only descriptive statistics are presented here

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: ng*h/mL				
median (standard deviation)	82 (± 71)	144 (± 60)	283 (± 115)	304 (± 143)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ng*h/mL				
median (standard deviation)	89 (± 66)	261 (± 137)	492 (± 373)	562 (± 374)

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 of vortioxetine

End point title	t1/2 of vortioxetine[3]

End point description:

Half-life of vortioxetine in plasma

End point type	Primary

End point timeframe:

Day 14, 16, 18 or 20, depending on assigned dose level

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 comparison between parameter was performed. Only descriptive statistics are presented here

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: hour				
median (standard deviation)	46 (± 33)	56 (± 19)	50 (± 16)	40 (± 10)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hour				
median (standard deviation)	45 (± 27)	52 (± 18)	71 (± 52)	62 (± 23)

Statistical analyses

No statistical analyses for this end point

Primary: Cmax of Lu AA34443

End point title	Cmax of Lu AA34443[4]

End point description:

Maximum plasma concentration of Lu AA34443 (the major inactive metabolite)

End point type	Primary

End point timeframe:

Day 14, 16, 18 or 20, depending on assigned dose level

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 comparison between parameter was performed. Only descriptive statistics are presented here

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: ng/mL				
median (standard deviation)	3.5 (± 2.2)	14 (± 7.1)	16 (± 5.3)	38 (± 12)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ng/mL				
median (standard deviation)	7.8 (± 3.4)	15 (± 5.4)	20 (± 13)	47 (± 17)

Statistical analyses

No statistical analyses for this end point

Primary: AUC(0-24h) of Lu AA34443

End point title	AUC(0-24h) of Lu AA34443[5]

End point description:

Area under the Lu AA34443 (the major inactive metabolite) plasma concentration curve

End point type	Primary

End point timeframe:

Day 14, 16, 18 or 20, depending on assigned dose level

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 comparison between parameter was performed. Only descriptive statistics are presented here.

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: ng*h/mL				
median (standard deviation)	56 (± 29)	223 (± 98)	266 (± 100)	544 (± 192)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: ng*h/mL				
median (standard deviation)	115 (± 47)	241 (± 93)	429 (± 232)	646 (± 251)

Statistical analyses

No statistical analyses for this end point

Primary: t1/2 of Lu AA34443

End point title	t1/2 of Lu AA34443[6]

End point description:

Half-life of Lu AA34443 (the major inactive metabolite) in plasma

End point type	Primary

End point timeframe:

Day 14, 16, 18 or 20, depending on assigned dose level

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparison between parameter was performed. Only descriptive statistics are presented here

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: hour				
median (standard deviation)	26 (± 9.3)	33 (± 13)	24 (± 11)	24 (± 5.1)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: hour				
median (standard deviation)	20 (± 24)	19 (± 9.6)	29 (± 6.1)	27 (± 8.8)

Statistical analyses

No statistical analyses for this end point

Primary: Oral clearance (CL/F) of vortioxetine

End point title	Oral clearance (CL/F) of vortioxetine[7]

End point description:

oral clearance expressed as a function of bioavailability

End point type	Primary

End point timeframe:

Day 14, 16, 18 or 20, depending on assigned dose level

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No comparison between parameter was performed. Only descriptive statistics are presented here

End point values	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort	Adolescents, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	6	6	6
Units: L/h				
median (standard deviation)	60 (± 55)	50 (± 16)	50 (± 23)	61 (± 20)

End point values	Children, 5 mg cohort	Children, 10 mg cohort	Children, 15 mg cohort	Children, 20 mg cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	6	6
Units: L/h				
median (standard deviation)	50 (± 16)	42 (± 25)	29 (± 33)	34 (± 17)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
First dose to follow-up	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Adolescents, 5 mg cohort
Reporting group description: -	
Reporting group title	Adolescents, 10 mg cohort
Reporting group description: -	
Reporting group title	Adolescents, 15 mg cohort
Reporting group description: -	
Reporting group title	Adolescents, 20 mg cohort
Reporting group description: -	
Reporting group title	Children, 5 mg cohort
Reporting group description: -	
Reporting group title	Children, 10 mg cohort
Reporting group description: -	
Reporting group title	Children, 15 mg cohort
Reporting group description: -	
Reporting group title	Children, 20 mg cohort
Reporting group description: -	

Serious adverse events	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Adolescents, 20 mg cohort	Children, 5 mg cohort	Children, 10 mg cohort
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Children, 15 mg cohort	Children, 20 mg cohort	

Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Adolescents, 5 mg cohort	Adolescents, 10 mg cohort	Adolescents, 15 mg cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 6 (66.67%)	4 / 6 (66.67%)	5 / 6 (83.33%)
Vascular disorders			
Hot flush			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	2	2	0
Infusion site pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Irritability			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	6	0	0
Pyrexia			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Frustration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hostility			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Restlessness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
White blood cells urine positive			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Ligament sprain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sunburn			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Akathisia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	3	1	2
Psychomotor hyperactivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Sedation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	1	1	3
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	3	1	6
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash generalised			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash macular			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Streptococcal infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Increased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pica			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Adolescents, 20 mg cohort	Children, 5 mg cohort	Children, 10 mg cohort
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	5 / 6 (83.33%)	5 / 6 (83.33%)
Vascular disorders			
Hot flush			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chills			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Infusion site pain			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Irritability			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Frustration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hostility			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Initial insomnia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Restlessness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			

White blood cells urine positive			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Ligament sprain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sunburn			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nervous system disorders			
Akathisia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Psychomotor hyperactivity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sedation			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 6 (33.33%)	3 / 6 (50.00%)	0 / 6 (0.00%)
occurrences (all)	2	3	0
Tremor			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Abdominal pain upper			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	3 / 6 (50.00%)	1 / 6 (16.67%)
occurrences (all)	0	5	2
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 6 (33.33%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	5	2	0
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Photosensitivity reaction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Rash generalised			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rash macular			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pollakiuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pharyngotonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Streptococcal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Increased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pica			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Children, 15 mg cohort	Children, 20 mg cohort	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	4 / 6 (66.67%)	
Vascular disorders			
Hot flush			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			

Chills			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Fatigue			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Infusion site pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Irritability			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Pyrexia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Frustration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Hostility			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Initial insomnia			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Restlessness			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Investigations			
White blood cells urine positive			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Ligament sprain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Sunburn			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Akathisia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Dizziness			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Headache			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	
occurrences (all)	3	1	
Psychomotor hyperactivity			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Sedation			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Tremor			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 6 (50.00%)	0 / 6 (0.00%)	
occurrences (all)	4	0	
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Toothache			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 6 (50.00%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Skin and subcutaneous tissue disorders			
Photosensitivity reaction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rash generalised			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Rash macular			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Urticaria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Dysuria			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Pharyngotonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Streptococcal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Increased appetite			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 6 (0.00%)	
occurrences (all)	0	0	
Pica			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2013	Visits 6 and 8: phone calls were replaced by visits to the clinic. Visit 9: new visit to the clinic added. PAERS, C-SSRS and vital signs assessments were added to Visits 6, 8, and 9. Confirmatory screening (re-screening for a different cohort) added. Comments/exceptions for Stimulants and other ADHD medications in the list of disallowed recent and concomitant medication was amended.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported