Clinical trial results:
Single Center, Therapeutic Exploratory Clinical Trial to Evaluate the Safety of Sodium Oxybate (Xyrem) 500 mg/mL Oral Solution on Potential Endocrine Changes at Currently Labeled Therapeutic Dose Regimens (4.5 - 9 g/Day Divided Into Two Equal Doses) During 12 Weeks of Treatment of Cataplexy in Adult Patients With Narcolepsy

Summary

EudraCT number	2005-004417-15
Trial protocol	BE
Global end of trial date	22 January 2008

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	14 June 2015

Trial information

Trial identification

Sponsor protocol code	C00301

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00345800
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma SA
Sponsor organisation address	Chemin du Foriest, Braine-l'Alleud, Belgium, B-1420
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 2173 4815 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 +49 2173 48 15 15, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 April 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 January 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

• To monitor for endocrine changes in response to treatment of cataplexy with Xyrem
• To focus on the hypothalamic pituitary axis

Protection of trial subjects:

Not applicable

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	10 April 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 25
Worldwide total number of subjects	25
EEA total number of subjects	25

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	1
Adults (18-64 years)	23
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This single-Center, therapeutic, exploratory study started to enroll subjects in April 2006.

Pre-assignment

Screening details:

Participant Flow refers to the Intention-to-Treat (ITT) population consisting of the 25 subjects enrolled in the study who took at least 1 dose of study medication.

Period 1

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

Arms

Arm title	Sodium Oxybate

Arm description:

Active Substance: Sodium Oxybate Pharmaceutical form: Oral Solution Concentration: 500 mg/mL oral solution from 4.5 to 9 g/day divided into two equal doses during 12 weeks Route of administration: Oral

Arm type	Experimental
Investigational medicinal product name	Sodium Oxybate
Investigational medicinal product code	Sodium Oxybate
Other name	Xyrem
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Active Substance: Sodium Oxybate
Concentration: 500 mg/mL oral solution from 4.5 to 9 g/day divided into two equal doses during 12 weeks

Number of subjects in period 1	Sodium Oxybate
Started	25
Completed	25

Baseline characteristics

Reporting groups	
Reporting group title	Sodium Oxybate
Reporting group description:	
Active Substance: Sodium Oxybate Pharmaceutical form: Oral Solution Concentration: 500 mg/mL oral solution from 4.5 to 9 g/day divided into two equal doses during 12 weeks Route of administration: Oral	

Reporting group values	Sodium Oxybate	Total	
Number of subjects	25	25	
Age Categorical Units: Subjects			
Adolescents (12-17 years)	1	1	
Adults (18-64 years)	23	23	
From 65-84 years	1	1	
Age Continuous Units:			
arithmetic mean	38.99		
standard deviation	± 13.94	-	
Gender Categorical Units: Subjects			
Male	13	13	
Female	12	12	

End points

End points reporting groups

Reporting group title	Sodium Oxybate

Reporting group description:

Active Substance: Sodium Oxybate Pharmaceutical form: Oral Solution Concentration: 500 mg/mL oral solution from 4.5 to 9 g/day divided into two equal doses during 12 weeks Route of administration: Oral

Primary: The insulin-like growth factor 1 (IGF-1) measured in fasting conditions at Baseline (Visit 2)

End point title	The insulin-like growth factor 1 (IGF-1) measured in fasting conditions at Baseline (Visit 2)[1]

End point description:

An assay of IGF-1 was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Primary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

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 confirmatory statistical hypothesis testing was planned for this study.

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	207.4 (± 86.5)			

Statistical analyses

No statistical analyses for this end point

Primary: The insulin-like growth factor 1 (IGF-1) measured in fasting conditions after 1 month of treatment (Visit 3)

End point title	The insulin-like growth factor 1 (IGF-1) measured in fasting conditions after 1 month of treatment (Visit 3)[2]

End point description:

An assay of IGF-1 was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Primary

End point timeframe:

After 1 month of treatment (Visit 3)

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 confirmatory statistical hypothesis testing was planned for this study.

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	200.4 (± 77.7)			

Statistical analyses

No statistical analyses for this end point

Primary: The insulin-like growth factor 1 (IGF-1) measured in fasting conditions after 3 months of treatment (Visit 4)

End point title	The insulin-like growth factor 1 (IGF-1) measured in fasting conditions after 3 months of treatment (Visit 4)[3]

End point description:

An assay of IGF-1 was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Primary

End point timeframe:

After 3 months of treatment (Visit 4)

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 confirmatory statistical hypothesis testing was planned for this study.

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	210.2 (± 90.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: The circadian rhythm of the growth hormone (GH) measured at Baseline (Visit 2)

End point title	The circadian rhythm of the growth hormone (GH) measured at Baseline (Visit 2)

End point description:

Blood was sampled at Baseline (Visit 2) at bedtime 10:00 pm and 1, 2, 4, 8, 12, 16, and 20 hours after bedtime for assaying GH.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
arithmetic mean (standard deviation)				
Bed time	1.821 (± 4.844)			
1h	1.225 (± 2.895)			
2h	1.408 (± 1.656)			
4h	1.236 (± 1.904)			
8h	0.576 (± 0.632)			
12h	0.293 (± 0.31)			
16h	0.309 (± 0.282)			
20h	0.313 (± 0.362)			

Statistical analyses

No statistical analyses for this end point

Secondary: The circadian rhythm of the growth hormone (GH) measured at Visit 3

End point title	The circadian rhythm of the growth hormone (GH) measured at Visit 3

End point description:

Blood was sampled predose and 1, 2, 4, 8, 12, 16, and 20 hours postdose at Visit 3 for assaying GH.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
arithmetic mean (standard deviation)				
Pre-dose	2.432 (± 7.118)			
1h	5.914 (± 9.743)			
2h	5.238 (± 8.557)			

4h	3.018 (± 4.332)			
8h	0.256 (± 0.326)			
12h	0.308 (± 0.664)			
16h	0.46 (± 0.767)			
20h	0.306 (± 0.342)			

Statistical analyses

No statistical analyses for this end point

Secondary: The circadian rhythm of the growth hormone (GH) measured at Visit 4

End point title	The circadian rhythm of the growth hormone (GH) measured at Visit 4

End point description:

Blood was sampled predose and 1, 2, 4, 8, 12, 16, and 20 hours postdose at Visit 4 for assaying GH.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ng/mL				
arithmetic mean (standard deviation)				
Pre-dose	0.816 (± 1.372)			
1h	3.804 (± 3.173)			
2h	3.864 (± 5.731)			
4h	2.712 (± 3.178)			
8h	0.224 (± 0.292)			
12h	0.42 (± 1.355)			
16h	0.296 (± 0.491)			
20h	0.244 (± 0.39)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cortisol measured at Baseline (Visit 2)

End point title	Cortisol measured at Baseline (Visit 2)

End point description:

Blood was sampled at Baseline (Visit 2) at bedtime 10:00 pm and 1, 2, 4, 8, 12, 16, and 20 hours after bedtime for assaying cortisol.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ug/L				
arithmetic mean (standard deviation)				
Bed time	42.21 (± 28.53)			
1h	27.91 (± 17.09)			
2h	22.8 (± 14.54)			
4h	36.06 (± 28.46)			
8h	115.79 (± 52.33)			
12h	143.39 (± 70.67)			
16h	90.84 (± 34.83)			
20h	68.48 (± 40.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cortisol measured at Visit 3

End point title	Cortisol measured at Visit 3

End point description:

Blood was sampled predose and and 1, 2, 4, 8, 12, 16, and 20 hours postdose at Visit 3 for assaying cortisol.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ug/L				
arithmetic mean (standard deviation)				
Pre-dose	35.84 (± 27.83)			
1h	24.75 (± 18.2)			
2h	34.62 (± 31.93)			
4h	44.28 (± 36.64)			
8h	95.61 (± 57.14)			
12h	130.21 (± 61.28)			
16h	77.33 (± 32.93)			
20h	70.49 (± 33.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Cortisol measured at Visit 4

End point title	Cortisol measured at Visit 4

End point description:

Blood was sampled predose and 1, 2, 4, 8, 12, 16, and 20 hours postdose at Visit 4 for assaying cortisol.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ug/L				
arithmetic mean (standard deviation)				
Pre-dose	34.46 (± 24.85)			
1h	25.61 (± 19.06)			
2h	30.06 (± 24.4)			
4h	45.27 (± 35.65)			
8h	113.84 (± 71.18)			

12h	146.33 (± 64.42)			
16h	92.48 (± 30.94)			
20h	75.55 (± 38.01)			

Statistical analyses

No statistical analyses for this end point

Secondary: The adrenocorticotropic hormone (ACTH) measured in fasting conditions at Baseline (Visit 2)

End point title	The adrenocorticotropic hormone (ACTH) measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of ACTH was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: pg/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	65.6 (± 46.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: The adrenocorticotropic hormone (ACTH) measured in fasting conditions at Visit 3

End point title	The adrenocorticotropic hormone (ACTH) measured in fasting conditions at Visit 3

End point description:

An assay of ACTH was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: pg/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	62.8 (± 37.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: The adrenocorticotropic hormone (ACTH) measured in fasting conditions at Visit 4

End point title	The adrenocorticotropic hormone (ACTH) measured in fasting conditions at Visit 4

End point description:

An assay of ACTH was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: pg/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	54.8 (± 27.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: The dehydroepiandrosterone sulfate (DHEA-S) measured in fasting conditions at Baseline (Visit 2)

End point title	The dehydroepiandrosterone sulfate (DHEA-S) measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of DHEA-S was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ug/L				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	1988.2 (± 1283.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: The dehydroepiandrosterone sulfate (DHEA-S) measured in fasting conditions at Visit 3

End point title	The dehydroepiandrosterone sulfate (DHEA-S) measured in fasting conditions at Visit 3

End point description:

An assay of DHEA-S was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ug/L				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	2200.9 (± 1517.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: The dehydroepiandrosterone sulfate (DHEA-S) measured in fasting conditions at Visit 4

End point title	The dehydroepiandrosterone sulfate (DHEA-S) measured in fasting conditions at Visit 4

End point description:

An assay of DHEA-S was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: ug/L				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	2130.7 (± 1450.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: The prolactin measured in fasting conditions at Baseline (Visit 2)

End point title	The prolactin measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of prolactin was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mUI/L				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	356.8 (± 185.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: The prolactin measured in fasting conditions at Visit 3

End point title	The prolactin measured in fasting conditions at Visit 3

End point description:

An assay of prolactin was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mUI/L				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	280 (± 162.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: The prolactin measured in fasting conditions at Visit 4

End point title	The prolactin measured in fasting conditions at Visit 4

End point description:

An assay of prolactin was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mUI/L				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	258.4 (± 113.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: The thyroid stimulating hormone (TSH) measured in fasting conditions at Baseline (Visit 2)

End point title	The thyroid stimulating hormone (TSH) measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of TSH was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: uU/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	1.366 (± 0.622)			

Statistical analyses

No statistical analyses for this end point

Secondary: The thyroid stimulating hormone (TSH) measured in fasting conditions at Visit 3

End point title	The thyroid stimulating hormone (TSH) measured in fasting conditions at Visit 3

End point description:

An assay of TSH was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: uU/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	1.292 (± 0.599)			

Statistical analyses

No statistical analyses for this end point

Secondary: The thyroid stimulating hormone (TSH) measured in fasting conditions

at Visit 4

End point title	The thyroid stimulating hormone (TSH) measured in fasting conditions at Visit 4

End point description:

An assay of TSH was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: uU/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	1.425 (± 0.818)			

Statistical analyses

No statistical analyses for this end point

Secondary: The total thyroxin (T4) measured in fasting conditions at Baseline (Visit 2)

End point title	The total thyroxin (T4) measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of T4 was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: pg/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	11.34 (± 1.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: The total thyroxin (T4) measured in fasting conditions at Visit 3

End point title	The total thyroxin (T4) measured in fasting conditions at Visit 3

End point description:

An assay of T4 was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: pg/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	11.47 (± 2.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: The total thyroxin (T4) measured in fasting conditions at Visit 4

End point title	The total thyroxin (T4) measured in fasting conditions at Visit 4

End point description:

An assay of T4 was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: pg/mL				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	11.65 (± 1.78)			

Statistical analyses

No statistical analyses for this end point

Secondary: The osmolality measured in fasting conditions at Baseline (Visit 2)

End point title	The osmolality measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of osmolality was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mosm/kg				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	291.6 (± 4.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: The osmolality measured in fasting conditions at Visit 3

End point title	The osmolality measured in fasting conditions at Visit 3

End point description:

An assay of osmolality was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mosm/kg				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	292.2 (± 4.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: The osmolality measured in fasting conditions at Visit 4

End point title	The osmolality measured in fasting conditions at Visit 4

End point description:

An assay of osmolality was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mosm/kg				
arithmetic mean (standard deviation)				
arithmetic mean (standard deviation)	292.1 (± 5.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Electrolytes (Na, K, Ca, P) measured in fasting conditions at Baseline (Visit 2)

End point title	Electrolytes (Na, K, Ca, P) measured in fasting conditions at Baseline (Visit 2)

End point description:

An assay of electrolytes (Na, K, Ca, P) was done from blood sampled about 10 hours after bedtime on Visit 2.

End point type	Secondary

End point timeframe:

Baseline (Visit 2) - approximately 1 day

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mmol/L and mg/L				
arithmetic mean (standard deviation)				
Na (Sodium in mmol/L)	141.4 (± 1.9)			
K (Potassium in mmol/L)	3.88 (± 0.21)			
Ca (Calcium in mmol/L)	2.257 (± 0.084)			
P (Phosphate in mg/L)	34.4 (± 6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Electrolytes (Na, K, Ca, P) measured in fasting conditions at Visit 3

End point title	Electrolytes (Na, K, Ca, P) measured in fasting conditions at Visit 3

End point description:

An assay of electrolytes (Na, K, Ca, P) was done from blood sampled about 10 hours postdose on Visit 3.

End point type	Secondary

End point timeframe:

Visit 3 (approximately 1 month)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mmol/L and mg/L				
arithmetic mean (standard deviation)				
Na (Sodium in mmol/L)	141.9 (± 2.1)			
K (Potassium in mmol/L)	3.9 (± 0.25)			
Ca (Calcium in mmol/L)	2.334 (± 0.071)			
P (Phosphate in mg/L)	34.2 (± 4.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Electrolytes (Na, K, Ca, P) measured in fasting conditions at Visit 4

End point title	Electrolytes (Na, K, Ca, P) measured in fasting conditions at Visit 4

End point description:

An assay of electrolytes (Na, K, Ca, P) was done from blood sampled about 10 hours postdose on Visit 4.

End point type	Secondary

End point timeframe:

Visit 4 (approximately 3 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: mmol/L and mg/L				
arithmetic mean (standard deviation)				
Na (Sodium in mmol/L)	141.2 (± 1.9)			
K (Potassium in mmol/L)	3.8 (± 0.27)			
Ca (Calcium in mmol/L)	2.29 (± 0.063)			
P (Phosphate in mg/L)	35 (± 3.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: The number of patients reporting at least one Adverse Event (AE) during the course of the study

End point title	The number of patients reporting at least one Adverse Event (AE) during the course of the study

End point description:

An AE was classified as a treatment-emergent AE (TEAE) if its onset date and time was on or after the first study drug administration.
Number of subjects with at least one TEAE is reported below.

End point type	Secondary

End point timeframe:

Visit 1 through the end of the study (approximately 4 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants				
Number of subjects	20			

Statistical analyses

No statistical analyses for this end point

Secondary: The number of patient withdrawal due to Adverse Events (AEs) during the course of the study

End point title	The number of patient withdrawal due to Adverse Events (AEs) during the course of the study

End point description:

An AE was classified as a treatment-emergent AE (TEAE) if its onset date and time was on or after the first study drug administration.
Number of subjects with TEAE that led to temporarily discontinuation of study drug is reported below.

End point type	Secondary

End point timeframe:

Visit 1 through the end of the study (approximately 4 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants				
Number of subjects	1			

Statistical analyses

No statistical analyses for this end point

Secondary: The number of patients reporting at least one Serious Adverse Event (SAE) during the course of the study

End point title	The number of patients reporting at least one Serious Adverse Event (SAE) during the course of the study

End point description:

A Serious Adverse Event is any untoward medical occurrence that at any dose
- results in death,
- is life threatening,
- requires in-patient hospitalization or prolongation of existing hospitalization,
- results in persistent or significant disability/incapacity
- is a congenital anomaly/birth defect

End point type	Secondary

End point timeframe:

Visit 1 through the end of the study (approximately 4 months)

End point values	Sodium Oxybate			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Participants				
Number of subjects	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Visit 1 through the end of the study (approximately 4 months).

Adverse event reporting additional description:

Adverse Events refer to the Safety Population which is identical to the Intention-to-Treat (ITT) population consisting of the 25 subjects enrolled in the study who took at least 1 dose of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.0

Reporting groups

Reporting group title	Sodium Oxybate

Reporting group description:

Active Substance: Sodium Oxybate
Pharmaceutical form: Oral Solution
Concentration: 500 mg/mL oral solution from 4.5 to 9 g/day divided into two equal doses during 12 weeks
Route of administration: Oral

Serious adverse events	Sodium Oxybate		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Rectal haemorrhage			
subjects affected / exposed	1 / 25 (4.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Sodium Oxybate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 25 (60.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	6 / 25 (24.00%)		
occurrences (all)	8		

Dizziness subjects affected / exposed occurrences (all)	2 / 25 (8.00%) 2		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all)	 5 / 25 (20.00%) 7 3 / 25 (12.00%) 7 2 / 25 (8.00%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 2 / 25 (8.00%) 3		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	 2 / 25 (8.00%) 2		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	 2 / 25 (8.00%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all)	 2 / 25 (8.00%) 2 2 / 25 (8.00%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 July 2007	The study protocol was amended on 24-Jul-2007 because of supply chain issues with the medications of the named patient program. The Discharge Visit, normally foreseen at the end of the last confinement period (Visit 4), was postponed for the subjects having benefited from the Xyrem treatment, to allow them to remain on medication. According to protocol, assays of IGF-1, ACTH, DHEA-S, prolactin, TSH, T4, and electrolytes at Baseline, Month 1 and Month 3 Visits were to be performed from blood sampled about 8 hours after bedtime dose (around 6:00 am). In the study, blood was sampled around 8:00 am (about 10 hours after bedtime dose).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported