# Clinical trial results:
# An Open-label, Extension Study to Assess the Long-Term Safety of Twice Daily Oxycodone Hydrochloride Controlled-release Tablets in Opioid Experienced Children Who Completed the OTR3001 Study

## Summary

| | |
|---|---|
| EudraCT number | 2011-002235-26 |
| Trial protocol | SE EE ES FI DE GR GB SK BE HU PL |
| Global end of trial date | 09 December 2013 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 21 July 2016 |
| First version publication date | 07 August 2015 |
| Summary attachment (see zip file) | OTR3002 Study report Synopsis (otr3002-synopsis.pdf) |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | OTR3002 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01369615 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Purdue Pharma L.P |
| Sponsor organisation address | One Stamford Forum, Stamford, United States, CT 06901-3431 |
| Public contact | Purdue Pediatric Call Centre, PRA International, +1 434 951 4115, PurduePediatric@praintl.com |
| Scientific contact | Purdue Pediatric Call Centre, PRA International, +1 434 951 4115, PurduePediatric@praintl.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 | 04 September 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 09 December 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 December 2013 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

To characterize the long-term safety of oxycodone HCl CR tablets in opioid experienced pediatric patients aged 6 to 17 years, inclusive, with moderate to severe malignant and/or non malignant pain requiring opioid therapy who completed the 4 -week treatment period in OTR3001.

Protection of trial subjects:

The DMC met periodically during the course of the study to review safety data and make recommendations to Purdue Pharma L.P. regarding early stopping of the study, continuation of the study, or modification of the study protocol, as needed.

Background therapy:

NA

Evidence for comparator:

NA

| | |
|---|---|
| Actual start date of recruitment | 05 January 2012 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Israel: 1 |
| Country: Number of subjects enrolled | United States: 22 |
| Worldwide total number of subjects | 23 |
| EEA total number of subjects | 0 |

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) | 9 |
| Adolescents (12-17 years) | 14 |
| Adults (18-64 years) | 0 |

| | |
|---|---|
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

First patient First Visit: 05 January 2012; Last Patient Last Visit: 09 December 2013. The study was conducted at 14 medical /research sites in the United States and Israel

### Pre-assignment

Screening details:

Opioid-experienced pediatric patients with moderate ot severe malignant and/or nonmalignant pain requiring around the clock opioid therapy were eligible for open-lable Extension Study OTR3002 if they completed the 4-week treatment period Core Study OTR3001 and could benefit from continued treatment with oxycodone HCI CR 20 to 240 mg total daily

### Period 1

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

Blinding implementation details:

This was an open lable study potential subjects were assigned a subject number at the time of screening

### Arms

| | |
|---|---|
| **Arm title** | Open label treatment |

Arm description:

Twice Daily Oxycodone Hydrochloride Controlled-release Tablets

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Oxycodone Hydrochloride Twice Daily Controlled-release |
| Investigational medicinal product code | Oxycodone HCl CR |
| Other name | NA |
| Pharmaceutical forms | Prolonged-release tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Oxycodone HCl controlled-release (CR) twice daily tablets, at strengths of 10, 15, 20, 30, or 40 mg (20 to 240 mg daily), every 12 hours taken orally with water

| **Number of subjects in period 1** | Open label treatment |
|---|---|
| Started | 23 |
| Completed | 21 |
| Not completed | 2 |
| Consent withdrawn by subject | 1 |
| Lost to follow-up | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Overall Study |

Reporting group description: -

| Reporting group values | Overall Study | Total | |
|---|---|---|---|
| Number of subjects | 23 | 23 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 9 | 9 | |
| Adolescents (12-17 years) | 14 | 14 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 12.6 | | |
| standard deviation | ± 2.69 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 13 | 13 | |
| Male | 10 | 10 | |
| Race/Ethnicity<br>Units: Subjects | | | |
| White | 16 | 16 | |
| Black or African American | 7 | 7 | |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | age group 6 to <12 years of age |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Children 6 to <12 years of age | |
| Subject analysis set title | age group >=12 to <=16 years of age |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Children 12 to <=16 years of age | |

| Reporting group values | age group 6 to <12 years of age | age group >=12 to <=16 years of age | |
|---|---|---|---|
| Number of subjects | 9 | 14 | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 9 | 0 | |
| Adolescents (12-17 years) | 0 | 14 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 9.9 | 14.3 | |
| standard deviation | ± 1.76 | ± 1.49 | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 6 | 7 | |
| Male | 3 | 7 | |
| Race/Ethnicity<br>Units: Subjects | | | |
| White | 6 | 10 | |
| Black or African American | 3 | 4 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Open label treatment |
| Reporting group description:<br>Twice Daily Oxycodone Hydrochloride Controlled-release Tablets | |
| Subject analysis set title | age group 6 to <12 years of age |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Children 6 to <12 years of age | |
| Subject analysis set title | age group >=12 to <=16 years of age |
| Subject analysis set type | Safety analysis |
| Subject analysis set description:<br>Children 12 to <=16 years of age | |

### Primary: Number of patients with adverse events as a mesure of safety

| | |
|---|---|
| End point title | Number of patients with adverse events as a mesure of |

End point description:

Safety assessments included adverse events ( AEs), vital sign measurements, clinical laboratory test results, and somnolence ( University of Michigan Sedation Scale (UMSS)). Safety variables were summarized descriptively within age group for the extension safety population

| | |
|---|---|
| End point type | Primary |

End point timeframe:

Up to 6 months ( during the study) and 7-10 days poststudy ( safety follow-up assessment)

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 comparative inferential analysis is performed for the data from this open-lable study in wich all patients receive oxycodone HCI CR treatment. No adjustments for covariates are necessary for the analysis of this study. Data will be summarized overall and by age group where appropriate

| End point values | age group 6 to <12 years of age | age group >=12 to <=16 years of age | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 9 | 14 | | |
| Units: participants | | | | |
| Serious adverse events | 3 | 2 | | |
| All other AE in more or equal than 5% of patients | 8 | 8 | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were reported from start of study participation through the period beyond study completion.

Adverse event reporting additional description:

AEs were learned of through spontaneous reports and/or patient interview, or were observed during physical examinations or other safety assessments. Ongoing AEs were followed until resolution/30 days after last study drug dose. SAEs up to 30 days following the last study drug visit were followed until the AE or sequelae resolved or stabilized

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 13.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | 6 to < 12 years |

Reporting group description:

children 6 to < 12 years

| | |
|---|---|
| Reporting group title | >=12 to <=16 years |

Reporting group description:

Children >=12 to <=16 years

| Serious adverse events | 6 to < 12 years | >=12 to <=16 years | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 2 / 14 (14.29%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Congenital, familial and genetic disorders | | | |
| Sickle cell anaemia with crisis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | 6 to < 12 years | >=12 to <=16 years | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 9 (88.89%) | 8 / 14 (57.14%) | |
| Vascular disorders | | | |
| flushing | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Surgical and medical procedures | | | |

| | | | |
|---|---|---|---|
| Scar excision | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| General disorders and administration site conditions | | | |
| Adverse drug reaction | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Cyst | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Fatigue | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 2 | |
| Inflammation | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 9 (33.33%) | 2 / 14 (14.29%) | |
| occurrences (all) | 4 | 2 | |
| Immune system disorders | | | |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| atelectasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| dyspnoea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |

| | | | |
|---|---|---|---|
| Epistaxis | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Respiratory depression | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Psychiatric disorders | | | |
| Depression | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Oxygen saturation decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Platelet count decreased | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Respiratory rate | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Transaminases increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| weight decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Congenital, familial and genetic disorders | | | |
| Sickle cell anaemia with crisis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 1 | |
| Nervous system disorders | | | |
| Headache | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 4 | |
| Sedation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 2 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Ear and labyrinth disorders | | | |
| Auricular swelling | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| External ear pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |

| | | | |
|---|---|---|---|
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Mydriasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 3 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 3 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 1 / 14 (7.14%) | |
| occurrences (all) | 1 | 4 | |
| Oral pain | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 9 (22.22%) | 2 / 14 (14.29%) | |
| occurrences (all) | 3 | 3 | |
| Skin and subcutaneous tissue disorders | | | |
| dry skin | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Photosensitivity reaction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 2 | 1 | |
| Rash | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Scar | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Seborrhoea | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Sinusitis | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| urinary tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 1 | |
| Vaginal infection | | | |
| subjects affected / exposed | 0 / 9 (0.00%) | 1 / 14 (7.14%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypocalcaemia | | | |
| subjects affected / exposed | 1 / 9 (11.11%) | 0 / 14 (0.00%) | |
| occurrences (all) | 1 | 0 | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 28 June 2011 | A. Provide more specific instructions for post-study opioid management, including a tapering procedure for patients no longer requiring opioid treatment and a method of conversion to other opioids.<br>B. Provide specific instructions for down-titration during the study to avoid potential opioid withdrawal syndrome. |
| 24 January 2012 | A. To increase the number of patients from 135 to 154 to account for the total number of patients required to be exposed to oxycodone for the evaluation of the safety of oxycodone in children, including all studies in the program.<br>B. To clarify that only a limited number of patients were expected to complete OTR3001 and enter OTR3002.<br>C. Based on spontaneous post-marketing reports, including reports of intestinal obstruction and exacerbation of diverticulitis, warnings and precautions were added to the OxyContin® package insert in Oct 2011 advising physicians to use caution when prescribing OxyContin® to patients who have an underlying gastrointestinal disorder<br>predisposing them to obstruction. To ensure adherence with the guidelines added to the package insert, similar language was included in the exclusion criteria such that patients who were predisposed to these types of conditions would not be enrolled into the study.<br>D. To correct an error and clarify that somnolence assessments would be performed by the parents/caregivers, rather than the patients.<br>E. To modify the values used to define ranges of bilirubin displayed in listings to be more inclusive and provide information on more patients with potentially clinically significant bilirubin levels<br>F. To revise the language in various sections as, in most cases, data would be presented only for the extension safety population and to clarify when data from OTR3001 would be included in the summary analyses.<br>G. To update language for reporting of CSPCs to reflect the current process. |
| 11 June 2012 | The amendment was submitted only to sites that requested it. The rationale for the amendment was the following:<br>A. To allow patients having difficulty getting to the site for a visit to have the visits conducted at the patient's home if deemed appropriate by the investigator. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Enrollement for study OTR3002 was closed by Purdue Pharma L.P on 01-January-2014 due to administrative reasons not related to safety. Interpretation is limited by the samall number of patients in each age group in this study

Notes: