ClinicalTrials.gov Protocol and Results Registration System (PRS) Receipt
Release Date: 07/16/2015

Grantor: CDER IND/IDE Number: 116020 Serial Number:

Pharmacokinetic, Efficacy and Safety Study of Tapentadol Oral Solution in Children With Postoperative Pain

This study has been completed.

Sponsor:	Grünenthal GmbH
Collaborators:	Janssen Research & Development, LLC
Information provided by (Responsible Party):	Grünenthal GmbH
ClinicalTrials.gov Identifier:	NCT01729728

Purpose

To find out if a drug called tapentadol administered by mouth safely relieves pain in children. Look at the amount of tapentadol in the blood after a single oral dose.

Tapentadol oral solution for children is still being tested and is not yet registered. Tapentadol tablets are effective in treating both acute and chronic pain in adults. This trial will help to understand how tapentadol oral solution works in children.

Condition	Intervention	Phase
Postoperative Pain Acute Pain	Drug: Tapentadol	Phase 2

Study Type: Interventional
Study Design: Treatment, Single Group Assignment, Open Label, Non-Randomized, Pharmacokinetics Study
Official Title: Open-label Evaluation of the Pharmacokinetic Profile, Safety, and Efficacy of Tapentadol Oral Solution for the Treatment of Post-surgical Pain in Children and Adolescents Aged From 2 Years to Less Than 18 Years.

Further study details as provided by Grünenthal GmbH:

Primary Outcome Measure:

- Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Older Children (Age 6 to Less Than 12 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Older Children (Age 6 to Less Than 12 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Younger Children (Age 3 to Less Than 6 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Younger Children (Age 3 to Less Than 6 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Very Young Children (Age 2 to Less Than 3 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
- Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Very Young Children (Age 2 to Less Than 3 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
- Non-Compartmental Pharmacokinetic (PK) Parameter of Tapentadol Area Under the Concentration-Time Curve (AUC 0-15) After a Single Dose of Tapentadol in Adolescent Participants (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The Area Under the Curve (AUC) from dose to 15 hours (AUC

0-15) is a summary measure of data from each pharmacokinetic blood sample taken over the 15 hour time period. The area is that below the line fitted to the data points.

- Non-Compartmental Pharmacokinetic (PK) Parameter: Cmax (Maximum Concentration) of Tapentadol After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The concentration of tapentadol (active drug) is assessed during absorption and distribution. The maximum concentration is derived from the Area Under the Curve, from dose to 15 hours (AUC 0-15). It is the highest amount of active drug observed in the blood sample
- Non-Compartmental Pharmacokinetic (PK) Parameter: Time to Maximum Concentration (Tmax) of Tapentadol After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. The time to maximum concentration is derived from the area under the curve from dose to 15 hours (AUC 0-15). The Tmax is the time after dosing at which the maximum concentration of the tapentadol (active drug) occurs. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours.
- Non-Compartmental Pharmacokinetic (PK) Parameter of Tapentadol-O-glucuronide Area Under the Concentration-Time Curve (AUC 0-15) After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The concentration of tapentadol (active drug) is assessed during absorption and distribution. The maximum concentration is derived from the Area Under the Curve, from dose to 15 hours (AUC 0-15). It is the highest amount of active drug observed in the blood sample.
- Non-Compartmental Pharmacokinetic (PK) Parameter: Cmax (Maximum Concentration) of Tapentadol-O-glucuronide After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The concentration of tapentadol-O-glucuronide (metabolite) is assessed to study absorption and distribution. The maximum concentration is derived from the Area Under the Curve, from dose to 15 hours (AUC 0-15). It is the highest amount of metabolite observed in the blood sample.
- Non-Compartmental Pharmacokinetic (PK) Parameter: Time to Maximum Concentration (Tmax) of Tapentadol-O-glucuronide After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18). [Time Frame: up to 15 hours] [Designated as safety issue: No]
  Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. The time to maximum concentration is derived from the area under the curve from dose to 15 hours (AUC 0-15). The Tmax is the time after dosing at which the maximum concentration of the tapentadol-O-glucuronide (metabolite) occurs. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours.

Secondary Outcome Measures:

- Pain Intensity Assessments Using the Visual Analog Scale (VAS) in Adolescents (Age 12 to Less Than 18 Years). [Time Frame: Baseline; 15 hours] [Designated as safety issue: No]
  At predefined times after investigational medicinal product administration, participants were asked to rate their pain on a 100 mm line (visual analog scale - VAS) by marking a point on the line in response to: "My pain at this time is". The mark was scored between "no pain" and " pain as bad as it could be". The distance was then measured by a clinician and reported. A value of 0 indicates "no pain". A value of 100 indicates "pain as bad as it could be".
- Pain Intensity Assessments Using the McGrath Color Analog Scale in Adolescent Participants and Older Children (Age 6 to Less Than 18 Years). [Time Frame: Baseline; 15 hours post-dose] [Designated as safety issue: No]

Pain intensity assessments were with a 0 (no pain) to 10 (worst pain) scored McGrath color analog scale (CAS) in participants aged 6 years to less than 18 years, i.e. in Adolescents and Older Children. Participants were presented with the CAS and instructed to place the sliding bar on the color that best represented their pain intensity level at the time of assessment. The CAS is a pocket size tool used to measure the self-reported pain intensity of the older participants. The CAS consists of a 145 mm long triangular shaped strip of plastic, varying in width and hue from 1 mm wide and light pink hue at the bottom (and text no pain), to 3 mm wide and deep red hue at the top (most pain). This instrument includes 2 sides. One side shows the color pain intensity scale as described and the other shows a graduated scale, which provides a specific numeric value for the participant-reported level of pain.

- Pain Intensity Assessments Using the Faces Pain Scale (Revised) in Children Age 3 to Less Than 12 Years. [Time Frame: Baseline; 15 hours post-dose] [Designated as safety issue: No]

  This assessment tool was used in 3 to less than 12 year old participants, i.e. Older Children and Young Children. The Faces Pain Scale (Revised) [FPS-R] score as allocated to a selected face by the participant. There are 6 faces and the participant is asked to indicate on a face to express how much it hurts. The numeric value 0 (no pain) to 10 (very much pain) is read off the reverse side of the scale by the clinician.
- Pain Intensity Assessment Using the Face, Legs, Activity, Cry, Consolability Scale in Young and Very Young Children (Age 2 to Less Than 6 Years). [Time Frame: Baseline; 15 hours post-dose] [Designated as safety issue: No]

  The Face Legs Activity Cry Consolability (FLACC) Scale was developed by the Department of Anesthesiology, University of Michigan Medical School and Health Systems. The FLACC Scale is a behavioral scale for scoring postoperative pain in children between the ages of two months and seven years or in persons unable to communicate. In this trial the scale was used in the young and very young children, i.e. in participants aged 2 to less than 6 years. This tool includes five categories of pain behaviors, including facial expression, leg movement, activity, cry, and consolability. The clinician observes the participant for 5 minutes or more and scores each category with a 0, 1 or 2. The scores are added together for a total score ranging from 0 (no pain) to 10 (worst pain). The higher the total score the higher the pain.
- Sum of Pain Intensity Differences Over the 4 Hours After Dosing Derived From the Different Pain Scales and for All Age Groups [Time Frame: Baseline; 4 hours post-dose] [Designated as safety issue: No]

  Different pain intensity assessment tools were used in the different age groups. Therefore the sum of pain intensities were calculated and are reported for each age group based on the tool used. Adolescents - Age 12 to Less Than 18 Years. Older Children - Age 6 to Less Than 12 Years. Young Children - Age 3 to Less Than 6 Years. Very Young Children - Age 2 to Less Than 3 Years. - CAS (McGrath color analog scale) [Theoretical Range: -40 to + 40], - VAS (100 mm Visual Analog Scale) [Theoretical Range: -400 to + 400], - FPS-R (6-point Faces Pain Scale - Revised) [Theoretical Range: -40 to + 40], - FLACC (Face, Legs, Activity, Cry, and Consolability score) [Theoretical Range: -40 to + 40]. A mean score of zero indicates that there was no pain intensity change over the 4 hours. The positive values indicate that in the group as a whole the sum of all pain intensity values over the first 4 hours lead to a reduction in pain in the time period.
- Respiratory Rate Assessments [Time Frame: Enrollment Visit; 15 hours post-dose] [Designated as safety issue: Yes]

  Respiratory rate assessments were performed at pre-defined times during the 15 hour period following investigational medicinal product intake. Pre-surgery data for these participants is also given from the enrollment Visit (Visit 1).
- Oxygen Saturation Assessments [Time Frame: Enrollment Visit; 15 hours post-dose] [Designated as safety issue: Yes]

  Oxygen saturation assessments were performed at pre-defined times during the 15 hour period following investigational medicinal product intake. Oxygen saturation was assessed using pulse oximetry. The uppermost value is 100%. Pre-surgery data for these participants is also given from the enrollment Visit (Visit 1).
- Systolic and Diastolic Blood Pressure Assessments [Time Frame: Enrollment Visit; 15 hours post-dose] [Designated as safety issue: Yes]

  Systolic and Diastolic blood pressure assessments were performed at pre-defined times during the 15 hour period following investigational medicinal product intake. Pre-surgery data for these participants is also given from the enrollment Visit (Visit 1).
- Change From Enrollment in 12-lead Electrocardiogram Parameters [Time Frame: Enrollment (pre-surgery); Discharge Visit] [Designated as safety issue: Yes]

  12-lead electrocardiograms (ECG) were part of the planned safety assessments. 12-lead Electrocardiograms were performed prior at the enrollment visit after informed consent and at the discharge visit. The discharge visit was as per standard of care. The changes in ECG parameters are reported. Negative mean values indicate that the millisecond intervals decreased from the enrollment to the discharge visit. Positive mean values indicate that the millisecond intervals increased from the enrollment to the discharge visit. The Letters P,Q,R,S and T refer to specific medically defined points on an ECG tracing and correspond to specific heart activities.

- Change From Enrollment in 12-lead Electrocardiogram Heart Rate Parameter [Time Frame: Enrollment; Discharge Visit] [Designated as safety issue: Yes]
  12-lead Electrocardiograms (ECG) were part of the planned safety assessments. 12-lead Electrocardiograms were performed prior at the enrollment visit after informed consent and at the discharge visit. The discharge visit was as per standard of care. The changes in heart rate (beats per minute) parameters are reported per treatment group between the visits. A positive value indicates that the heart rate was higher at discharge than at enrollment.
- Treatment Emergent Adverse Events by Intensity [Time Frame: Baseline; 48 hours post dosing] [Designated as safety issue: Yes]
  The intensity of all treatment emergent adverse events (TEAEs) were scored by the investigator. Treatment emergent adverse events were those adverse events documented from the time of investigational medicinal product (IMP), study drug, up to 48 hours post dosing. The clinical "intensity" of an adverse event was classified as: - Mild: Signs and symptoms that can be easily tolerated. Symptoms can be ignored and disappear when the subject is distracted. - Moderate: Symptoms cause discomfort but are tolerable; they cannot be ignored and affect concentration. - Severe: Symptoms which affect usual daily activity. For adverse events where the intensity changes over time, the maximum intensity observed was documented.
- Intake of Additional Analgesic Medication During the Trial [Time Frame: Baseline; 15 hours post dosing] [Designated as safety issue: No]
  Number of participants with intakes of supplemental analgesic medication between investigational medicinal product (IMP) intake and Site Discharge grouped according to preparation taken (non-opioid/opioid).
- Hematology Safety Laboratory Assessments: Hemoglobin Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  The hemoglobin test is a commonly ordered blood test and was done as part of a complete blood count (CBC). It is routinely done before and after surgery to check for anemia, the presence of chronic kidney disease or other chronic medical problems. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Hematology Safety Laboratory Assessments: Hematocrit [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  Hematocrit is a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells (RBC). This measurement depends on the number of red blood cells and the size of red blood cells. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Hematology Safety Laboratory Assessments: Erythrocyte Mean Corpuscular Volume (Mean Corpuscular Volume) [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  Erythrocyte Mean Corpuscular volume is a measurement of the average size of Red Blood Cells (RBC). It is also referred to as Mean Corpuscular Volume. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Hematology Safety Laboratory Assessments: Platelet Count [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  Platelets are cell fragments that are vital for normal blood clotting. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Hematology Safety Laboratory Assessments: Leukocyte Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  Leukocytes are also called white blood cells (WBC). These were measured to assess immune function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Blood Glucose Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  A blood glucose test measures the amount of a sugar called glucose in blood. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.

- Biochemistry Safety Laboratory Parameters: Blood Sodium Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Sodium is required by the body for the body to function properly. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Blood Potassium Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Potassium is a mineral that the body needs to work normally. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Blood Calcium Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  All cells need calcium in order to function. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Blood Chloride Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Chloride with other electrolytes help keep the proper balance of body fluids and maintain the body's acid-base balance. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care
- Biochemistry Safety Laboratory Parameters: Blood Phosphate Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Phosphate is needed by the body. This test was done to see how much phosphate is in the blood. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Blood Urea Nitrogen (BUN) Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  This test is to measure the amount of urea nitrogen in the blood. It was used to test liver and kidney function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Creatinine Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Creatinine is removed from the body entirely by the kidneys. If kidney function is not normal, creatinine level increases in the blood. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Aspartate Aminotransferase (AST) Enzyme Activity [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  AST is considered to be one of the two most important tests to detect liver injury. During liver damage the enzyme is released into the blood. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Triglycerides Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

Triglycerides are a group of fat. Triglycerides were measured as part of metabolic and cardiac assessments. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.

- Biochemistry Safety Laboratory Parameters: Serum Albumin Concentration [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Albumin is a protein made by the liver. Albumin prevents fluid leaking into the tissues. Albumin also transports many small molecules. Serum albumin was measured in the clear liquid portion of the blood called serum. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Urate in the Blood [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Uric acid (urate is the salt) is a chemical created when the body breaks down substances called purines. Most urate dissolves in blood and travels to the kidneys. From there, it passes out in the urine. The test is used to determine kidney function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Calculated Glomerular Filtration Rate [Time Frame: Enrollment Visit; Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  Glomerular filtration rate (GFR) was done to check how well the kidneys are working. It estimates how much blood passes through the glomeruli in the kidney each minute. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Urine Specific Gravity [Time Frame: Enrollment Visit and Discharge Visit] [Designated as safety issue: Yes]

  This test was used to test for the water balance and urine concentration. A urine sample was tested right away. A dipstick with a color-sensitive pad was used. The color the dipstick changes and the specific gravity of the urine was read off the color chart. In the study there were 2 planned safety urine collections. At Visit 1 in the enrollment period, after consent and assent obtained. The second sample was obtained at Visit 3 prior to discharge from the hospital. The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Urine pH (Acid, Alkalinity) Test [Time Frame: Enrollment Visit and Discharge Visit] [Designated as safety issue: Yes]

  A urine sample was tested right away. A dipstick made with a color-sensitive pad was used. The color indicated the acidity of the urine. In the study there were 2 planned safety urine collections. At Visit 1 in the enrollment period, after consent and assent obtained. The second sample was obtained at Visit 3 prior to discharge from the hospital. The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Liver Function Test - Alanine Aminotransferase (ALT) Enzyme Activity [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  This test was done in combination with other tests (such as AST, ALP, and bilirubin) to diagnose and monitor the liver function. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Liver Function Test - Gamma-Glutamyl Transferase (GGT) Enzyme Activity [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

  The gamma-glutamyl transferase (GGT) test was used in combination with the alkaline phosphatase (ALP) test. Both ALP and GGT can be elevated in bile duct or liver complications. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Liver Function Test - Bilirubin Concentration [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]

Old red blood cells are replaced by new blood cells every day. Bilirubin is made by the body when the old blood cells are removed. The concentration of bilirubin in the blood measures liver function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.

- Biochemistry Safety Laboratory Parameters: Liver Function Test - Lactate Dehydrogenase (LDH) Enzyme Activity [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  Lactate Dehydrogenase (LDH) was used to check for tissue damage. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Blood Protein Concentration [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  The test was done to verify kidney and liver function. It is done in combination with the albumin test. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Creatine Kinase (CK) Enzyme Activity [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  The creatine kinase (CK) test was used to detect inflammation of muscles. The test was done in combination with other tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Alkaline Phosphatase (ALP) Enzyme Activity [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  The Alkaline Phosphatase activity was used to detect bone or hepatobiliary disease. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
- Biochemistry Safety Laboratory Parameters: Triacylglycerol Lipase (TL) Enzyme Activity [Time Frame: Enrollment Visit, Visit 2 and Discharge Visit] [Designated as safety issue: Yes]
  A triacylglycerol lipase test was done to check for pancreatic function. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to investigational medicinal product administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.

Enrollment: 86
Study Start Date: November 2012
Primary Completion Date: February 2014
Study Completion Date: February 2014

Arms	Assigned Interventions
Experimental: Tapentadol	Drug: Tapentadol Tapentadol oral solution single dose (1mg/kg body weight)

Detailed Description:

The lower age limit for the clinical trial was initially set to 3 years of age in the protocol. The trial planned for the inclusion of participants in three age categories. Age 3 to less than 6 years (young children), age 6 to less than 12 years (older children) and age 12 to less than 18 years of age (adolescents). There was a

request by the Paediatric Committee (PDCO) at the European Medicines Agency to include participants 2 years of age (very young children). The protocol amendment thus planned to combine the two youngest age groups into a single reporting group. The protocol amendment only planned that the very young children group would have separate analysis for the Faces Pain Scale Revised (FPS-R) Scale and for the presentation of the serum concentrations, because the pharmacokinetic sampling scheme used in the 2 year old participants was different from the young children group (aged 3 to less than 6 years).

Eligibility

Ages Eligible for Study: 2 Years to 17 Years
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- A maximum body weight of 85.0 kg.
- A minimum body weight of 10 kg for participants aged 2 years to less than 3 years old.
- If female and post-menarchal, or 12 years or older, the subject has a negative urine pregnancy test within 24 hours before surgery.
- Having completed either dental surgery or tonsillectomy with or without adenoidectomy surgery (age group: 6 to less than 18 years of age).
- Having completed ear, nose, or throat surgery (including but not limited to tonsillectomy (age group: 2 to less than 3 years of age).
- Participant aged 6 to less than 18 years has a post-operative pain intensity score greater than or equal to 4 on the Color Analog Scale (CAS) as a result of the surgical procedure or the participant has a pain level that the usual standard of care following the surgical procedure (which reliably produces moderate to severe pain) requires opioid treatment.
- Participant aged 2 years to less than 6 years has a pain level following a surgical procedure that reliably produces moderate to severe pain, for which the usual standard of care requires opioid treatment.
- Participant is alert, orientated, and able to follow commands and complete the post-operative required procedures.

Exclusion Criteria:

- History of brain injury.
- Clinically relevant abnormal ECG.
- Clinically unstable vital signs and/or a saturation of oxygen saturation (SpO2) less than 93%. During surgery SpO2 may decrease <93%.
- Clinically relevant abnormal values for clinical chemistry, hematology, or urinalysis at enrollment.
- Body temperature above 38.5°C within 48 hours prior to dosing.
- Positive drugs of abuse test result.

Contacts and Locations

Locations
United States, Utah
Jean Brown Research
Salt Lake City, Utah, United States, 84124

Investigators

Study Director:	Study Director	Grünenthal GmbH

More Information

Responsible Party: Grünenthal GmbH
Study ID Numbers: KF5503/68
2013-002016-27 [EudraCT Number]
Health Authority: United States: Food and Drug Administration

Study Results

Participant Flow

Recruitment Details	The first participant was enrolled on the 15 Nov 2012 and the last participant completed the trial on the 24 Feb 2014.
Pre-Assignment Details	Consent was obtained for 86 participants in the trial. 66 participants were allocated and received study drug (investigational medicinal product). Pharmacokinetic data was obtained for the planned 56 participants.

Reporting Groups

	Description
Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight)
Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight)
Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight)

Overall Study

	Adolescents	Older Children	Young and Very Young Children
Started	21	28	17
Completed	20	22	16
Not Completed	1	6	1
Adverse Event	0	6	0
Protocol Violation	1	0	1

Baseline Characteristics

Analysis Population Description

Number of participants that were dosed.

Reporting Groups

	Description
Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Baseline Measures

	Adolescents	Older Children	Young and Very Young Children	Total
Number of Participants	21	28	17	66
Age, Continuous [units: years] Mean (Standard Deviation)	15.5 (1.6)	8.3 (1.6)	3.4 (1.1)	9.3 (4.9)
Gender, Male/Female [units: participants]				
Female	9	17	8	34
Male	12	11	9	32
Race (NIH/OMB) [units: participants]				
American Indian or Alaska Native	0	0	0	0
Asian	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	0	1	0	1
White	21	27	15	63
More than one race	0	0	0	0
Unknown or Not Reported	0	0	2	2

	Adolescents	Older Children	Young and Very Young Children	Total
Region of Enrollment United States [units: participants]	21	28	17	66
Weight [units: kilograms] Mean (Standard Deviation)	61.30 (9.78)	28.85 (5.89)	16.34 (2.20)	35.95 (19.36)
Height [units: centimeter] Mean (Standard Deviation)	170.6 (10.7)	132.9 (11.1)	101.7 (8.1)	136.9 (28.3)

Outcome Measures

1. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Adolescents (Age 12 to Less Than 18 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Tapentadol Serum Concentrations: Adolescents	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 12 years and less than 18 years of age.

Measured Values

	Tapentadol Serum Concentrations: Adolescents
Number of Participants Analyzed	19
Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Adolescents (Age 12 to Less Than 18 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
15 minutes post-dose (N = 19)	23.2 (34.0)

	Tapentadol Serum Concentrations: Adolescents
30 minutes post-dose (N=18)	45.6 (33.0)
1 hour post-dose (N=18)	49.4 (21.2)
2 hours post-dose (N=18)	43.1 (14.2)
4 hours post-dose (N=17)	32.8 (10.8)
6 hours post-dose (N=18)	22.3 (11.9)
11 hours post-dose (N=18)	8.14 (6.35)
15 hours post-dose (N=17)	3.66 (3.26)

2. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Adolescents (Age 12 to Less Than 18 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Tapentadol-O-glucuronide Serum Concentrations: Adolescents	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 12 years and less than 18 years of age.

Measured Values

	Tapentadol-O-glucuronide Serum Concentrations: Adolescents
Number of Participants Analyzed	18

	Tapentadol-O-glucuronide Serum Concentrations: Adolescents
Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Adolescents (Age 12 to Less Than 18 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
15 minutes post-dose (N = 18)	404 (581)
30 minutes post-dose (N=17)	855 (672)
1 hour post-dose (N=17)	1424 (542)
2 hours post-dose (N=18)	1202 (366)
4 hours post-dose (N=17)	824 (191)
6 hours post-dose (N=18)	497 (138)
11 hours post-dose (N=18)	150 (69.0)
15 hours post-dose (N=17)	66.9 (35.4)

3. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Older Children (Age 6 to Less Than 12 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Tapentadol Serum Concentrations: Older Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 6 years and less than 12 years of age.

Measured Values

	Tapentadol Serum Concentrations: Older Children
Number of Participants Analyzed	22
Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Older Children (Age 6 to Less Than 12 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
15 minutes to 1 hour post-dose (N=22)	36.5 (21.8)
1 to 4 hours post-dose (N=22)	36.5 (15.7)
4 to 11 hours post-dose (N=22)	13.5 (6.52)
11 to 15 hours post-dose (N=22)	3.71 (1.96)

4. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Older Children (Age 6 to Less Than 12 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Tapentadol-O-glucuronide Serum Concentrations: Older Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 6 years and less than 12 years of age.

Measured Values

	Tapentadol-O-glucuronide Serum Concentrations: Older Children
Number of Participants Analyzed	22
Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Older Children (Age 6 to Less Than 12 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
15 minutes to 1 hour post-dose (N = 20)	676 (343)
1 to 4 hours post-dose (N=22)	900 (330)
4 to 11 hours post-dose (N=22)	321 (123)
11 to 15 hours post-dose (N=22)	86.3 (37.8)

5. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Younger Children (Age 3 to Less Than 6 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Tapentadol Serum Concentrations: Younger Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 3 years and less than 6 years of age.

Measured Values

	Tapentadol Serum Concentrations: Younger Children
Number of Participants Analyzed	11

	Tapentadol Serum Concentrations: Younger Children
Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Younger Children (Age 3 to Less Than 6 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
15 minutes to 1 hour post-dose (N = 11)	30.1 (19.2)
4 to 11 hours post-dose (N=11)	26.4 (10.7)

6. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Younger Children (Age 3 to Less Than 6 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Tapentadol-O-glucuronide Serum Concentrations Younger Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 3 years and less than 6 years of age.

Measured Values

	Tapentadol-O-glucuronide Serum Concentrations Younger Children
Number of Participants Analyzed	11
Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Younger Children (Age 3 to Less Than 6 Years).	

	Tapentadol-O-glucuronide Serum Concentrations Younger Children
[units: nanogram per milliliter] Mean (Standard Deviation)	
15 minutes to 1 hour post-dose (N = 10)	494 (377)
4 to 11 hours post-dose (N=11)	504 (112)

7. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Very Young Children (Age 2 to Less Than 3 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 0.2 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

[Not Specified]

Reporting Groups

	Description
Tapentadol Serum Concentrations: Very Young Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 2 years and less than 3 years of age.

Measured Values

	Tapentadol Serum Concentrations: Very Young Children
Number of Participants Analyzed	4
Pharmacokinetic Profile of Serum Concentrations of Tapentadol After a Single Dose of Tapentadol Oral Solution in Very Young Children (Age 2 to Less Than 3 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
1.25 hours post-dose (N = 4)	19.9 (13.2)
3 hours post-dose (N=4)	37.7 (18.2)
5 hours post-dose (N=3)	23.4 (6.36)

	Tapentadol Serum Concentrations: Very Young Children
8 hours post-dose (N=4)	10.0 (4.33)

8. Primary Outcome Measure:

Measure Title	Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Very Young Children (Age 2 to Less Than 3 Years).
Measure Description	Mean and Standard Deviation of Serum Concentrations of Tapentadol-O-glucuronide. Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Tapentadol-O-glucuronide concentrations were measured in participants. Serum was analyzed by means of liquid chromatography coupled to tandem mass spectrometry with a lower limit of quantification (LLOQ) at 10 ng/mL.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description
[Not Specified]

Reporting Groups

	Description
Tapentadol-O-glucuronide Concentrations: Very Young Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 2 years and less than 3 years of age.

Measured Values

	Tapentadol-O-glucuronide Concentrations: Very Young Children
Number of Participants Analyzed	4
Pharmacokinetic Profile of Serum Concentrations of Tapentadol-O-glucuronide After a Single Dose of Tapentadol Oral Solution in Very Young Children (Age 2 to Less Than 3 Years). [units: nanogram per milliliter] Mean (Standard Deviation)	
1.25 hours after administration (N = 4)	497 (513)
3 hours after administration (N=4)	938 (407)
5 hours after administration (N=3)	624 (235)

	Tapentadol-O-glucuronide Concentrations: Very Young Children
8 hours after administration (N=4)	253 (103)

9. Primary Outcome Measure:

Measure Title	Non-Compartmental Pharmacokinetic (PK) Parameter of Tapentadol Area Under the Concentration-Time Curve (AUC 0-15) After a Single Dose of Tapentadol in Adolescent Participants (Age 12 to Less Than 18 Years).
Measure Description	Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The Area Under the Curve (AUC) from dose to 15 hours (AUC 0-15) is a summary measure of data from each pharmacokinetic blood sample taken over the 15 hour time period. The area is that below the line fitted to the data points.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

The protocol planned that this analysis would only be performed for the adolescent participants.

Reporting Groups

	Description
Tapentadol Non-Compartmental PK Parameter: AUC	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Tapentadol Non-Compartmental PK Parameter: AUC
Number of Participants Analyzed	18
Non-Compartmental Pharmacokinetic (PK) Parameter of Tapentadol Area Under the Concentration-Time Curve (AUC 0-15) After a Single Dose of Tapentadol in Adolescent Participants (Age 12 to Less Than 18 Years). [units: ng*hr/mL] Mean (Full Range)	302 (218 to 636)

10. Primary Outcome Measure:

Measure Title	Non-Compartmental Pharmacokinetic (PK) Parameter: Cmax (Maximum Concentration) of Tapentadol After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years).
Measure Description	Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The concentration of tapentadol (active drug) is assessed during absorption and distribution. The maximum concentration is derived from the Area Under the Curve, from dose to 15 hours (AUC 0-15). It is the highest amount of active drug observed in the blood sample
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

The protocol planned that this analysis would only be performed for the adolescent participants.

Reporting Groups

	Description
Tapentadol Non-Compartmental PK Parameter: Cmax	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Tapentadol Non-Compartmental PK Parameter: Cmax
Number of Participants Analyzed	18
Non-Compartmental Pharmacokinetic (PK) Parameter: Cmax (Maximum Concentration) of Tapentadol After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [units: nanograms/millilitre] Mean (Standard Error)	67.5 (26.3)

11. Primary Outcome Measure:

Measure Title	Non-Compartmental Pharmacokinetic (PK) Parameter: Time to Maximum Concentration (Tmax) of Tapentadol After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years).

Measure Description	Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. The time to maximum concentration is derived from the area under the curve from dose to 15 hours (AUC 0-15). The Tmax is the time after dosing at which the maximum concentration of the tapentadol (active drug) occurs. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

The protocol planned that this analysis would only be performed for the adolescent participants.

Reporting Groups

	Description
Tapentadol Non-Compartmental PK Parameter: Tmax	Tapentadol oral solution single dose (1mg/kg body weight) of participants aged 12 years to less than 18 years old.

Measured Values

	Tapentadol Non-Compartmental PK Parameter: Tmax
Number of Participants Analyzed	18
Non-Compartmental Pharmacokinetic (PK) Parameter: Time to Maximum Concentration (Tmax) of Tapentadol After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [units: hours] Mean (Standard Deviation)	1.4 (1.10)

12. Primary Outcome Measure:

Measure Title	Non-Compartmental Pharmacokinetic (PK) Parameter of Tapentadol-O-glucuronide Area Under the Concentration-Time Curve (AUC 0-15) After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years).
Measure Description	Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The concentration of tapentadol (active drug) is assessed during absorption and distribution. The maximum concentration is derived from the Area Under the Curve, from dose to 15 hours (AUC 0-15). It is the highest amount of active drug observed in the blood sample.

Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

The protocol planned that this analysis would only be performed for the adolescent participants.

Reporting Groups

	Description
Tapentadol-O-glucuronide Non-Compartmental PK Parameter: AUC	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Tapentadol-O-glucuronide Non-Compartmental PK Parameter: AUC
Number of Participants Analyzed	18
Non-Compartmental Pharmacokinetic (PK) Parameter of Tapentadol-O-glucuronide Area Under the Concentration-Time Curve (AUC 0-15) After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [units: ng*hr/mL] Mean (Full Range)	7082 (4946 to 9689)

13. Primary Outcome Measure:

Measure Title	Non-Compartmental Pharmacokinetic (PK) Parameter: Cmax (Maximum Concentration) of Tapentadol-O-glucuronide After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years).
Measure Description	Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours. The concentration of tapentadol-O-glucuronide (metabolite) is assessed to study absorption and distribution. The maximum concentration is derived from the Area Under the Curve, from dose to 15 hours (AUC 0-15). It is the highest amount of metabolite observed in the blood sample.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

The protocol planned that this analysis would only be performed for the adolescent participants.

Reporting Groups

	Description
Tapentadol-O-glucuronide Non-Compartmental PK Parameter: Cmax	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Tapentadol-O-glucuronide Non-Compartmental PK Parameter: Cmax
Number of Participants Analyzed	18
Non-Compartmental Pharmacokinetic (PK) Parameter: Cmax (Maximum Concentration) of Tapentadol-O-glucuronide After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18 Years). [units: nanogramsg/millilitre] Mean (Standard Error)	1487 (495)

14. Primary Outcome Measure:

Measure Title	Non-Compartmental Pharmacokinetic (PK) Parameter: Time to Maximum Concentration (Tmax) of Tapentadol-O-glucuronide After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18).
Measure Description	Tapentadol-O-glucuronide is the metabolite of tapentadol. Metabolites are sometimes referred to as "breakdown products". The body alters the administered medication to a metabolite so that it can be more easily or quickly removed from the body. Serum samples for pharmacokinetic analysis were obtained using frequent sampling techniques in participants 12 years to less than 18 years of age. The time to maximum concentration is derived from the area under the curve from dose to 15 hours (AUC 0-15). The Tmax is the time after dosing at which the maximum concentration of the tapentadol-O-glucuronide (metabolite) occurs. Serum samples (frequent sampling) were drawn at 0.25, 0.5, 1, 2, 4, 6, 11, and 15 hours.
Time Frame	up to 15 hours
Safety Issue?	No

Analysis Population Description

The protocol planned that this analysis would only be performed for the adolescent participants.

Reporting Groups

	Description
Tapentadol-O-glucuronide Non-Compartmental PK Parameter: Tmax	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Tapentadol-O-glucuronide Non-Compartmental PK Parameter: Tmax
Number of Participants Analyzed	18
Non-Compartmental Pharmacokinetic (PK) Parameter: Time to Maximum Concentration (Tmax) of Tapentadol-O-glucuronide After a Single Dose of Tapentadol in Adolescents (Age 12 to Less Than 18). [units: hours] Mean (Standard Deviation)	1.70 (1.19)

15. Secondary Outcome Measure:

Measure Title	Pain Intensity Assessments Using the Visual Analog Scale (VAS) in Adolescents (Age 12 to Less Than 18 Years).
Measure Description	At predefined times after investigational medicinal product administration, participants were asked to rate their pain on a 100 mm line (visual analog scale - VAS) by marking a point on the line in response to: “My pain at this time is”. The mark was scored between “no pain” and ” pain as bad as it could be”. The distance was then measured by a clinician and reported. A value of 0 indicates "no pain". A value of 100 indicates "pain as bad as it could be".
Time Frame	Baseline; 15 hours
Safety Issue?	No

Analysis Population Description

Protocol pre-specified reporting groups.

Reporting Groups

	Description
Visual Analog Scale: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Visual Analog Scale: Adolescents
Number of Participants Analyzed	21
Pain Intensity Assessments Using the Visual Analog Scale (VAS) in Adolescents (Age 12 to Less Than 18 Years). [units: units on a scale] Mean (Standard Deviation)	
Pre-dose (N=21)	71.5 (13.3)
15 minutes post-dose (N=21)	63.6 (24.4)
30 minutes post-dose (N=21)	53.2 (27.3)
1 hour post-dose (N=21)	46.3 (26.5)
2 hours post-dose (N=20)	34.0 (24.6)
4 hours post-dose (N=20)	43.5 (26.8)
6 hours post-dose (N=20)	34.8 (24.3)
11 hours post-dose (N=20)	32.7 (21.1)
15 hours post-dose (N=20)	33.4 (20.1)

16. Secondary Outcome Measure:

Measure Title	Pain Intensity Assessments Using the McGrath Color Analog Scale in Adolescent Participants and Older Children (Age 6 to Less Than 18 Years).
Measure Description	Pain intensity assessments were with a 0 (no pain) to 10 (worst pain) scored McGrath color analog scale (CAS) in participants aged 6 years to less than 18 years, i.e. in Adolescents and Older Children. Participants were presented with the CAS and instructed to place the sliding bar on the color that best represented their pain intensity level at the time of assessment. The CAS is a pocket size tool used to measure the self-reported pain intensity of the older participants. The CAS consists of a 145 mm long triangular shaped strip of plastic, varying in width and hue from 1 mm wide and light pink hue at the bottom (and text no pain), to 3 mm wide and deep red hue at the top (most pain). This instrument includes 2 sides. One side shows the color pain intensity scale as described and the other shows a graduated scale, which provides a specific numeric value for the participant-reported level of pain.
Time Frame	Baseline; 15 hours post-dose
Safety Issue?	No

Analysis Population Description

Protocol pre-specified reporting groups.

Reporting Groups

	Description
McGrath Color Analog Scale: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
McGrath Color Analog Scale: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	McGrath Color Analog Scale: Adolescents	McGrath Color Analog Scale: Older Children
Number of Participants Analyzed	21	28
Pain Intensity Assessments Using the McGrath Color Analog Scale in Adolescent Participants and Older Children (Age 6 to Less Than 18 Years). [units: units on a scale] Mean (Standard Deviation)		
Pre-dose	6.643 (1.461)	4.670 (1.602)
15 minutes post-dose	6.131 (2.180)	3.071 (1.718)
30 minutes after dosing	5.262 (2.311)	2.571 (1.824)
1 hour post-dose	4.393 (2.299)	2.407 (1.723)
2 hours post-dose	3.475 (2.173)	2.292 (1.793)
4 hours post-dose	4.200 (2.113)	2.341 (1.899)
6 hours post-dose	3.438 (1.960)	2.636 (2.152)
11 hours post-dose	3.350 (1.836)	3.352 (1.851)
15 hours post-dose	3.288 (1.578)	3.568 (2.549)

17. Secondary Outcome Measure:

Measure Title	Pain Intensity Assessments Using the Faces Pain Scale (Revised) in Children Age 3 to Less Than 12 Years.

Measure Description	This assessment tool was used in 3 to less than 12 year old participants, i.e. Older Children and Young Children. The Faces Pain Scale (Revised) [FPS-R] score as allocated to a selected face by the participant. There are 6 faces and the participant is asked to indicate on a face to express how much it hurts. The numeric value 0 (no pain) to 10 (very much pain) is read off the reverse side of the scale by the clinician.
Time Frame	Baseline; 15 hours post-dose
Safety Issue?	No

Analysis Population Description

The protocol pre-specified that the Faces Pain Scale (Revised) would not be administered in the very young participants (aged 2 to less than 3 years).

Reporting Groups

	Description
Faces Pain Scale: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight)
Faces Pain Scale: Young Children	Single Dose of Tapentadol Oral Solution in Children Age 3 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight). The children aged 2 were assessed using the FLACC (Face, Legs, Activity, Cry, Consolability) Scale and not the 6-point Faces Pain Scale - Revised.

Measured Values

	Faces Pain Scale: Older Children	Faces Pain Scale: Young Children
Number of Participants Analyzed	28	12
Pain Intensity Assessments Using the Faces Pain Scale (Revised) in Children Age 3 to Less Than 12 Years. [units: units on a scale] Mean (Standard Deviation)		
Pre-dose	4.8 (1.6)	6.8 (3.2)
15 minutes post-dose	3.5 (1.8)	4.5 (4.0)
30 minutes post-dose	2.9 (1.8)	2.8 (3.2)
1 hour post-dose	2.4 (1.6)	1.8 (3.3)
2 hours post-dose	2.6 (1.7)	1.2 (2.9)
4 hours post-dose	2.5 (1.6)	3.5 (3.2)
6 hours post-dose	2.7 (2.1)	1.8 (2.3)
11 hours post-dose	2.7 (1.7)	2.3 (2.4)

	Faces Pain Scale: Older Children	Faces Pain Scale: Young Children
15 hours post-dose	3.5 (2.2)	2.8 (2.9)

18. Secondary Outcome Measure:

Measure Title	Pain Intensity Assessment Using the Face, Legs, Activity, Cry, Consolability Scale in Young and Very Young Children (Age 2 to Less Than 6 Years).
Measure Description	The Face Legs Activity Cry Consolability (FLACC) Scale was developed by the Department of Anesthesiology, University of Michigan Medical School and Health Systems. The FLACC Scale is a behavioral scale for scoring postoperative pain in children between the ages of two months and seven years or in persons unable to communicate. In this trial the scale was used in the young and very young children, i.e. in participants aged 2 to less than 6 years. This tool includes five categories of pain behaviors, including facial expression, leg movement, activity, cry, and consolability. The clinician observes the participant for 5 minutes or more and scores each category with a 0, 1 or 2. The scores are added together for a total score ranging from 0 (no pain) to 10 (worst pain). The higher the total score the higher the pain.
Time Frame	Baseline; 15 hours post-dose
Safety Issue?	No

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

Reporting Groups

	Description
Face, Legs, Activity, Cry, Consolability Scale	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Face, Legs, Activity, Cry, Consolability Scale
Number of Participants Analyzed	17
Pain Intensity Assessment Using the Face, Legs, Activity, Cry, Consolability Scale in Young and Very Young Children (Age 2 to Less Than 6 Years). [units: units on a scale] Mean (Standard Deviation)	
Pre-dose	4.2 (2.2)
15 minutes post-dose	1.8 (1.6)

	Face, Legs, Activity, Cry, Consolability Scale
30 minutes post-dose	1.2 (1.6)
1 hour post-dose	1.1 (1.4)
2 hours post-dose	0.8 (1.1)
4 hours post-dose	1.5 (1.7)
6 hours post-dose	0.8 (1.6)
11 hours post-dose	0.9 (2.1)
15 hours post-dose	0.8 (1.2)

19. Secondary Outcome Measure:

Measure Title	Sum of Pain Intensity Differences Over the 4 Hours After Dosing Derived From the Different Pain Scales and for All Age Groups
Measure Description	Different pain intensity assessment tools were used in the different age groups. Therefore the sum of pain intensities were calculated and are reported for each age group based on the tool used. Adolescents - Age 12 to Less Than 18 Years. Older Children - Age 6 to Less Than 12 Years. Young Children - Age 3 to Less Than 6 Years. Very Young Children - Age 2 to Less Than 3 Years. • CAS (McGrath color analog scale) [Theoretical Range: -40 to + 40], • VAS (100 mm Visual Analog Scale) [Theoretical Range: -400 to + 400], • FPS-R (6-point Faces Pain Scale - Revised) [Theoretical Range: -40 to + 40], • FLACC (Face, Legs, Activity, Cry, and Consolability score) [Theoretical Range: -40 to + 40]. A mean score of zero indicates that there was no pain intensity change over the 4 hours. The positive values indicate that in the group as a whole the sum of all pain intensity values over the first 4 hours lead to a reduction in pain in the time period.
Time Frame	Baseline; 4 hours post-dose
Safety Issue?	No

Analysis Population Description

Protocol pre-specified reporting groups.

Reporting Groups

	Description
Sum of Pain Intensity Differences	The sum of pain intensity difference over 4 hours (SPID4) were calculated as the weighted sum of the scheduled pain intensity difference collected up to 4 hours after tapentadol oral solution administration. The time elapsed (in hours) since the previous measurement is multiplied with the pain intensity difference (PID) at the respective time, and defines the weight in the calculation of the weighted sum of pain intensity differences.

Measured Values

	Sum of Pain Intensity Differences
Number of Participants Analyzed	65
Sum of Pain Intensity Differences Over the 4 Hours After Dosing Derived From the Different Pain Scales and for All Age Groups [units: units on a scale] Mean (Standard Deviation)	
Adolescents SPID for VAS (N=20)	106.282 (75.350)
Adolescents SPID for CAS (N=20)	8.925 (6.347)
Older Children SPID for CAS (N=22)	9.698 (7.610)
Older Children SPID for FPS-R (N=22)	8.724 (6.868)
Young Children SPID for FPS-R (N=11)	17.646 (14.674)
Young Children SPID for FLACC (N=12)	11.614 (8.334)
Very Young Children SPID for FLACC (N=4)	12.483 (8.955)

20. Secondary Outcome Measure:

Measure Title	Respiratory Rate Assessments
Measure Description	Respiratory rate assessments were performed at pre-defined times during the 15 hour period following investigational medicinal product intake. Pre-surgery data for these participants is also given from the enrollment Visit (Visit 1).
Time Frame	Enrollment Visit; 15 hours post-dose
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at and after 2 hours: N=20; Older Children Group at 30 minutes and 1 hour N=27, at 2 hours N=24, and at and after 4 hours N=22; Young and Very Young Children Group at and after 4 hours: N=16).

Reporting Groups

	Description
Respiratory Rates: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Respiratory Rates: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Respiratory Rates: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Respiratory Rates: Adolescents	Respiratory Rates: Older Children	Respiratory Rates: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Respiratory Rate Assessments [units: breaths per minute] Mean (Standard Deviation)			
Visit 1	17.8 (3.2)	18.4 (3.1)	25.1 (3.4)
Pre-dose	16.4 (2.5)	19.2 (2.5)	25.1 (3.3)
15 minutes post-dose	16.8 (2.6)	19.7 (2.5)	24.0 (3.1)
30 minutes post-dose	17.5 (2.5)	19.4 (2.4)	22.6 (4.3)
1 hours post-dose	15.9 (2.3)	19.0 (2.0)	21.8 (3.5)
2 hours post-dose	17.3 (2.8)	19.3 (2.5)	22.5 (3.3)
4 hours post-dose	16.4 (2.1)	19.5 (2.8)	22.5 (2.1)
6 hours post-dose	16.9 (2.9)	19.0 (3.8)	22.1 (3.5)
11 hours post-dose	17.4 (3.6)	18.4 (2.9)	22.4 (3.4)
15 hours post-dose	16.1 (2.5)	17.3 (3.0)	21.1 (3.9)

21. Secondary Outcome Measure:

Measure Title	Oxygen Saturation Assessments
Measure Description	Oxygen saturation assessments were performed at pre-defined times during the 15 hour period following investigational medicinal product intake. Oxygen saturation was assessed using pulse oximetry. The uppermost value is 100%. Pre-surgery data for these participants is also given from the enrollment Visit (Visit 1).
Time Frame	Enrollment Visit; 15 hours post-dose
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at and after 2 hours: N=20; Older Children Group at 30 minutes and 1 hour N=27, at 2 hours N=24, at and after 4 hours N=22; Young and Very Young Children Group at and after 4 hours: N=16).

Reporting Groups

	Description
Oxygen Saturation: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Oxygen Saturation: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Oxygen Saturation: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Oxygen Saturation: Adolescents	Oxygen Saturation: Older Children	Oxygen Saturation: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Oxygen Saturation Assessments [units: percentage of oxygen saturation] Mean (Standard Deviation)			
Visit 1	97.8 (1.1)	97.4 (1.7)	97.4 (1.4)
Pre-dose	97.7 (1.4)	96.7 (1.4)	96.8 (1.0)
15 minutes post-dose	97.3 (1.2)	96.8 (1.3)	96.5 (1.9)
30 minutes post-dose	97.0 (1.4)	96.4 (1.3)	96.8 (1.6)

	Oxygen Saturation: Adolescents	Oxygen Saturation: Older Children	Oxygen Saturation: Young and Very Young Children
1 hour post-dose	97.3 (1.2)	96.0 (1.6)	96.2 (2.0)
2 hours post-dose	97.1 (1.3)	95.8 (1.4)	95.8 (1.7)
4 hours post-dose	96.9 (1.4)	96.5 (1.2)	96.5 (1.5)
6 hours post-dose	97.1 (1.5)	96.7 (1.3)	96.7 (1.7)
11 hours post-dose	96.8 (1.4)	96.8 (1.4)	96.4 (1.5)
15 hours post-dose	96.7 (1.0)	96.5 (1.4)	97.1 (1.5)

22. Secondary Outcome Measure:

Measure Title	Systolic and Diastolic Blood Pressure Assessments
Measure Description	Systolic and Diastolic blood pressure assessments were performed at pre-defined times during the 15 hour period following investigational medicinal product intake. Pre-surgery data for these participants is also given from the enrollment Visit (Visit 1).
Time Frame	Enrollment Visit; 15 hours post-dose
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at and after 2 hours: N=20; Older Children Group at 30 minutes and 1 hour N=27, at 2 hours N=24, at and after 4 hours N=22; Young and Very Young Children Group at and after 4 hours: N=16).

Reporting Groups

	Description
Blood Pressure: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Pressure: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Pressure: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Pressure: Adolescents	Blood Pressure: Older Children	Blood Pressure: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Systolic and Diastolic Blood Pressure Assessments [units: mmHg] Mean (Standard Deviation)			
Visit 1 Enrollment Systolic blood pressure	110.2 (9.0)	103.8 (9.6)	98.7 (7.0)
Pre-dose Systolic Blood Pressure	122.9 (13.9)	107.1 (9.1)	105.1 (15.6)
15 minutes post-dose Systolic Blood Pressure	126.9 (17.7)	104.1 (8.3)	101.8 (7.5)
30 minutes post-dose Systolic Blood Pressure	126.8 (17.9)	104.1 (7.2)	100.1 (6.2)
1 hour post-dose Systolic Blood Pressure	127.0 (17.7)	104.0 (9.6)	97.6 (7.6)
2 hours post-dose Systolic Blood Pressure	124.9 (16.7)	103.9 (8.2)	98.4 (6.6)
4 hours post-dose Systolic Blood Pressure	122.8 (13.9)	104.8 (10.5)	100.1 (7.4)
6 hours post-dose Systolic Blood Pressure	116.8 (14.1)	106.7 (7.9)	102.0 (8.5)
11 hours post-dose Systolic Blood Pressure	115.1 (11.2)	102.0 (9.1)	99.4 (14.2)
15 hours post-dose Systolic Blood Pressure	113.8 (14.2)	100.3 (8.7)	93.3 (9.9)
Visit 1 Enrollment Diastolic blood pressure	66.5 (9.0)	66.3 (8.3)	62.8 (5.3)
Pre-dose Diastolic blood pressure	74.8 (11.8)	64.2 (9.4)	65.6 (11.2)
15 minutes post-dose Diastolic blood pressure	78.9 (15.7)	62.4 (7.8)	62.4 (7.7)
30 minutes post-dose Diastolic blood pressure	76.1 (12.0)	61.3 (5.7)	60.2 (6.1)
1 hour post-dose Diastolic blood pressure	77.6 (13.0)	61.1 (7.1)	59.6 (6.9)
2 hours post-dose Diastolic blood pressure	74.7 (13.4)	59.7 (7.0)	59.7 (7.4)
4 hours post-dose Diastolic blood pressure	73.2 (12.1)	60.0 (7.1)	58.7 (5.9)
6 hours post-dose Diastolic blood pressure	66.0 (10.3)	59.0 (8.3)	58.8 (7.3)
11 hours post-dose Diastolic blood pressure	65.4 (8.4)	54.6 (8.5)	57.3 (11.2)
15 hours post-dose Diastolic blood pressure	67.1 (10.8)	56.8 (8.5)	57.0 (8.7)

23. Secondary Outcome Measure:

Measure Title	Change From Enrollment in 12-lead Electrocardiogram Parameters
Measure Description	12-lead electrocardiograms (ECG) were part of the planned safety assessments. 12-lead Electrocardiograms were performed prior at the enrollment visit after informed consent and at the discharge visit. The discharge visit was as per standard of care. The changes in ECG parameters are reported. Negative mean values indicate that the millisecond intervals decreased from the enrollment to the discharge visit. Positive mean values indicate that the millisecond intervals increased from the enrollment to the discharge visit. The Letters P,Q,R,S and T refer to specific medically defined points on an ECG tracing and correspond to specific heart activities.
Time Frame	Enrollment (pre-surgery); Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(For older children N=27 at Visit 1)

Reporting Groups

	Description
ECG Changes: Adolescents	Single Dose of Tapentadol Oral Solution in Children and Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ECG Changes: Older Children	Single Dose of Tapentadol Oral Solution in Children and Adolescents Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ECG Changes: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children and Adolescents Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	ECG Changes: Adolescents	ECG Changes: Older Children	ECG Changes: Young and Very Young Children
Number of Participants Analyzed	21	27	17
Change From Enrollment in 12-lead Electrocardiogram Parameters [units: milliseconds] Mean (Standard Deviation)			
QTcF change	-3.6 (16.4)	15.7 (21.7)	5.6 (20.7)
QT Duration change	-8.0 (33.1)	8.5 (32.0)	-4.1 (29.6)
QRS Duration change	0.5 (4.5)	-0.2 (4.7)	0.5 (5.8)

	ECG Changes: Adolescents	ECG Changes: Older Children	ECG Changes: Young and Very Young Children
PR Duration change	-3.5 (11.7)	-1.8 (11.3)	-2.4 (12.6)
RR Duration change	-32.2 (193.8)	-35.2 (156.5)	-48.1 (102.8)

24. Secondary Outcome Measure:

Measure Title	Change From Enrollment in 12-lead Electrocardiogram Heart Rate Parameter
Measure Description	12-lead Electrocardiograms (ECG) were part of the planned safety assessments. 12-lead Electrocardiograms were performed prior at the enrollment visit after informed consent and at the discharge visit. The discharge visit was as per standard of care. The changes in heart rate (beats per minute) parameters are reported per treatment group between the visits. A positive value indicates that the heart rate was higher at discharge than at enrollment.
Time Frame	Enrollment; Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(For older children: N=27 at Visit 1)

Reporting Groups

	Description
ECG Heart Rate Change: Adolescents	Single Dose of Tapentadol Oral Solution in Children and Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ECG Heart Rate Change: Older Children	Single Dose of Tapentadol Oral Solution in Children and Adolescents Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ECG Heart Rate Change: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children and Adolescents Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	ECG Heart Rate Change: Adolescents	ECG Heart Rate Change: Older Children	ECG Heart Rate Change: Young and Very Young Children
Number of Participants Analyzed	21	28	17

	ECG Heart Rate Change: Adolescents	ECG Heart Rate Change: Older Children	ECG Heart Rate Change: Young and Very Young Children
Change From Enrollment in 12-lead Electrocardiogram Heart Rate Parameter [units: beats per minute] Mean (Standard Deviation)	2.0 (16.4)	4.3 (16.2)	10.7 (16.4)

25. Secondary Outcome Measure:

Measure Title	Treatment Emergent Adverse Events by Intensity
Measure Description	The intensity of all treatment emergent adverse events (TEAEs) were scored by the investigator. Treatment emergent adverse events were those adverse events documented from the time of investigational medicinal product (IMP), study drug, up to 48 hours post dosing. The clinical “intensity” of an adverse event was classified as: • Mild: Signs and symptoms that can be easily tolerated. Symptoms can be ignored and disappear when the subject is distracted. • Moderate: Symptoms cause discomfort but are tolerable; they cannot be ignored and affect concentration. • Severe: Symptoms which affect usual daily activity. For adverse events where the intensity changes over time, the maximum intensity observed was documented.
Time Frame	Baseline; 48 hours post dosing
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

Reporting Groups

	Description
Number of TEAEs: Adolescents	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 12 years and less than 18 years of age.
Number of TEAEs: Older Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 6 years and less than 12 years of age.
Number of TEAEs: Young and Very Young Children	Tapentadol oral solution single dose (1mg/kg body weight). Participants aged 2 years and less than 6 years of age.

Measured Values

	Number of TEAEs: Adolescents	Number of TEAEs: Older Children	Number of TEAEs: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Treatment Emergent Adverse Events by Intensity [units: number of events]			
Total number of TEAEs	22	33	11
Total number of mild TEAEs	10	16	10
Total number of moderate TEAEs	12	17	1

26. Secondary Outcome Measure:

Measure Title	Intake of Additional Analgesic Medication During the Trial
Measure Description	Number of participants with intakes of supplemental analgesic medication between investigational medicinal product (IMP) intake and Site Discharge grouped according to preparation taken (non-opioid/opioid).
Time Frame	Baseline; 15 hours post dosing
Safety Issue?	No

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

Reporting Groups

	Description
Adolescents With Supplementary Analgesic	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Older Children With Supplementary Analgesic	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Young and Very Young Children With Supplementary Analgesic	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Adolescents With Supplementary Analgesic	Older Children With Supplementary Analgesic	Young and Very Young Children With Supplementary Analgesic
Number of Participants Analyzed	21	28	17
Intake of Additional Analgesic Medication During the Trial [units: participants]			
Supplemental analgesic medication taken	12	18	15
Supplemental opioid analgesic taken	3	3	8
Supplemental non-opioid analgesic taken	12	18	15

27. Secondary Outcome Measure:

Measure Title	Hematology Safety Laboratory Assessments: Hemoglobin Concentration
Measure Description	The hemoglobin test is a commonly ordered blood test and was done as part of a complete blood count (CBC). It is routinely done before and after surgery to check for anemia, the presence of chronic kidney disease or other chronic medical problems. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visits 2 and 3: N=16 one participant with missing data at each of these visits).

Reporting Groups

	Description
Hemoglobin Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Hemoglobin Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).

	Description
Hemoglobin Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Hemoglobin Concentration: Adolescents	Hemoglobin Concentration: Older Children	Hemoglobin Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Hematology Safety Laboratory Assessments: Hemoglobin Concentration [units: g/L] Mean (Standard Deviation)			
Visit 1	151.10 (13.82)	140.04 (6.66)	127.47 (7.60)
Visit 2	145.67 (21.44)	128.64 (7.88)	121.75 (7.91)
Visit 3	139.00 (19.20)	126.54 (9.10)	117.00 (7.63)

28. Secondary Outcome Measure:

Measure Title	Hematology Safety Laboratory Assessments: Hematocrit
Measure Description	Hematocrit is a blood test that measures the percentage of the volume of whole blood that is made up of red blood cells (RBC). This measurement depends on the number of red blood cells and the size of red blood cells. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visits 2 and 3: N=16 one participant with missing data at each of these visits).

Reporting Groups

	Description
Hematocrit: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Hematocrit: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Hematocrit: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Hematocrit: Adolescents	Hematocrit: Older Children	Hematocrit: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Hematology Safety Laboratory Assessments: Hematocrit [units: fraction of blood volume] Mean (Standard Deviation)			
Visit 1	0.436 (0.037)	0.400 (0.018)	0.368 (0.018)
Visit 2	0.421 (0.060)	0.372 (0.024)	0.363 (0.023)
Visit 3	0.402 (0.054)	0.364 (0.025)	0.356 (0.022)

29. Secondary Outcome Measure:

Measure Title	Hematology Safety Laboratory Assessments: Erythrocyte Mean Corpuscular Volume (Mean Corpuscular Volume)
Measure Description	Erythrocyte Mean Corpuscular volume is a measurement of the average size of Red Blood Cells (RBC). It is also referred to as Mean Corpuscular Volume. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visits 2 and 3: N=16 one participant with missing data at each of these visits).

Reporting Groups

	Description
Mean Corpuscular Volume: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Mean Corpuscular Volume: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Mean Corpuscular Volume: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Mean Corpuscular Volume: Adolescents	Mean Corpuscular Volume: Older Children	Mean Corpuscular Volume: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Hematology Safety Laboratory Assessments: Erythrocyte Mean Corpuscular Volume (Mean Corpuscular Volume) [units: fL] Mean (Standard Deviation)			
Visit 1	86.1 (2.9)	82.3 (3.1)	79.6 (3.6)
Visit 2	86.5 (2.1)	83.1 (3.5)	81.8 (3.7)
Visit 3	86.9 (3.5)	83.1 (3.5)	82.7 (3.6)

30. Secondary Outcome Measure:

Measure Title	Hematology Safety Laboratory Assessments: Platelet Count
Measure Description	Platelets are cell fragments that are vital for normal blood clotting. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visits 2 and 3: N=16 one participant with missing data at each of these visits).

Reporting Groups

	Description
Platelet Count: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Platelet Count: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Platelet Count: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Platelet Count: Adolescents	Platelet Count: Older Children	Platelet Count: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Hematology Safety Laboratory Assessments: Platelet Count [units: GI/L] Mean (Standard Deviation)			
Visit 1	297.0 (59.8)	347.1 (86.2)	357.4 (67.5)
Visit 2	266.1 (73.0)	303.4 (73.9)	312.6 (111.2)
Visit 3	263.9 (57.9)	316.9 (71.3)	307.3 (50.0)

31. Secondary Outcome Measure:

Measure Title	Hematology Safety Laboratory Assessments: Leukocyte Concentration
Measure Description	Leukocytes are also called white blood cells (WBC). These were measured to assess immune function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visits 2 and 3: N=16 one participant with missing data at each visit).

Reporting Groups

	Description
Leukocyte Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Leukocyte Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Leukocyte Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Leukocyte Concentration: Adolescents	Leukocyte Concentration: Older Children	Leukocyte Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Hematology Safety Laboratory Assessments: Leukocyte Concentration [units: GI/L] Mean (Standard Deviation)			
Visit 1	6.631 (1.682)	7.594 (3.984)	6.555 (1.278)
Visit 2	8.537 (2.514)	12.509 (4.209)	10.751 (3.272)
Visit 3	10.052 (3.253)	14.806 (4.031)	13.160 (2.907)

32. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Glucose Concentration
Measure Description	A blood glucose test measures the amount of a sugar called glucose in blood. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Blood Glucose Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Glucose Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Glucose Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Glucose Concentration: Adolescents	Blood Glucose Concentration: Older Children	Blood Glucose Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Glucose Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	4.77 (0.51)	4.81 (0.52)	5.01 (1.38)
Visit 2	5.10 (0.68)	6.39 (1.49)	5.89 (1.17)
Visit 3	5.51 (0.90)	5.69 (1.21)	4.90 (0.54)

33. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Sodium Concentration
Measure Description	Sodium is required by the body for the body to function properly. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Blood Sodium Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Sodium Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Sodium Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Sodium Concentration: Adolescents	Blood Sodium Concentration: Older Children	Blood Sodium Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Sodium Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	140.9 (1.4)	140.4 (2.1)	139.3 (1.3)
Visit 2	140.3 (1.5)	138.4 (2.6)	139.1 (1.2)
Visit 3	138.1 (1.2)	138.7 (1.8)	138.8 (1.9)

34. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Potassium Concentration
Measure Description	Potassium is a mineral that the body needs to work normally. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit

Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Blood Potassium Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Potassium Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Potassium Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Potassium Concentration: Adolescents	Blood Potassium Concentration: Older Children	Blood Potassium Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Potassium Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	4.20 (0.31)	4.20 (0.32)	4.09 (0.33)
Visit 2	3.90 (0.36)	3.83 (0.32)	4.04 (0.36)
Visit 3	3.94 (0.26)	3.93 (0.29)	3.93 (0.27)

35. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Calcium Concentration
Measure Description	All cells need calcium in order to function. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.

Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older children Group at Visit 2: N=27 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Blood Calcium Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Calcium Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Calcium Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Calcium Concentration: Adolescents	Blood Calcium Concentration: Older Children	Blood Calcium Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Calcium Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	2.455 (0.065)	2.482 (0.100)	2.519 (0.055)
Visit 2	2.268 (0.166)	2.267 (0.108)	2.343 (0.160)
Visit 3	2.359 (0.104)	2.266 (0.157)	2.369 (0.123)

36. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Chloride Concentration

Measure Description	Chloride with other electrolytes help keep the proper balance of body fluids and maintain the body's acid-base balance. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older children Group at Visit 2: N=27 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Blood Chloride Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Chloride Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Chloride Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Chloride Concentration: Adolescents	Blood Chloride Concentration: Older Children	Blood Chloride Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Chloride Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	103.3 (1.9)	103.4 (2.2)	103.8 (1.7)
Visit 2	106.6 (2.2)	104.9 (2.8)	106.2 (3.0)
Visit 3	103.0 (2.2)	105.1 (2.6)	105.1 (2.4)

37. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Phosphate Concentration
Measure Description	Phosphate is needed by the body. This test was done to see how much phosphate is in the blood. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Blood Phosphate Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Phosphate Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Blood Phosphate Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Blood Phosphate Concentration: Adolescents	Blood Phosphate Concentration: Older Children	Blood Phosphate Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Phosphate Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	1.384 (0.185)	1.560 (0.146)	1.689 (0.165)
Visit 2	1.234 (0.194)	1.248 (0.241)	1.412 (0.179)
Visit 3	1.500 (0.199)	1.535 (0.178)	1.611 (0.181)

38. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Urea Nitrogen (BUN) Concentration
Measure Description	This test is to measure the amount of urea nitrogen in the blood. It was used to test liver and kidney function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
BUN Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
BUN Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
BUN Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	BUN Concentration: Adolescents	BUN Concentration: Older Children	BUN Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Urea Nitrogen (BUN) Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	4.55 (1.19)	4.47 (1.30)	5.15 (1.19)
Visit 2	4.54 (1.32)	4.38 (0.95)	4.19 (0.93)
Visit 3	3.88 (0.98)	4.31 (1.21)	4.11 (0.82)

39. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Creatinine Concentration
Measure Description	Creatinine is removed from the body entirely by the kidneys. If kidney function is not normal, creatinine level increases in the blood. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Creatinine Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Creatinine Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Creatinine Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Creatinine Concentration: Adolescents	Creatinine Concentration: Older Children	Creatinine Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Creatinine Concentration [units: µmol/L] Mean (Standard Deviation)			
Visit 1	73.3 (14.7)	49.5 (6.2)	35.6 (4.8)

	Creatinine Concentration: Adolescents	Creatinine Concentration: Older Children	Creatinine Concentration: Young and Very Young Children
Visit 2	67.8 (15.1)	44.1 (9.3)	31.6 (6.7)
Visit 3	68.6 (16.2)	41.5 (8.0)	33.0 (5.8)

40. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Aspartate Aminotransferase (AST) Enzyme Activity
Measure Description	AST is considered to be one of the two most important tests to detect liver injury. During liver damage the enzyme is released into the blood. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older children at Visits 2 and 3: N=26 two participants with missing data; Young and Very Young Children Group at Visits 1 and 3: N=16 one participant with missing data).

Reporting Groups

	Description
AST Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
AST Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
AST Activity: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	AST Activity: Adolescents	AST Activity: Older Children	AST Activity: Young and Very Young Children
Number of Participants Analyzed	21	28	17

	AST Activity: Adolescents	AST Activity: Older Children	AST Activity: Young and Very Young Children
Biochemistry Safety Laboratory Parameters: Aspartate Aminotransferase (AST) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	21.5 (5.1)	27.9 (6.5)	33.4 (3.8)
Visit 2	21.6 (4.5)	29.9 (5.1)	37.9 (7.5)
Visit 3	21.6 (12.9)	30.2 (7.2)	33.8 (4.4)

41. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Triglycerides Concentration
Measure Description	Triglycerides are a group of fat. Triglycerides were measured as part of metabolic and cardiac assessments. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant data missing; Older children Visits 2 and 3: N=27 and N=26 one and two participant data missing; Young and Very Young Children Group at Visits 2 and 3: N=16 one participant data missing).

Reporting Groups

	Description
Triglycerides Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Triglycerides Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Triglycerides Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Triglycerides Concentration: Adolescents	Triglycerides Concentration: Older Children	Triglycerides Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Triglycerides Concentration [units: mmol/L] Mean (Standard Deviation)			
Visit 1	1.118 (0.459)	1.129 (0.495)	1.223 (0.511)
Visit 2	0.666 (0.318)	0.499 (0.245)	0.556 (0.173)
Visit 3	0.634 (0.224)	0.646 (0.225)	0.789 (0.227)

42. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Serum Albumin Concentration
Measure Description	Albumin is a protein made by the liver. Albumin prevents fluid leaking into the tissues. Albumin also transports many small molecules. Serum albumin was measured in the clear liquid portion of the blood called serum. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older children N=27 at Visit 1; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Albumin Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Albumin Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).

	Description
Albumin Concentration: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Albumin Concentration: Adolescents	Albumin Concentration: Older Children	Albumin Concentration: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Serum Albumin Concentration [units: g/L] Mean (Standard Deviation)			
Visit 1	43.4 (2.5)	43.4 (3.0)	42.6 (2.4)
Visit 2	38.4 (3.1)	37.1 (2.5)	38.9 (3.4)
Visit 3	38.4 (2.8)	37.2 (3.5)	37.5 (3.3)

43. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Urate in the Blood
Measure Description	Uric acid (urate is the salt) is a chemical created when the body breaks down substances called purines. Most urate dissolves in blood and travels to the kidneys. From there, it passes out in the urine. The test is used to determine kidney function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Urate: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Urate: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Urate: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Urate: Adolescents	Urate: Older Children	Urate: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Urate in the Blood [units: µmol/L] Mean (Standard Deviation)			
Visit 1	301.62 (69.35)	228.32 (41.87)	214.82 (39.67)
Visit 2	305.57 (85.12)	225.39 (44.74)	205.65 (34.51)
Visit 3	291.45 (69.06)	213.68 (57.96)	195.94 (48.68)

44. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Calculated Glomerular Filtration Rate
Measure Description	Glomerular filtration rate (GFR) was done to check how well the kidneys are working. It estimates how much blood passes through the glomeruli in the kidney each minute. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit; Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Glomerular Filtration Rate: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Glomerular Filtration Rate: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Glomerular Filtration Rate: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Glomerular Filtration Rate: Adolescents	Glomerular Filtration Rate: Older Children	Glomerular Filtration Rate: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Calculated Glomerular Filtration Rate [units: mL/min/1.73m^2] Mean (Standard Deviation)			
Visit 1	133.6 (20.7)	133.9 (16.6)	141.5 (18.4)
Visit 2	146.6 (25.2)	155.1 (38.0)	166.9 (42.5)
Visit 3	142.6 (23.3)	158.7 (31.5)	164.0 (37.3)

45. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Urine Specific Gravity
Measure Description	This test was used to test for the water balance and urine concentration. A urine sample was tested right away. A dipstick with a color-sensitive pad was used. The color the dipstick changes and the specific gravity of the urine was read off the color chart. In the study there were 2 planned safety urine collections. At Visit 1 in the enrollment period, after consent and assent obtained. The second sample was obtained at Visit 3 prior to discharge from the hospital. The discharge visit was as per standard of care.
Time Frame	Enrollment Visit and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Young and Very Young Children Group at Visits 1: N=9 thus 8 participants with missing data; at Visit 3: N=7 thus 10 participants with missing data).

Reporting Groups

	Description
Specific Gravity Urine: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Specific Gravity Urine: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Specific Gravity Urine: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Specific Gravity Urine: Adolescents	Specific Gravity Urine: Older Children	Specific Gravity Urine: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Urine Specific Gravity [units: units on a scale] Mean (Standard Deviation)			
Visit 1	1.025 (0.007)	1.024 (0.004)	1.021 (0.007)
Visit 3	1.022 (0.007)	1.024 (0.004)	1.024 (0.002)

46. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Urine pH (Acid, Alkalinity) Test
Measure Description	A urine sample was tested right away. A dipstick made with a color-sensitive pad was used. The color indicated the acidity of the urine. In the study there were 2 planned safety urine collections. At Visit 1 in the enrollment period, after consent and assent obtained. The second sample was obtained at Visit 3 prior to discharge from the hospital. The discharge visit was as per standard of care.
Time Frame	Enrollment Visit and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Young and Very Young Children Group at Visits 1: N=9 thus 8 participants with missing data; at Visit 3: N=7 thus 10 participants with missing data).

Reporting Groups

	Description
Urine pH: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Urine pH: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Urine pH: Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Urine pH: Adolescents	Urine pH: Older Children	Urine pH: Young and Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Urine pH (Acid, Alkalinity) Test [units: units on a scale] Mean (Standard Deviation)			
Visit 1	6.2 (0.5)	6.5 (0.4)	6.2 (0.6)
Visit 3	6.1 (0.2)	6.2 (0.4)	6.4 (0.9)

47. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Liver Function Test - Alanine Aminotransferase (ALT) Enzyme Activity
Measure Description	This test was done in combination with other tests (such as AST, ALP, and bilirubin) to diagnose and monitor the liver function. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=19 two participants with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
ALT Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ALT Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ALT Activity: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	ALT Activity: Adolescents	ALT Activity: Older Children	ALT Activity: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Liver Function Test - Alanine Aminotransferase (ALT) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	16.2 (6.3)	15.9 (4.1)	16.4 (3.4)
Visit 2	14.1 (4.6)	15.7 (3.4)	17.9 (5.3)
Visit 3	14.2 (4.5)	15.4 (3.4)	17.1 (4.1)

48. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Liver Function Test - Gamma-Glutamyl Transferase (GGT) Enzyme Activity
Measure Description	The gamma-glutamyl transferase (GGT) test was used in combination with the alkaline phosphatase (ALP) test. Both ALP and GGT can be elevated in bile duct or liver complications. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 2 and 3: N=20 one participant with missing data; Older Children at Visit 2: N=27 one participant with missing data; Young and Very Young Children Group at Visit 2: N=16 one participant with missing data).

Reporting Groups

	Description
GGT Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
GGT Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
GGT Activity: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	GGT Activity: Adolescents	GGT Activity: Older Children	GGT Activity: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Liver Function Test - Gamma-Glutamyl Transferase (GGT) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	12.0 (4.0)	10.6 (2.9)	9.4 (1.7)
Visit 2	10.4 (3.9)	8.7 (2.0)	8.6 (1.9)
Visit 3	10.8 (4.2)	8.8 (1.9)	8.3 (2.0)

49. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Liver Function Test - Bilirubin Concentration
Measure Description	Old red blood cells are replaced by new blood cells every day. Bilirubin is made by the body when the old blood cells are removed. The concentration of bilirubin in the blood measures liver function. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents-Visit 2 & 3: N=20 - 1 participant with data missing; Older Children-Visit 1 & 2: N=26 thus 2 participants with data missing; Young and Very Young Children-Visits 1 & 3: N=12 (5 with data missing) & at Visit 2 N=9 (8 with data missing).

Reporting Groups

	Description
Bilirubin Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Bilirubin Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Bilirubin Concentration: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Bilirubin Concentration: Adolescents	Bilirubin Concentration: Older Children	Bilirubin Concentration: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Liver Function Test - Bilirubin Concentration [units: µmol/L] Mean (Standard Deviation)			
Visit 1	12.0 (7.0)	6.8 (3.5)	4.8 (1.8)
Visit 2	10.9 (7.8)	6.3 (2.3)	3.7 (1.0)
Visit 3	17.8 (10.8)	9.3 (4.5)	5.8 (2.6)

50. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Liver Function Test - Lactate Dehydrogenase (LDH) Enzyme Activity
Measure Description	Lactate Dehydrogenase (LDH) was used to check for tissue damage. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older Children at Visits 1 and 3: N=26 and at Visit 2 N=24 participants; Young and Very Young Children Group at Visits 1 and 3: N=16 participant with missing data).

Reporting Groups

	Description
LDH Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
LDH Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
LDH Activity: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	LDH Activity: Adolescents	LDH Activity: Older Children	LDH Activity: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Liver Function Test - Lactate Dehydrogenase (LDH) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	157.7 (23.0)	210.5 (31.7)	243.8 (23.3)
Visit 2	154.5 (27.9)	199.1 (27.2)	256.3 (36.8)
Visit 3	143.9 (28.8)	197.8 (28.5)	238.6 (24.6)

51. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Blood Protein Concentration
Measure Description	The test was done to verify kidney and liver function. It is done in combination with the albumin test. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit

Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older Children at Visit 2: N=27 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data).

Reporting Groups

	Description
Protein Concentration: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Protein Concentration: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Protein Concentration: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	Protein Concentration: Adolescents	Protein Concentration: Older Children	Protein Concentration: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Blood Protein Concentration [units: g/L] Mean (Standard Deviation)			
Visit 1	72.3 (3.5)	73.3 (4.4)	68.6 (4.7)
Visit 2	64.2 (4.6)	61.8 (4.4)	62.1 (4.9)
Visit 3	64.9 (4.4)	62.1 (5.5)	61.8 (4.6)

52. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Creatine Kinase (CK) Enzyme Activity
Measure Description	The creatine kinase (CK) test was used to detect inflammation of muscles. The test was done in combination with other tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.

Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older children at Visit 1: N=27 (1 participant missing); Young and Very Young Children Group at Visit 3: N=16 one participant with missing data at this visit).

Reporting Groups

	Description
CK Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
CK Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
CK Activity: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	CK Activity: Adolescents	CK Activity: Older Children	CK Activity: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Creatine Kinase (CK) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	126.0 (66.0)	109.8 (31.7)	133.4 (35.2)
Visit 2	186.8 (216.2)	283.3 (158.5)	275.8 (87.5)
Visit 3	264.6 (564.4)	288.1 (214.8)	203.6 (84.5)

53. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Alkaline Phosphatase (ALP) Enzyme Activity

Measure Description	The Alkaline Phosphatase activity was used to detect bone or hepatobiliary disease. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to study drug administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 2 and 3: N=20 one participant with missing data; Young and Very Young Children Group at Visits 3: N=16 one participant with missing data at this visit).

Reporting Groups

	Description
ALP Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ALP Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
ALP Activity: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	ALP Activity: Adolescents	ALP Activity: Older Children	ALP Activity: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Alkaline Phosphatase (ALP) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	124.7 (62.7)	240.0 (50.8)	230.1 (26.7)
Visit 2	114.7 (53.9)	207.5 (42.2)	210.2 (31.5)
Visit 3	107.6 (54.3)	204.1 (46.7)	199.2 (26.2)

54. Secondary Outcome Measure:

Measure Title	Biochemistry Safety Laboratory Parameters: Triacylglycerol Lipase (TL) Enzyme Activity
Measure Description	A triacylglycerol lipase test was done to check for pancreatic function. In the study there were 3 planned safety blood draws for routine blood tests. In the study there were 3 planned safety blood draws for routine blood tests: at Visit 1 (during the enrollment period, including surgery), at Visit 2 (prior to investigational medicinal product administration) and at Visit 3 (prior to discharge from the hospital). The discharge visit was as per standard of care.
Time Frame	Enrollment Visit, Visit 2 and Discharge Visit
Safety Issue?	Yes

Analysis Population Description

The protocol pre-specified that the young and very young children will be reported as one group.

(Adolescents Group at Visit 3: N=20 one participant with missing data; Older Children N=27 at Visit 1 one participant with missing data; Young and Very Young Children Group at Visit 3: N=16 one participant with missing data at visit).

Reporting Groups

	Description
TL Activity: Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
TL Activity: Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
TL Activity: Young & Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Measured Values

	TL Activity: Adolescents	TL Activity: Older Children	TL Activity: Young & Very Young Children
Number of Participants Analyzed	21	28	17
Biochemistry Safety Laboratory Parameters: Triacylglycerol Lipase (TL) Enzyme Activity [units: U/L] Mean (Standard Deviation)			
Visit 1	29.5 (10.5)	30.3 (9.4)	26.3 (8.7)
Visit 2	22.7 (8.3)	22.6 (8.8)	19.6 (6.3)
Visit 3	24.8 (18.3)	22.2 (9.2)	19.3 (6.0)

Reported Adverse Events

Time Frame	Any adverse event that started on the intake of tapentadol up to 48 hours thereafter.
Additional Description	For tapentadol oral solution, the therapeutic reach is defined as 48 hours after intake. The age groups reported were prespecified in the protocol.

Reporting Groups

	Description
Adolescents	Single Dose of Tapentadol Oral Solution in Adolescents Age 12 to Less Than 18 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Older Children	Single Dose of Tapentadol Oral Solution in Children Age 6 to Less Than 12 Years. Tapentadol oral solution single dose (1mg/kg body weight).
Young and Very Young Children	Single Dose of Tapentadol Oral Solution in Children Age 2 to Less Than 6 Years. Tapentadol oral solution single dose (1mg/kg body weight).

Serious Adverse Events

	Adolescents	Older Children	Young and Very Young Children
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Surgical and medical procedures			
post-procedural hemorrhage A [1] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA 16.1

[1] Post-procedural hemorrhage occurred 6 days following tonsillectomy. Outside the therapeutic range of the investigational product.

Other Adverse Events

Frequency Threshold Above Which Other Adverse Events are Reported: 3.6%

	Adolescents	Older Children	Young and Very Young Children
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Total	12/21 (57.14%)	20/28 (71.43%)	6/17 (35.29%)
Eye disorders			

	Adolescents	Older Children	Young and Very Young Children
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Diplopia [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Gastrointestinal disorders			
Abdominal pain upper [A] *	0/21 (0%)	0/28 (0%)	1/17 (5.88%)
Constipation [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Enlarged uvula [A] *	0/21 (0%)	0/28 (0%)	1/17 (5.88%)
Nausea [A] *	6/21 (28.57%)	9/28 (32.14%)	1/17 (5.88%)
Vomiting [A] *	3/21 (14.29%)	8/28 (28.57%)	0/17 (0%)
General disorders			
Chest pain [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Infusion site irritation [A] *	0/21 (0%)	0/28 (0%)	1/17 (5.88%)
Pyrexia [A] *	1/21 (4.76%)	1/28 (3.57%)	0/17 (0%)
Vessel puncture site bruise [A] *	0/21 (0%)	0/28 (0%)	1/17 (5.88%)
Infections and infestations			
Otitis media [A] *	1/21 (4.76%)	0/28 (0%)	0/17 (0%)
Otitis media viral [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Investigations			
Aspartate aminotransferase increased [A] †	1/21 (4.76%)	0/28 (0%)	0/17 (0%)
Blood creatine phosphokinase increased [A] †	1/21 (4.76%)	0/28 (0%)	0/17 (0%)
Cardiac murmur [A] †	0/21 (0%)	0/28 (0%)	1/17 (5.88%)
Nervous system disorders			
Dizziness [A] *	3/21 (14.29%)	3/28 (10.71%)	0/17 (0%)
Headache [A] *	2/21 (9.52%)	0/28 (0%)	2/17 (11.76%)
Somnolence [A] *	1/21 (4.76%)	1/28 (3.57%)	0/17 (0%)

	Adolescents	Older Children	Young and Very Young Children
	Affected/At Risk (%)	Affected/At Risk (%)	Affected/At Risk (%)
Tremor [A] *	1/21 (4.76%)	0/28 (0%)	0/17 (0%)
Respiratory, thoracic and mediastinal disorders			
Cough [A] *	0/21 (0%)	0/28 (0%)	2/17 (11.76%)
Epistaxis [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Nasal discomfort [A] *	0/21 (0%)	0/28 (0%)	1/17 (5.88%)
Skin and subcutaneous tissue disorders			
Hyperhidrosis [A] *	1/21 (4.76%)	0/28 (0%)	0/17 (0%)
Pruritus [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)
Rash [A] *	1/21 (4.76%)	0/28 (0%)	0/17 (0%)
Vascular disorders			
Hot flush [A] *	0/21 (0%)	1/28 (3.57%)	0/17 (0%)

† Indicates events were collected by systematic assessment.
* Indicates events were collected by non-systematic methods.
A Term from vocabulary, MedDRA 16.1

Limitations and Caveats

Another opioid may been given according to medical judgment/standard of care if the participant had persistent intolerable pain 2 hours or more after administration of tapentadol oral solution despite having received a non-opioid analgesic.

More Information

Certain Agreements:

Principal Investigators are NOT employed by the organization sponsoring the study.

There IS an agreement between the Principal Investigator and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

The sponsor reserves the right to review any publication pertaining to the trial before it is submitted for publication. Neither party has the right to prohibit publication unless publication can be shown to affect possible patent rights.

Results Point of Contact:

Name/Official Title: Director of Clinical Trials
Organization: Grünenthal GmbH
Phone: +49 241 569 3223
Email: Clinical-Trials@grunenthal.com