SYNOPSIS

INN : PARACETAMOL

Study number : PARAC_L_00859

Study title : Non-comparative, open-label, multicentre study of the acceptability and tolerability of 4.8% paediatric paracetamol oral suspension

CSR date : 25 May 2007

The study results and synopsis are supplied for informational purposes only.

Not all of the study results have necessarily been reviewed by the Regulatory Authorities.

The decision to prescribe and take a product should always be made on the basis of the most recent version of the product information and product package insert in the country of prescription.

PDF name: Paracetamol – Study 3

EMA request May 2011 – Publication of result-related information on paediatric studies submitted under Article 45 of Regulation (EC) No 1901/2006 (‘Paediatric Regulation’)

August 2011
Study title:
Non-comparative, open-label, multicentre study of the acceptability and tolerability of 4.8% paediatric paracetamol oral suspension
Protocol n°: PARAC_L_00859

Investigators:
15 paediatricians or general practitioners practicing in private offices, in France.
Coordinating investigator: Dr Jean LALAU KERALY – PARIS XVI.

Publication: Not applicable

Study duration:
Date of first inclusion: October 30, 2006
Date of last inclusion: January 27, 2007

Development phase: IIIb

Objectives:
Primary objective:
To evaluate the acceptability over 24 hours of a new paracetamol formulation, 4.8% paediatric oral suspension in children weighing between 3 and 26 kg inclusive
Secondary objectives:
Evaluate the general tolerability of treatment

Design:
Non-comparative open-label, multicentre, phase IIIb study of the acceptability of paediatric 4.8% paracetamol oral suspension in children prescribed antipyretic and/or analgesic treatment with paracetamol over a minimum period of 24 hours.

Number of patients:
Planned: 48 children.
Included: 55 patients
ITT: 55 patients
PP: 55 patients
Tolerability: 55 patients

Diagnosis and inclusion criteria:
- Child of either sex, weighing between 3 and 26 kg (included)
  presenting fever and/or pain justifying treatment by paracetamol for a minimum duration of 24 hours.
- May be followed up throughout the study period on an outpatient basis.
- Informed consent obtained in writing from parents, legal guardian or from the child him/herself if sufficiently old.
Sponsor: Study table: (Reserved for national authorities)

sanofi-aventis otc

Reference to Part or Dossier

Name of finished product: SUGAR-FREE 4.8% DOLIPRANE, oral suspension sweetened with liquid maltitol, sorbitol and saccharin sodium.

Name of active ingredients
Paracetamol

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Exclusion criteria:
- Patient with gastrointestinal disorders, vomiting.
- Hypersensitivity to paracetamol or to one of the components of the study medication
- Hepatic insufficiency.
- Fructose intolerance
- Serious concomitant disease such as cancer, immune deficiency or a serious renal, hepatic, cardiac, neurological, psychiatric or metabolic disease.
- Significant history of laboratory abnormalities.
- Treated by Kayexalate®
- Not benefiting from the social security system
- Parents incapable of understanding.
- Unable to return for the final evaluation and/or comply with the constraints of the study.
- Participation in another clinical study during the 30 days before inclusion
- Close relative of the investigator

Study product:
- Active ingredient: Paracetamol
- Pharmaceutical form: Sugar-free, paediatric, oral suspension
- Dosage strength: 4.8%
- Route of administration: Orally, either pure, or diluted in a small quantity of drink
- Dosage: 60 mg/kg/day. The presentation is adjusted for administration 4 times daily, i.e. approximately 15 mg/kg/6 hours
- Duration of prescription: 24h, if the investigator wants to continue treatment he/she must prescribe marketed paracetamol
- Batch number(s): 60031

Reference product:
Not applicable

Endpoints:
- Primary endpoint:
Global assessment of treatment by parents, guardian or childminder, measured using a 4-level semi-quantitative scale (very acceptable, acceptable, indifferent, refusal), over 24 hours (4 evaluations at 6-hour intervals).
- Secondary endpoints
Global assessment by the child (from 3 years), using a Hedonic Visual Scale during last dose before visit V2

Tolerability:
Events reported by the child, parents or legal guardian during visit V2
Events collected in the child’s diary
Events noted by the investigator during Visit 2
**Statistical methods:**
Primary analysis: Per protocol population (PP).
Determination of the 80% two-sided confidence interval of the proportion of patients finding treatment unacceptable (rounded mean of the 4 evaluations > 1). Treatment is considered to be acceptable if this interval excludes 25% and contains 10% or if the upper limit of the interval is < 10%.

**Summary - Conclusions:**
Fifty five patients were included by 11 investigators. All patients took at least one dose of the study treatment. No major deviation from the protocol was identified.
Thirty-nine patients terminated the study according to the protocol, 16 prematurely discontinued the study including 7 who refused treatment and 9 in whom the fever did not persist. Treatment discontinuations were taken into account for the evaluation of acceptability.
The 3 populations analyzed (tolerability, ITT and PP) were identical and comprised the 55 included patients.
There were 30 boys (54.5 %) and 25 girls (45.5 %), aged on average 3.3 ± 1.9 years (mean ± SD), 31 children (56.4 %) were aged 3 years or more. They weighed 14.5 ± 4.8 kg for a mean height of 93.8 ± 16.4 cm, i.e. a mean body mass index of 16.3 ± 2.5 kg/m².
Prescription of paracetamol was justified by a fever for 54 patients (98.2%) (including 24 with concomitant pain), and pain for 25 patients (45.5%) (including 24 with concomitant fever).
39 patients (70.9 %) took the 4 doses of treatment planned in the protocol, 6 patients (10.9 %) only took 3 doses, 7 patients (12.7%) 2 doses and 3 patients (5.5 %) only a single dose.

**Acceptability**
Treatment was considered to be globally acceptable for 47 patients (85.5 %) and unacceptable for the 8 others (14.5 %). The 80 % two-sided confidence interval of the percentage of patients for whom treatment was considered to be unacceptable was [8.7 %; 22.6 %]. This did not reach 25%, the threshold defined a priori as “intolerable” but, on the contrary, included 10% the expected threshold of non-acceptability. Consequently, 4.8% paracetamol oral suspension was considered to be acceptable by the patients.
The mean acceptability score over 24 hours was 2.14 ± 0.92 (on a scale ranging from 0 = refusal to 3= very acceptable), and for all 191 evaluations, treatment was considered to be “acceptable” 176 times (92.1 %).
For the 31 children aged 3 years or more in whom the hedonic visual scale was applied, 44.4 % considered the treatment to be “not good” (80 % two-sided CI [31.1 %; 58.5 %])

**Tolerability:**
No serious or unexpected adverse event or any treatment-related event was reported.
A single intercurrent event was reported during the study: “Vomiting of food”, of moderate severity, not related to treatment according to the investigator.
### Study Table

**Sponsor:** sanofi-aventis otc

**Name of finished product:** SUGAR-FREE 4.8% DOLIPRANE, oral suspension sweetened with liquid maltitol, sorbitol and saccharin sodium.

**Name of active ingredients:** Paracetamol

**CONCLUSION:**
- 4.8% paracetamol oral suspension was considered to be acceptable by the patients.
- Tolerability was good.

**Date of report:** 25 May 2007

**Reference to Part or Dossier:**

**Volume:**

**Page:**

(Reserved for national authorities)