EMA/703629/2011

European Medicines Agency decision

P/222/2011

of 27 September 2011

on the acceptance of a modification of an agreed paediatric investigation plan for rabeprazole (sodium) (Pariet and associated names), (EMEA-000055-PIP01-07-M04) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

Disclaimer

This Decision does not constitute entitlement to the rewards and incentives referred to in Title V of Regulation (EC) No 1901/2006.

Only the English text is authentic.

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The European Medicines Agency,

Having regard to the Treaty on the Functioning of the European Union,

Having regard to Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No. 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004[1],

Having regard to Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/50/2008 issued on 20 July 2008, the decision P/34/2010 issued on 19 March 2010, and the decision P/101/2010 issued on 4 June 2010,

Having regard to the application submitted by Eisai Limited on 27 May 2011 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 12 August 2011, in accordance with Article 22 of Regulation (EC) No 1901/2006,

Having regard to Article 25 of Regulation (EC) No 1901/2006,

Whereas:

(1) The Paediatric Committee of the European Medicines Agency has given an opinion on the acceptance of changes to the agreed paediatric investigation plan.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[1] OJ L 378, 27.12.2006, p.1.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for rabeprazole (sodium) (Pariet and associated names), gastro-resistant granules, gastro-resistant tablet, modified-release capsule, hard, oral use, are hereby accepted in the scope set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices.

Article 2

This decision is addressed to Eisai Limited, European Knowledge Centre, Mosquito Way, AL10 9SN - Hatfield, United Kingdom.

Done at London, 27 September 2011

For the European Medicines Agency
Andreas Pott
Acting Executive Director
(Signature on file)

EMA/PDCO/591125/2011

Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan

EMEA-000055-PIP01-07-M04

Scope of the application

Active substance(s):

Rabeprazole (sodium)

Invented name:

Pariet and associated names

Condition(s):

Treatment of gastro-oesophageal reflux disease

Treatment of Zollinger-Ellison Syndrome

Treatment of duodenal ulcer

Treatment of gastric ulcer

Treatment of Helicobacter pylori in patients with peptic ulcer disease

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Gastro-resistant granules

Gastro-resistant tablet

Modified-release capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Eisai Limited

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Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Eisai Limited submitted to the European Medicines Agency on 27 May 2011 an application for modification of the agreed paediatric investigation plan with a deferral and a waiver as set out in the European Medicines Agency's decision P/50/2008 issued on 20 July 2008, the decision P/34/2010 issued on 19 March 2010, and the decision P/101/2010 issued on 4 June 2010.

The application for modification proposed changes to the agreed paediatric investigation plan.

The procedure started on 15 June 2011.

A meeting with the Paediatric Committee took place on 10 August 2011.

Scope of the modification

Some clinical measures and timelines of the Paediatric Investigation Plan have been modified.

Opinion

1. The Paediatric Committee, having assessed the application in accordance with Article 22 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree to changes to the paediatric investigation plan in the scope set out in the Annex I of this opinion.

   The Icelandic and the Norwegian Paediatric Committee members agree with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver are set out in the Annex I.

This opinion is forwarded to the applicant and the Executive Director of the European Medicines Agency, together with its annexes and appendix.

London, 12 August 2011

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

Annex I

The subset(s) of the paediatric population and condition(s) covered by the waiver and the measures and timelines of the agreed Paediatric Investigation Plan

1. Waiver

1.1. Condition: treatment of Zollinger-Ellison syndrome

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for gastro-resistant granules, oral use, gastro-resistant tablet, oral use, and modified-release capsule, hard, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

1.2. Condition: treatment of duodenal ulcer

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for gastro-resistant granules, oral use, gastro-resistant tablet, oral use, and modified-release capsule, hard, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

1.3. Condition: treatment of gastric ulcer

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age;
- for gastro-resistant granules, oral use, gastro-resistant tablet, oral use, and modified-release capsule, hard, oral use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric Investigation Plan

2.1. Condition: treatment of gastro-oesophageal reflux disease

2.1.1. Indication(s) targeted by the PIP

Treatment of neonates infants, children and adolescents with gastro-oesophageal reflux disease.

2.1.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Gastro-resistant granules

Gastro-resistant tablet

Modified-release capsule, hard

2.1.4. Studies

Area	Number of studies	Description
Quality	2	Elimination or minimisation of phthalates and their degradation products. Age-appropriate strength and formulation of modified-release capsule, hard, for use from 6 years to less than 12 years of age.
Non-clinical	0	Not applicable.
Clinical	9	Study 1: Multi-centre, open-label, randomised, pharmacokinetics, pharmacodynamics and safety of rabeprazole single and multiple dose in neonates and preterm infants with a corrected age less than 44 weeks. Study 2: Multi-centre, open-label, randomised, pharmacokinetics, pharmacodynamics and safety of single and multiple daily doses of rabeprazole in patients 1 month to 11 months of age with GORD. Study 3: Double-blind, randomised, placebo-controlled, parallel-group, withdrawal Phase 3 study to determine efficacy and safety of rabeprazole in 2 different doses in children 1 month to 11 months of age with GORD. Study 4: Multi-centre, open label, randomised, dose-ranging phase II study to evaluate the pharmacokinetics and safety of rabeprazole after single and multiple daily administration in 2 dose levels in paediatric subjects from 1 year to 11 years of age with endoscopically proven GORD. Study 5: Randomised, double-blind, dose ranging, Phase 2 study to determine the efficacy and safety of rabeprazole delayed release in paediatric subjects from 1 year to 11 years of age. Study 6: Double-blind, extension of long term, maintenance safety and efficacy of rabeprazole delayed release in paediatric subjects 1 year to 11 years of age with GORD. Study 8: Open-label, randomized, open-label, single and multiple dose trial to evaluate pharmacokinetics and safety of rabeprazole sodium modified-release capsules in adolescents from 12 years to less than 18 years of age. Study 9: Open-label, randomized trial to evaluate safety and efficacy of rabeprazole sodium modified- release in adolescents from 12 years to less than 18 years of age. Study 10: Trial to evaluate pharmacokinetics, safety and acceptability of rabeprazole sodium modified-release capsule in children and adolescents from 6 years to less than 12 years of age.

2.2. Condition: treatment of Helicobacter pylori infection in patients with peptic ulcer disease

2.2.1. Indication(s) targeted by the PIP

Treatment of infants, children and adolescents with Helicobacter pylori infection.

2.2.2. Subset(s) of the paediatric population concerned by the paediatric development

From birth to less than 18 years of age.

2.2.3. Pharmaceutical form(s)

Gastro-resistant granules

Gastro-resistant tablet

Modified-release capsule, hard

2.2.4. Studies

Area	Number of studies	Description
Quality	2	As for condition treatment of gastro-oesophageal reflux disease.
Non-clinical	0	Not applicable.
Clinical	1	Study 7: Extrapolation of existing adult data and paediatric data generated in the gastro-oesophageal reflux disease studies to determine dose and dosing regime for the management of Helicobacter pylori eradication.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By July 2014
Deferral for one or more studies contained in the paediatric investigation plan:	Yes