EMA/354482/2010

European Medicines Agency decision

P/101/2010

of 4 June 2010

on the acceptance of a modification of an agreed paediatric investigation plan for rabeprazole (sodium) (Pariet and associated names) (EMEA-000055-PIP01-07-M03) 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,

Having regard to the application submitted by Eisai Limited on 30 March 2010 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation planwith a deferral and a waiver,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 May 2010, 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 micro-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, 4 June 2010

For the European Medicines Agency
Thomas Lönngren
Executive Director

(Signature on file)

EMA/PDCO/314156/2010

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

EMEA-000055-PIP01-07-M03

Scope of the application

Active substance(s):

Rabeprazole (sodium)

Invented name:

Pariet and associated names

Condition(s):

Gastro-oesophageal reflux disease

Zollinger-Ellison syndrome

Duodenal ulcer

Gastric ulcer

Helicobacter pylori infection in patients with peptic ulcer disease

Pharmaceutical form(s):

Gastro-resistant micro-granules

Gastro-resistant tablet

Modified-release capsule, hard

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Eisai Limited

Information about the authorised medicinal product:

See Annex II

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Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Eisai Limited submitted to the European Medicines Agency on 30 March 2010 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/34/2010 issued on 19 March 2010 and the decision P/50/2008 issued on 20 July 2008.

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

The procedure started on 15 April 2010.

Scope of the modification

A clinical measure of the paediatric investigation plan has 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 Norwegian Paediatric Committee member agrees 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 annex(es) and appendix.

London, 21 May 2010

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman

(Signature on file)

Annex I

The measures and timelines of the agreed paediatric investigation plan and the subset(s) of the paediatric population and condition(s) covered by the waiver

1. Condition(s)

Gastro-oesophageal reflux disease
Zollinger-Ellison syndrome
Duodenal ulcer
Gastric ulcer
Helicobacter pylori infection in patients with peptic ulcer disease

2. Waiver

2.1. Condition

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 micro-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.

2.2. Condition

Duodenal ulcer

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age
- for gastro-resistant micro-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.

2.3. Condition

Gastric ulcer

The waiver applies to:

- all subsets of the paediatric population from birth to less than 18 years of age
- for gastro-resistant micro-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.

3. Paediatric Investigation Plan

3.1. Condition to be investigated

Gastro-oesophageal reflux disease

3.1.1. Indication targeted by the PIP

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

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

From birth to less than 18 years of age.

3.1.3. Pharmaceutical form(s)

Gastro-resistant micro-granules
Gastro-resistant tablet
Modified-release capsule, hard

3.1.4. 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: Open-label, extension of long term, maintenance safety and efficacy of rabeprazole delayed release in paediatric subjects 1 year to

Area	Number of studies	Description
		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

3.2. Condition to be investigated

Helicobacter pylori infection in patients with peptic ulcer disease

3.2.1. Indication targeted by the PIP

Treatment of infants, children and adolescents with Helicobacter pylori infection

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

From birth to less than 18 years of age.

3.2.3. Pharmaceutical form(s)

Gastro-resistant micro-granules
Gastro-resistant tablet
Modified-release capsule, hard

3.2.4. Studies

Area	Number of studies	Description
Quality	2	As for condition 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

4. Follow-up, completion and deferral of pip

Measures to address long term follow-up of potential 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

ANNEX II

INFORMATION ABOUT THE AUTHORISED MEDICINAL PRODUCT

Invented name **Name**	**Strength**	**Pharmaceutical form**	**Route of administration**
Pariet and associated names	10 mg, 20 mg	Gastro-resistant tablets	Oral use