

EMA/823217/2018

## European Medicines Agency decision

P/0401/2018

of 3 December 2018

on the acceptance of a modification of an agreed paediatric investigation plan for rabeprazole (sodium) (Pariet and associated names), (EMA-000055-PIP01-07-M06) 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<sup>1</sup>,

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<sup>2</sup>,

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, the decision P/101/2010 issued on 4 June 2010, decision P/222/2011 issued on 27 September 2011 and the decision P/0055/2012 issued on 26 March 2012,

Having regard to the application submitted by Eisai Limited on 13 August 2018 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 16 November 2018, in accordance with Article 22 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.

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<sup>1</sup> OJ L 378, 27.12.2006, p.1.

<sup>2</sup> 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, 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, Hertfordshire, United Kingdom.

EMA/PDCO/570225/2018  
London, 16 November 2018

## Opinion of the Paediatric Committee on the acceptance of a modification of an agreed Paediatric Investigation Plan EMA-000055-PIP01-07-M06

### 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

**Route(s) of administration:**

Oral use

**Name/corporate name of the PIP applicant:**

Eisai Limited

**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 13 August 2018 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, the decision P/101/2010 issued on 4 June 2010, decision P/222/2011 issued on 27 September 2011 and the decision P/0055/2012 issued on 26 March 2012.

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

The procedure started on 18 September 2018.

## **Scope of the modification**

Some measures 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 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 annexes and appendix.

## **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 (PIP)**

## **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, and gastro-resistant tablet, 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, and gastro-resistant tablet, 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, and gastro-resistant tablet, 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

#### 2.1.4. Studies

| Area         | Number of studies | Description                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
|--------------|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality      | 1                 | Elimination or minimisation of phthalates and their degradation products.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Non-clinical | 0                 | Not applicable.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Clinical     | 6                 | <p><b>Study 1:</b> 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.</p> <p><b>Study 2:</b> 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.</p> <p><b>Study 3:</b> 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.</p> <p><b>Study 4:</b> 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.</p> <p><b>Study 5:</b> 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.</p> <p><b>Study 6:</b> 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.</p> |

### **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

#### 2.2.4. Studies

| Area         | Number of studies | Description                                                                                                                                                                                                                           |
|--------------|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Quality      | 1                 | As for condition treatment of gastro-oesophageal reflux disease.                                                                                                                                                                      |
| Non-clinical | 0                 | Not applicable.                                                                                                                                                                                                                       |
| Clinical     | 1                 | <b>Study 7:</b> 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 <i>Helicobacter pylori</i> 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 February 2013 |
| Deferral for one or more studies contained in the paediatric investigation plan: | Yes              |

## Annex II

### Information about the authorised medicinal product

#### Condition(s) and authorised indication(s):

1. Treatment of gastro-oesophageal reflux disease

Authorised indications:

Treatment of symptomatic erosive or ulcerative gastro-oesophageal reflux disease (GORD), gastro-oesophageal reflux disease long term maintenance (GORD maintenance), symptomatic treatment of moderate to very severe gastro-oesophageal reflux disease (symptomatic GORD)

2. Treatment of Zollinger-Ellison syndrome

Authorised indications:

Treatment of Zollinger-Ellison syndrome

3. Treatment of duodenal ulcer

Authorised indication:

Treatment of active duodenal ulcer

4. Treatment of gastric ulcer

Authorised indication:

Treatment of active benign gastric ulcer

5. Treatment of *Helicobacter pylori* infection in patients with peptic ulcer disease

Authorised indication:

in combination with appropriate antibacterial regimens for the eradication of *Helicobacter pylori* in patients with peptic ulcer disease.

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