EMA/249406/2016

European Medicines Agency decision

P/0118/2016

of 22 April 2016

on the acceptance of a modification of an agreed paediatric investigation plan for perampanel (Fycompa), (EMEA-000467-PIP01-08-M07) 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/79/2010 issued on 7 May 2010, the decision P/248/2011 issued on 25 October 2011, the decision P/0123/2012 issued on 4 July 2012, the decision P/0161/2013 issued on 29 July 2013, the decision P/0307/2013 issued on 13 December 2013, the decision P/0160/2014 issued on 11 June 2014, and the decision P/0301/2014 issued on 24 November 2014,

Having regard to the application submitted by Eisai Europe Limited on 4 January 2016 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 1 April 2016, 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 perampanel (Fycompa), tablet, oral suspension, 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 Europe Limited, European Knowledge Centre, Mosquito Way, AL10 9SN - Hatfield, United Kingdom.

Done at London, 22 April 2016

For the European Medicines Agency
Zaïde Frias
Head of Division
Human Medicines Research and Development Support
(Signature on file)

EMA/PDCO/18299/2016 Corr
London, 1 April 2016

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

EMEA-000467-PIP01-08-M07

Scope of the application

Active substance(s):

Perampanel

Invented name:

Fycompa

Condition(s):

Treatment of treatment-resistant epilepsies

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Oral suspension

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Eisai Europe 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 Europe Limited submitted to the European Medicines Agency on 4 January 2016 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/79/2010 issued on 7 May 2010, the decision P/248/2011 issued on 25 October 2011, the decision P/0123/2012 issued on 4 July 2012, the decision P/0161/2013 issued on 29 July 2013, the decision P/0307/2013 issued on 13 December 2013, the decision P/0160/2014 issued on 11 June 2014, and the decision P/0301/2014 issued on 24 November 2014.

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

The procedure started on 2 February 2016.

Scope of the modification

Some 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 Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan 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

Not applicable.

2. Paediatric Investigation Plan

2.1. Condition:

Treatment of treatment-resistant epilepsies

2.1.1. Indication(s) targeted by the PIP

Adjunctive therapy in patients with refractory partial onset seizures including secondarily generalised seizures

Adjunctive therapy in patients with other paediatric epilepsies

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)

Tablet

Oral suspension

2.1.4. Studies

Area	Number of studies	Description
Quality-related studies	1	**Study 1** Development of an oral liquid formulation (≤ 0.5mg/ml) and a dosing device suitable for treatment of children of all ages including preterm neonates.
Non-clinical Studies	1	**Study 2** 33-week oral gavage toxicity study in the juvenile dog.
Clinical Studies	9	**Study 3** Pooled subgroup analyses of the efficacy, pharmacokinetics and safety of perampanel in the adolescent population included in three double-blind, placebo-controlled studies in patients with refractory partial seizures. **Study 4** Open-label extension to double-blind, placebo-controlled, dose-escalation, parallel-group studies to evaluate the efficacy, pharmacokinetics and safety of perampanel as adjunctive therapy in adolescents and adults with refractory partial seizures.

		Study 5 Randomized, double-blind, placebo-controlled, parallel-group study with open-label extension phases to evaluate the effect of perampanel on cognition, safety, tolerability and pharmacokinetics when administered as an adjunctive therapy in adolescents with inadequately controlled partial onset seizures. **Study 6** Randomized, open-label, crossover study to demonstrate relative bioavailability between a 4 mg oral suspension of perampanel and a 4 mg tablet of perampanel in healthy adult subjects. **Study 7** Open-label pilot study with an extension phase to evaluate the pharmacokinetics, and to generate preliminary safety, tolerability, and efficacy data of perampanel oral suspension as an adjunctive treatment in paediatric subjects with epilepsy from 2 to less than 12 years of age. **Study 8** Exploratory, open-label study with an extension phase to evaluate preliminary efficacy, safety and tolerability of perampanel administered as an adjunctive therapy in paediatric patients (age 1 month to less than 18 years) with childhood epilepsy. **Study 9** Open-label, multicentre, uncontrolled, study with an extension phase to evaluate safety, tolerability and exposure-efficacy of perampanel suspension when administered as an adjunctive therapy in paediatric patients (from 4 to less than 12 years of age) with partial onset seizures. (E2007-G000-311) **Study 10** Open-label, multiple-dose study to explore the safety, tolerability and pharmacokinetics of perampanel as an adjunctive therapy in neonates with seizures, aged from birth to less than 28 days, followed by an open label extension study (up to 1 year). **Study 11** Open-label pilot study with an extension phase to evaluate the pharmacokinetics, and to generate preliminary safety, tolerability, and efficacy data of perampanel oral suspension as an adjunctive treatment in paediatric subjects with epilepsy from 1 to less than 24 months of age.
Extrapolation, modelling and simulation studies	2	**Study 12** Population PK and PK/PD analyses (regarding study 9, patients 4-12 years)

		Study 13 Population PK analysis (regarding study 11; patients 1-24 month of age)
Other studies	1	**Study 14** Systematic meta-analysis of the literature to substantiate the possibility of extrapolating efficacy from adults to paediatric patients with PGCTS
Other measures	0	**Not applicable.**

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	No
Date of completion of the paediatric investigation plan:	By April 2021
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 treatment-resistant epilepsies (localisation-related or generalised epilepsies and age-related epilepsy syndromes)

Authorised indication(s):

- adjunctive treatment of partial-onset seizures with or without secondarily generalised seizures in patients with epilepsy aged 12 years and older.

Authorised pharmaceutical form(s):

Film-coated tablet

Authorised route(s) of administration:

Oral use