EMA/195548/2014

European Medicines Agency decision

P/0120/2014

of 7 May 2014

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for pradigastat (EMEA-001333-PIP02-13) 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.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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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 application submitted by Novartis Europharm Limited on 10 June 2013 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 21 March 2014, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation and Article 13 of said Regulation,

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 agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver.

(2) It is therefore appropriate to adopt a decision agreeing a paediatric investigation plan.

(3) It is therefore appropriate to adopt a decision granting a deferral.

(4) It is therefore appropriate to adopt a decision granting a waiver.

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

Has adopted this decision:

Article 1

A paediatric investigation plan for pradigastat, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby agreed.

Article 2

A deferral for pradigastat, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 3

A waiver for pradigastat, film-coated tablet, oral use, the details of which are set out in the opinion of the Paediatric Committee of the European Medicines Agency annexed hereto, together with its appendices, is hereby granted.

Article 4

This decision is addressed to Novartis Europharm Limited, Wimblehurst Road Horsham, West Sussex, RH12 5AB - Horsham, United Kingdom.

Done at London, 7 May 2014

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/25448/2014

Opinion of the Paediatric Committee on the agreement of a Paediatric Investigation Plan and a deferral and a waiver

EMEA-001333-PIP02-13

Scope of the application

Active substance(s):

Pradigastat

Condition(s):

Treatment of familial chylomicronaemia syndrome (type I hyperlipoproteinaemia)

Pharmaceutical form(s):

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Novartis Europharm Limited submitted for agreement to the European Medicines Agency on 10 June 2013 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 17 July 2013.

Supplementary information was provided by the applicant on 20 December 2013. The applicant proposed modifications to the paediatric investigation plan.

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Opinion

1. The Paediatric Committee, having assessed the proposed paediatric investigation plan in accordance with Article 17 of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

   - to agree the paediatric investigation plan in accordance with Article 18 of said Regulation;
   - to grant a deferral in accordance with Article 21 of said Regulation;
   - to grant a waiver for one or more subsets of the paediatric population in accordance with Article 13 of said Regulation and concluded in accordance with Article 11(1)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   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 agreed 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 and appendix.

London, 21 March 2014

On behalf of the Paediatric Committee
Dr Dirk Mentzer, 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 familial chylomicronaemia syndrome (type I hyperlipoproteinaemia)

The waiver applies to:

- the paediatric population from birth to Tanner stage III;
- for film-coated tablet, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric Investigation Plan

2.1. Condition: treatment of familial chylomicronaemia syndrome (type I hyperlipoproteinaemia)

2.1.1. Indication(s) targeted by the PIP

Treatment of familial chylomicronaemia syndrome (type I hyperlipoproteinaemia).

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

At Tanner stage IV or above.

2.1.3. Pharmaceutical form(s)

Film-coated tablet.

2.1.4. Measures

Area	Number of studies	Description
Quality-related studies	0	Not applicable.
Non-clinical studies	5	**Study 1: 1070498** Oral gavage repeated-dose, follow-up study to evaluate adverse effects of pradigastat on female rats during gestation and lactation and the development of the pups and their survival, physical development, behaviour and reproductive performance. **Study 2: 1170661** Oral gavage repeated-dose study to investigate the causes of adverse effects of pradigastat on rat pups during lactation, to determine the toxicokinetic characteristics of pradigastat in the maternal and offspring plasma, and to analyse maternal milk samples for nutrient content.

		Study 3: 1170233 Three-week oral gavage dose range-finding toxicity study in juvenile rats to determine toxicokinetics of pradigastat and to characterise potential differences in toxicity between pre-pubescent and pubescent rats. **Study 4: 1170234** Nine-week oral gavage toxicity study in juvenile rats to evaluate the adverse effects of pradigastat on the postnatal development of the rat, the potential for recovery and the toxicokinetic characteristics of pradigastat. **Study 5: 1270085** Three-week oral gavage toxicity study in juvenile male rats to investigate the toxicologic effects of pradigastat versus its inactive structural analogue on the male reproductive organs.
Clinical studies	2	**Study 6: CLCQ908B2306** Fifty two-week open-label, single treatment arm trial with a 6-week low fat dietary lead-in period to evaluate efficacy, safety and pharmacokinetics of pradigastat in children at Tanner stage IV or above with familial chylomicronaemia syndrome (type I hyperlipoproteinaemia). **Study 7: CLCQ908B2306E** Fifty two-week open-label extension study to evaluate safety and tolerability of pradigastat in children at Tanner stage IV or above of age with familial chylomicronaemia syndrome (type I hyperlipoproteinaemia).
Extrapolation, modelling & simulation studies	2	**Study 8** Extrapolation study to estimate exposure and to support correct dosing of pradigastat in paediatric patients at Tanner stage IV or above with familial chylomicronaemia syndrome (type I hyperlipoproteinaemia). **Study 9** Modelling and simulation study to characterise the pharmacokinetics and pharmacodynamics of pradigastat in paediatric patients at Tanner stage IV or above with familial chylomicronaemia syndrome (type I hyperlipoproteinaemia).

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 September 2018
Deferral for one or more measures contained in the paediatric investigation plan:	Yes