EMA/439456/2014

European Medicines Agency decision

P/0199/2014

of 8 August 2014

on the acceptance of a modification of an agreed paediatric investigation plan for deferasirox (Exjade), (EMEA-001103-PIP01-10-M01) 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/216/2011 issued on 9 September 2011,

Having regard to the application submitted by Novartis Europharm Limited on 28 March 2014 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 20 June 2014, in accordance with Article 22 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 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 deferasirox (Exjade), dispersible tablet, film-coated tablet, granules, 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 Novartis Europharm Limited, Wimblehurst Road, RH125AB - Horsham, West Sussex, United Kingdom.

Done at London, 8 August 2014

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

EMA/PDCO/195881/2014

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

EMEA-001103-PIP01-10-M01

Scope of the application

Active substance(s):

Deferasirox

Invented name:

Exjade

Condition(s):

Treatment of chronic iron overload requiring chelation therapy

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Dispersible tablet

Film-coated tablet

Granules

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Novartis Europharm 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, Novartis Europharm Limited submitted to the European Medicines Agency on 28 March 2014 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/216/2011 issued on 9 September 2011.

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

The procedure started on 23 April 2014.

Scope of the modification

Two new pharmaceutical forms, and related measures have been added.

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, 20 June 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 (PIP)

1. Waiver

1.1. Condition:

Treatment of chronic iron overload requiring chelation therapy

The waiver applies to:

- All subsets of the paediatric population from birth to less than 2 years of age;
- for dispersible tablets, film-coated tablet, granules, oral use;
- on the grounds that clinical studies cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the paediatric population.

2. Paediatric investigation plan

2.1. Condition:

Treatment of chronic iron overload requiring chelation therapy

2.1.1. Indication(s) targeted by the PIP

- Treatment of chronic transfusional iron overload in patients with beta thalassaemia major.
- Treatment of chronic iron overload in patients with non-transfusion-dependent thalassaemia.
- Treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in patients with other anaemias.

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

From 2 to less than 18 years of age.

2.1.3. Pharmaceutical form(s)

Dispersible tablet

Film-coated tablet

Granules

2.1.4. Measures

Area	Number of measures/ studies	Description
Quality-related measures	1	**Study 1:** Analysis of the palatability of the currently approved posology of deferasirox in paediatric patients 3 to 10 years of age with transfusional haemosiderosis

Non-clinical studies	0	Not applicable.
Clinical studies	5	**Study 2:** Double-blind, randomised, multicentre, placebo-controlled study of the efficacy and safety of deferasirox in paediatric and adult patients (10 years of age and older) with non-transfusion dependent thalassaemia syndromes (Completed study at the time of the initial PDCO review.) **Study 3:** Open-label, multicentre 5-year observational study (registry) in children from 2 to less than 6 years of age at enrolment with transfusional haemosiderosis treated with deferasirox (Ongoing study at the time of the initial PDCO review.) **Study 5:** Open-label, randomised, crossover study to evaluate the pharmacokinetic comparability of deferasirox new tablet formulation with the reference dispersible formulation in healthy adult subjects. (Completed study at the time of the initial PDCO review (Study added in M01).) **Study 6:** Open label, randomised, cross-over study to evaluate the pharmacokinetic comparability of deferasirox new granule formulation with the reference dispersible formulation in healthy adult subjects. (Completed study at the time of the initial PDCO review (Study added in M01).) **Study 7:** Open label, randomised, cross-over study to evaluate the pharmacokinetic comparability of two different doses of the deferasirox granule formulation with the reference dispersible formulation in healthy adult subjects.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	1	**Study 4:** Quantitative assessment (meta-analysis) of safety and efficacy profiles by age, blood intake rate, iron burden and average dose groups from six long-term clinical trials of deferasirox in paediatric

		and adult patients from 2 years of age with β-thalassaemias and transfusional iron overload (Ongoing study at the time of the initial PDCO review.)
Other measures	0	Not applicable.

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety or efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By June 2015
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Treatment of chronic iron overload requiring chelation therapy

Authorised indications:

- EXJADE is indicated for the treatment of chronic iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older.
- EXJADE is also indicated for the treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups:
  - in patients with beta thalassaemia major with iron overload due to frequent blood transfusions (≥ 7 ml/kg/month of packed red blood cells) aged 2 to 5 years,
  - in patients with beta thalassaemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells) aged 2 years and older,
  - in patients with other anaemias aged 2 years and older.

Authorised pharmaceutical form(s):

Dispersible tablet

Authorised route(s) of administration:

Oral use