EMA/900464/2018

European Medicines Agency decision

P/0031/2019

of 11 February 2019

on the acceptance of a modification of an agreed paediatric investigation plan for empagliflozin (Jardiance), (EMEA-000828-PIP04-16-M02) 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/0162/2017 issued on 30 June 2017 and the decision P/0165/2018 issued on 15 June 2018,

Having regard to the application submitted by Boehringer Ingelheim International GmbH on 7 September 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 14 December 2018, 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, an opinion on the acceptance of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan, including changes to the deferral.

[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 empagliflozin (Jardiance), film-coated tablet, age-appropriate formulation, oral use, including changes to the deferral, 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 covers all conditions, indications, pharmaceutical forms, routes of administration, measures, timelines, waivers and deferrals, as agreed in the decision P/33/2011 issued on 28 January 2011, including subsequent modifications thereof.

Article 3

This decision is addressed to Boehringer Ingelheim International GmbH, Binger Strasse 173, 55216 - Ingelheim am Rhein, Germany.

EMA/PDCO/46124/2019
London, 1 February 2019

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

EMEA-000828-PIP04-16-M02

Scope of the application

Active substance(s):

Empagliflozin

Invented name:

Jardiance

Condition(s):

Treatment of type 1 diabetes mellitus

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Age-appropriate formulation

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Boehringer Ingelheim International GmbH

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, Boehringer Ingelheim International GmbH submitted to the European Medicines Agency on 7 September 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/0162/2017 issued on 30 June 2017 and the decision P/0165/2018 issued on 15 June 2018.

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

An Opinion was adopted by the Paediatric Committee on 14 December 2018 for the above mentioned product. Boehringer Ingelheim International GmbH received the Paediatric Committee Opinion on 20 December 2018.

On 16 January 2019 Boehringer Ingelheim International GmbH submitted to the European Medicines Agency a written request including detailed grounds for a re-examination of the Opinion.

The re-examination procedure started on 17 January 2019.

Scope of the modification

Some measures and timelines of the Paediatric Investigation Plan have been modified.

Final Opinion

1. The Paediatric Committee, having assessed the detailed grounds for re-examination, in accordance with Article 25(3) of Regulation (EC) No 1901/2006 as amended, recommends as set out in the appended summary report:

1.1. to maintain its opinion and

- to agree to changes to the paediatric investigation plan and to the deferral 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 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 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 type 1 diabetes mellitus

The waiver applies to:

- the paediatric population from birth to less than 2 years;
- film-coated tablet and age-appropriate formulation, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of type 1 diabetes mellitus

2.1.1. Indication(s) targeted by the PIP

Adjunct to insulin for the treatment of type 1 diabetes mellitus to improve glycaemic control

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate formulation

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	1	**Study 1** Development of an oral age appropriate formulation for children below 6 years of age.
Non-clinical studies	1	**Study 2** Juvenile toxicity study, with specific focus on kidney, stomach and bone in juvenile rats (post-natal day 21)
Clinical studies	5	**Study 3** Relative bioavailability study in adults to compare selected age appropriate formulation approach(es) with the solid oral dosage form used in adult/adolescent patients

		Study 4 Open-label, randomised, single-dose, parallel group, pharmacokinetics and pharmacodynamics study in the age group from 6 to less than18 years, comparing four different dose levels of empagliflozin in children with type 1 diabetes. (1245.76, P-EASE 1) **Study 5** Double-blind, randomised, placebo controlled, parallel group trial to evaluate efficacy and safety as adjunct to insulin therapy over 52 weeks in children and adolescents from 6 to less than18 years with type 1 diabetes mellitus. (1245.77, P-EASE 2) **Study 6** Open-label, randomised, single-dose, parallel group, pharmacokinetics and pharmacodynamics study in the age group from 2 to less than 6 years, comparing different dose levels of empagliflozin in children with type 1 diabetes. (1245.163, P-EASE-3) **Study 7** Randomised, placebo-controlled crossover trial to evaluate efficacy and safety as adjunct to insulin therapy in children from 2 to less than 6 years with type 1 diabetes mellitus. (1245.164, P-EASE-4)
Extrapolation, modelling and simulation studies	1	**Study 8** Exposure-response model to characterize the influence of empagliflozin exposure on change from baseline in 24 h urinary glucose excretion after a single drug administration of empagliflozin in paediatric patients
Other studies	0	Not applicable
Other measures	0	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long term safety/efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By August 2029
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 type 2 diabetes mellitus

Authorised indication(s):

Jardiance is indicated in the treatment of type 2 diabetes mellitus to improve glycaemic control in adults as:

- Monotherapy:

When diet and exercise alone do not provide adequate glycaemic control in patients for whom use of metformin is considered inappropriate due to intolerance.

- Add-on combination therapy:

In combination with other glucose-lowering medicinal products including insulin, when these, together with diet and exercise, do not provide adequate glycaemic control

Authorised pharmaceutical form(s):

Film-coated tablets

Authorised route(s) of administration:

Oral use