EMA/398408/2017

European Medicines Agency decision

P/0162/2017

of 30 June 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for empagliflozin (Jardiance), (EMEA-000828-PIP04-16) 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 application submitted by Boehringer Ingelheim International GmbH on 9 September 2016 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 19 May 2017, 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 empagliflozin (Jardiance), film-coated tablet, age-appropriate formulation, 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 empagliflozin (Jardiance), film-coated tablet, age-appropriate formulation, 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 empagliflozin (Jardiance), film-coated tablet, age-appropriate formulation, 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 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 5

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

EMA/PDCO/162685/2017
London, 19 May 2017

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

EMEA-000828-PIP04-16

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

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Boehringer Ingelheim International GmbH submitted for agreement to the European Medicines Agency on 9 September 2016 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 18 October 2016.

Supplementary information was provided by the applicant on 27 February 2017. The applicant proposed modifications to the paediatric investigation plan.

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 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;
- for film-coated tablet and age-appropriate oral 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 age appropriate formulation
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 6-<18years, 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 6-<18years 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 2-<6years, 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 2-<6years 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 December 2028
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