EMA/584740/2018

European Medicines Agency decision

P/0307/2018

of 12 September 2018

on the acceptance of a modification of an agreed paediatric investigation plan for dapagliflozin (Forxiga), (EMEA-000694-PIP01-09-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/100/2010 issued on 11 June 2010, the decision P/0207/2012 issued on 21 September 2012, the decision P/0008/2013 issued on 22 January 2013, the decision P/0292/2013 issued on 29 November 2013, the decision P/0310/2014 issued on 25 November 2014, the decision P/0161/2015 issued on 9 July 2015 and the decision P/0247/2015 issued on 30 October 2015,

Having regard to the application submitted by AstraZeneca AB on 2 May 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 27 July 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 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 dapagliflozin (Forxiga), tablet, 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 is addressed to AstraZeneca AB, SE-151 85 Södertälje, SE-151 85 – Södertälje, Sweden.

EMA/PDCO/298074/2018
London, 27 July 2018

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

EMEA-000694-PIP01-09-M07

Scope of the application

Active substance(s):

Dapagliflozin

Invented name:

Forxiga

Condition(s):

Treatment of type 2 diabetes mellitus

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

AstraZeneca AB

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, AstraZeneca AB submitted to the European Medicines Agency on 2 May 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/100/2010 issued on 11 June 2010, the decision P/0207/2012 issued on 21 September 2012, the decision P/0008/2013 issued on 22 January 2013, the decision P/0292/2013 issued on 29 November 2013, the decision P/0310/2014 issued on 25 November 2014, the decision P/0161/2015 issued on 9 July 2015 and the decision P/0247/2015 issued on 30 October 2015.

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

The procedure started on 29 May 2018.

Scope of the modification

Some 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 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 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 2 diabetes mellitus

The waiver applies to:

- the paediatric population from birth to less than 10 years of age;
- tablets, oral use;
- on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified paediatric subset(s).

1. Paediatric Investigation Plan

1.1. Condition

Treatment of type 2 diabetes mellitus

1.1.1. Indication(s) targeted by the PIP

Treatment of type 2 diabetes mellitus

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

From 10 to less than 18 years of age

1.1.3. Pharmaceutical form(s)

Tablet

1.1.4. Measures

Area	Number of studies	Description
Quality	1	**Study 1** Assessment of acceptability of tablets in children (ability to swallow 2.5, 5 or 10 mg tablets) in the paediatric PK/PD study.
Non-clinical	2	**Study 2** Oral carcinogenicity study in mice. **Study 3** Oral carcinogenicity study in rats.
Clinical	2	**Study 4** Randomised, multi-centre, parallel, single-dose study to explore the pharmacokinetics and pharmacodynamics of dapagliflozin in children, 10 to less than 18years of age with Type 2 Diabetes receiving one of three dose levels of dapagliflozin: 2.5, 5, or 10 mg.

		Study 5 Randomised, double-blind, placebo-controlled, 24 week efficacy and safety study of dapagliflozin 10 mg as compared to placebo with a 28-week open label safety extension phase, in patients aged 10 to less than 18 years of age (and young adults from 18 to less than 25 years of age) with type 2 diabetes mellitus who have inadequate glycaemic control on diet and exercise with: either metformin only, or insulin only or with metformin and insulin.
Extrapolation, modelling and simulation studies	0	Not applicable.
Other studies	0	Not applicable.
Other measures	0	Not applicable.

2. 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 November 2019.
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):

- Forxiga is indicated in adults aged 18 years and older with type-2 diabetes mellitus to improve glycaemic control 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 tablet

Authorised route(s) of administration

Oral use