EMA/629978/2019

European Medicines Agency decision

P/0402/2019

of 20 December 2019

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for 3-[5-[(1R,2S)-2-(2,2-difluoropropanoylamino)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)propoxy]indazol-1-yl]-N-[(3R)-tetrahydrofuran-3-yl]benzamide (AZD7594), (EMEA-001976-PIP02-18) 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 AstraZeneca AB on 7 September 2018 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 11 December 2019, in accordance with Article 17 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, following a re-examination procedure of the Paediatric Committee's opinion according to Article 25(3) of Regulation (EC) No 1901/2006, 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 3-[5-[(1R,2S)-2-(2,2-difluoropropanoylamino)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)propoxy]indazol-1-yl]-N-[(3R)-tetrahydrofuran-3-yl]benzamide (AZD7594), inhalation powder, nebuliser suspension, pressurised inhalation suspension, inhalation 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 3-[5-[(1R,2S)-2-(2,2-difluoropropanoylamino)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)propoxy]indazol-1-yl]-N-[(3R)-tetrahydrofuran-3-yl]benzamide (AZD7594), inhalation powder, nebuliser suspension, pressurised inhalation suspension, inhalation 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 3-[5-[(1R,2S)-2-(2,2-difluoropropanoylamino)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)propoxy]indazol-1-yl]-N-[(3R)-tetrahydrofuran-3-yl]benzamide (AZD7594), inhalation powder, nebuliser suspension, pressurised inhalation suspension, inhalation 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 AstraZeneca AB, SE-151 85 – Sodertalje, Sweden.

EMA/PDCO/666499/2019
Amsterdam, 11 December 2019

Final opinion of the Paediatric Committee on the agreement of a Paediatric Investigation plan and a deferral and a waiver

EMEA-001976-PIP02-18

Scope of the application

Active substance(s):

3-[5-[(1R,2S)-2-(2,2-difluoropropanoylamino)-1-(2,3-dihydro-1,4-benzodioxin-6-yl)propoxy]indazol-1-yl]-N-[(3R)-tetrahydrofuran-3-yl]benzamide (AZD7594)

Condition(s):

Treatment of asthma

Pharmaceutical form(s):

Inhalation powder

Nebuliser suspension

Pressurised inhalation suspension

Route(s) of administration:

Inhalation use

Name/corporate name of the PIP applicant:

AstraZeneca AB

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, AstraZeneca AB submitted for agreement to the European Medicines Agency on 7 September 2018 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.

An Opinion was adopted by the Paediatric Committee on 18 October 2019 for the above mentioned product. AstraZeneca AB received the Paediatric Committee Opinion on 25 October 2019.

On 22 November 2019 AstraZeneca AB submitted to the European Medicines Agency a written request, including detailed grounds for re-examination of the Opinion.

The re-examination procedure started on 23 November 2019.

A meeting with the Paediatric Committee took place on 10 December 2019.

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, by a majority of 23 out of 31 votes:

   1.1. to revise its opinion and

   - to agree the paediatric investigation plan in accordance with Article 17(1) 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)(c) of said Regulation, on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments for paediatric patients.

   1.2. following re-examination, to amend the measures of the paediatric investigation plan.

The divergent position(s) is (are) appended to 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 annex 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 asthma

The waiver applies to:

- the paediatric population from birth to less than 6 months of age;
- inhalation powder, nebuliser suspension, pressurised inhalation suspension, inhalation use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments.

2. Paediatric investigation plan

2.1. Condition:

Treatment of asthma

2.1.1. Indication(s) targeted by the PIP

Treatment of persistent asthma

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

From 6 months to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Inhalation powder

Nebuliser suspension

Pressurised inhalation suspension

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	**Study 1** Development of a nebuliser suspension, for paediatric use (or spacer pressurised inhalation suspension for Metered Dose Inhaler (MDI)with spacer) for the paediatric population between 6 months and 5 years of age to be used in Study 12 **Study 2** Development of an age-appropriate (lower strength) inhalation dry powder formulation(s) for paediatric use (dry-powder inhaler (DPI))

Non-clinical studies	2	**Study 3** Pre- and postnatal development study in the rat following inhalation administration to mated females from day 6 of gestation to day 20 of lactation, inclusive (MT19MC) **Study 4** Juvenile toxicity study in dog
Clinical studies	8	**Study 5** Open-label study to assess PK, PD and safety of AZD7594 in paediatric subjects from 12 to less than 18 years of age with asthma controlled on low dose inhaled corticosteroid (ICS) or leukotriene receptor antagonists (LTRA) Global Initiative for Asthma grade 2 (GINA 2) at baseline (D3741C00012) **Study 6** Randomized, double-blind, placebo- and active-controlled, 3-parallel arms, multi-centre study to evaluate the efficacy and safety of AZD7594 in paediatric subjects from 12 to less than 18 years of age (and adults) with asthma (GINA 2) (D3741C000A2) **Study 7** Randomized, double-blind, active-controlled, 3-parallel arms, multi-centre study to evaluate the efficacy and safety of AZD7594 in paediatric subjects from 12 to less than 18 years of age (and adults) with asthma (GINA 3) (D3741C000A3) **Study 8** Randomized, 3-period incomplete block cross-over design with a 2-week treatment period, placebo and active control, dose-ranging study to assess efficacy, safety and PK of AZD7594 to establish effective dose in paediatric subjects from 5 to less than 12 years of age (D3741C000P1) **Study 9** Randomized, double-blind, placebo-controlled two period cross-over study to assess effect on short term growth rate in pre-pubertal children as measured by knenometer (D3741C000P2) **Study 10** Randomized, double-blind, double-dummy, parallel group, placebo- and active-controlled 3-arms study to assess efficacy and safety of AZD7594 in paediatric patients from 5 to less than 12 years of age with asthma (GINA 2) (D3741C000P3a) **Study 11** Randomized, double-blind, double-dummy, parallel group, active-controlled 2-arms study to assess efficacy and safety of AZD7594 in paediatric patients from 5 to less than 12 years of age with asthma (GINA 3) (D3741C000P3b)

		Study 12 Randomized, double-blind, parallel, placebo- and active-controlled 5-arms, dose-ranging, efficacy and safety study of AZD7594 in paeditric patients aged 6 months to less than 6 years (D3741C000P5)
Extrapolation, modelling and simulation studies	0	Not applicable
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:	No
Date of completion of the paediatric investigation plan:	By September 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes