EMA/27242/2020

European Medicines Agency decision

P/0058/2020

of 14 February 2020

on the refusal of a modification of an agreed paediatric investigation plan for fluticasone furoate / umeclidinium bromide / vilanterol trifenatate (Trelegy Ellipta / Elebrato Ellipta / Temybric Ellipta), (EMEA-002153-PIP01-17-M01) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0076/2018 issued on 16 March 2018,

Having regard to the application submitted by GlaxoSmithKline Trading Services Limited on 6 September 2019 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 11 December 2019, 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 refusal of changes to the agreed paediatric investigation plan and to the deferral.

(2) It is therefore appropriate to adopt a decision on the refusal 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 fluticasone furoate / umeclidinium bromide / vilanterol trifenatate (Trelegy Ellipta / Elebrato Ellipta / Temybric Ellipta), inhalation powder, pre-dispensed, inhalation use, including changes to the deferral, 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, are hereby refused.

Article 2

This decision is addressed to GlaxoSmithKline Trading Services Limited, 12 Riverwalk, Citywest Business Campus, Dublin 24 – Dublin, Ireland.

EMA/PDCO/530590/2019
Amsterdam, 11 December 2019

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

EMEA-002153-PIP01-17-M01

Scope of the application

Active substance(s):

Fluticasone furoate / umeclidinium bromide / vilanterol trifenatate

Invented name:

Trelegy Ellipta

Elebrato Ellipta

Temybric Ellipta

Condition(s):

Treatment of asthma

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Inhalation powder, pre-dispensed

Route(s) of administration:

Inhalation use

Name/corporate name of the PIP applicant:

GlaxoSmithKline Trading Services Limited

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, GlaxoSmithKline Trading Services Limited submitted to the European Medicines Agency on 6 September 2019 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/0076/2018 issued on 16 March 2018.

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

The procedure started on 15 October 2019.

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 refuse the changes proposed by the applicant regarding the timelines of the paediatric investigation plan and the deferral.

   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 remain unchanged and are set out in the Annex I.

3. The scientific conclusions and the grounds for refusal are set out in the summary report appended to this opinion.

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 asthma

The waiver applies to:

- the paediatric population from birth to less than 5 years;
- inhalation powder, pre-dispensed, inhalation use;
- on the grounds that the specific medicinal product does not represent a significant therapeutic benefit as clinical studies(s) are not feasible.

2. Paediatric investigation plan

2.1. Condition

Treatment of asthma

2.1.1. Indication(s) targeted by the PIP

Maintenance treatment of asthma in patients aged 5 years or older who have inadequately controlled asthma despite therapy with inhaled corticosteroids and long acting beta agonists

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

From 5 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Inhalation powder, pre-dispensed

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	0	Not applicable
Clinical studies	3	***Study 1 (206867)*** Double-blind, randomised 52-week study comparing the safety and efficacy and pharmacokinetics (PK) of fluticasone furoate (FF) / umeclidinium bromide (UMEC)/ vilanterol (VI) with FF/VI in adolescents with inadequately controlled asthma on stable maintenance therapy with inhaled corticosteroids (ICS) and long-acting β adrenoceptor agonists (LABA).

		Study 2 (206868) Double-blind, 3-period, 4 treatment balanced incomplete block cross-over, single-dose study to evaluate the PK and bronchodilatory effect of UMEC when added to FF/VI in children 5 to less than 12 years of age with asthma ***Study 3 (207717)*** Double-blind, randomised 52-week study comparing the safety and efficacy of FF / UMEC/ VI with FF/VI in children with asthma 5 to less than 12 years of age
Extrapolation, modelling and simulation studies	2	***Study 4*** Population PK models to predict the systemic exposure for each analyte in children and adolescents with asthma ***Study 5*** Physiological based pharmacokinetics (PBPK) model to predict the UMEC systemic PK following inhalation of FF/UMEC/VI in children 5 to less than 12 years of age and to evaluate the CYP2D6 activity.
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 2027
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 Obstructive Pulmonary Disease

Authorised indication(s):

- Maintenance treatment in adult patients with moderate to severe chronic obstructive pulmonary disease (COPD) who are not adequately treated by a combination of an inhaled corticosteroid and a long-acting β2-agonist or a combination of a long-acting β2-agonist and a long-acting muscarinic antagonist

Authorised pharmaceutical form(s):

Inhalation powder, pre-dispensed

Authorised route(s) of administration:

Inhalation use