EMA/152108/2021

European Medicines Agency decision

P/0150/2021

of 16 April 2021

on the agreement of a paediatric investigation plan and on the granting of a waiver for metformin (hydrochloride) / pioglitazone (hydrochloride) / spironolactone, (EMEA-002187-PIP01-17) 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 Katholieke Universiteit Leuven (KUL) Research & Development on 13 July 2020 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 26 February 2021, in accordance with Article 17 of Regulation (EC) No 1901/2006 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 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 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 metformin (hydrochloride) / pioglitazone (hydrochloride) / spironolactone, film-coated tablet, 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 waiver for metformin (hydrochloride) / pioglitazone (hydrochloride) / spironolactone, film-coated tablet, 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

This decision is addressed to Katholieke Universiteit Leuven (KUL) Research & Development, Waaistraat 6 - box 5105, 3000 - Leuven Belgium.

EMA/PDCO/669910/2020
Amsterdam, 26 February 2021

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

EMEA-002187-PIP01-17

Scope of the application

Active substance(s):

Metformin (hydrochloride) / pioglitazone (hydrochloride) / spironolactone

Condition(s):

Treatment of polycystic ovary syndrome

Pharmaceutical form(s):

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Katholieke Universiteit Leuven (KUL) Research & Development

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Katholieke Universiteit Leuven (KUL) Research & Development submitted for agreement to the European Medicines Agency on 13 July 2020 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 18 August 2020.

Supplementary information was provided by the applicant on 30 November 2020. 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 17(1) 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)(b) of said Regulation, on the grounds that the disease or condition for which the specific medicinal product is intended does not occur in the specified subset(s) of the paediatric population; 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.

   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 polycystic ovary syndrome

The waiver applies to:

- boys from birth to less than 18 years and premenarcheal girls;
- film-coated tablet, 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 subsets.

And to

- post-menarcheal girls less than 2 years post-menarche or below 14 years of age for girls with primary amenorrhea;
- film-coated tablet, oral use;
- on the grounds that clinical studies with the specific medicinal product cannot be expected to be of significant therapeutic benefit to or fulfil a therapeutic need of the specified paediatric subsets.

2. Paediatric investigation plan

2.1. Condition:

Treatment of polycystic ovary syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of adolescent polycystic ovary syndrome (PCOS) in post-menarche adolescents <18 years.

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

Post-menarche adolescents (from 2 years post-menarche or above 14 years of age for girls with primary amenorrhea) to less than 18 years.

2.1.3. Pharmaceutical form(s)

Film-coated tablet.

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** (Phase II SPIOMET4Health) Double-blind, randomised, active-controlled/placebo-controlled trial to evaluate safety, efficacy and tolerability of the fixed dose combination SPIOMET (metformin hydrochloride/pioglitazone hydrochloride/spironolactone) in adolescents (and adults) with polycystic ovary syndrome (PCOS). **Study 2** (SPIOMET Phase III-A) Double-blind, randomised, parallel-group, placebo-controlled trial to evaluate safety and efficacy of the fixed dose combination SPIOMET in adolescents (and adults) with PCOS. **Study 3** (SPIOMET Phase III-B) Double-blind, randomised, parallel-group, placebo-controlled trial to evaluate safety and efficacy of the fixed dose combination SPIOMET in adolescents (and adults) with PCOS.
Extrapolation, modelling and simulation studies		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 December 2028
Deferral for one or more measures contained in the paediatric investigation plan:	No