EMA/134574/2023

European Medicines Agency decision

P/0135/2023

of 14 April 2023

on the acceptance of a modification of an agreed paediatric investigation plan for osilodrostat (Isturisa), (EMEA-000315-PIP02-15-M03) 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 Union procedures for the authorisation and supervision of medicinal products for human use and establishing a European Medicines Agency[2],

Having regard to the European Medicines Agency's decision P/0011/2016 issued on 29 January 2016, the decision P/0064/2018 issued on 16 March 2018 and the decision P/0252/2018 issued on 15 August 2018,

Having regard to the application submitted by Recordati Rare Diseases SARL on 21 November 2022 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 24 February 2023, 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for osilodrostat (Isturisa), film-coated 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 Recordati Rare Diseases SARL, Immeuble Le Wilson, 70 Avenue du Général de Gaulle, 92800 – Puteaux, France.

EMA/PDCO/905370/2022
Amsterdam, 24 February 2023

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

EMEA-000315-PIP02-15-M03

Scope of the application

Active substance(s):

Osilodrostat

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of adrenal cortical hyperfunction

Pharmaceutical form(s):

Film-coated tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Recordati Rare Diseases SARL

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Recordati Rare Diseases SARL submitted to the European Medicines Agency on 21 November 2022 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/0011/2016 issued on 29 January 2016, the decision P/0064/2018 issued on 16 March 2018 and the decision P/0252/2018 issued on 15 August 2018.

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

The procedure started on 3 January 2023.

Scope of the modification

The 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 Paediatric Committee member of Norway 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 adrenal cortical hyperfunction

The waiver applies to:

- the paediatric population from birth to less than 6 years of age;
- film-coated tablet, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition

Treatment of adrenal cortical hyperfunction

2.1.1. Indication(s) targeted by the PIP

Treatment of endogenous Cushing's syndrome in adults and children aged 6 years and older

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

From 6 to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

2.1.4. Measures

Area	Description
Quality-related studies	Not applicable
Non-clinical studies	**Study 1** 4-week dose-ranging study in juvenile animals **Study 2** 10-week toxicity study in juvenile animals
Clinical studies	**Study 3** Open-label, non-comparative study to evaluate the tolerability, pharmacokinetics and pharmacodynamics of osilodrostat in children and adolescent patients with Cushing disease

Extrapolation, modelling and simulation studies	**Study 4** Population PK modelling and simulation study to evaluate the use of osilodrostat in children and adolescent patients from 6 to 18 years of age
Other measures	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 August 2024
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Information provided by the applicant:

Condition(s) and authorised indication(s)

1. Treatment of of adrenal cortical hyperfunction

Authorised indication(s):

- EU: Isturisa is indicated for the treatment of endogenous Cushing's syndrome in adults.
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure
- Australia: Isturisa is indicated for the treatment of endogenous Cushing's syndrome in adults.
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure
- Colombia: Isturisa is indicated for the treatment of endogenous Cushing's syndrome for whom surgery is not an option or has not been curative
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure
- Israel: Isturisa is indicated for the treatment of endogenous Cushing's syndrome in adult patients for whom surgery is not an option or has not been curative
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure
- Japan: Cushing's syndrome (when surgical treatment is insufficiently effective or difficult to perform)
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure

- Switzerland: Treatment of Cushing's syndrome and other causes of endogenous hypercortisolism (e.g., adrenal cortex adenoma, bilateral adrenal hyperplasia, ectopic ACTH secretion) in adults provided that pharmacotherapy is indicated
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure
- USA: Isturisa is a cortisol synthesis inhibitor indicated for the treatment of adult patients with Cushing’s disease for whom pituitary surgery is not an option or has not been curative
  - Invented name(s): Isturisa
  - Authorised pharmaceutical form(s): film-coated tablets
  - Authorised route(s) of administration: oral use
  - Authorised via centralised procedure