EMA/328837/2024

European Medicines Agency decision

P/0268/2024

of 17 July 2024

on the acceptance of a modification of an agreed paediatric investigation plan for doravirine / islatravir (EMEA-002707-PIP01-19-M02) 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/0395/2020 issued on 23 October 2020 and the decision P/0073/2021 issued on 17 March 2021,

Having regard to the application submitted by MSD Europe Belgium SRL on 22 February 2024 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 31 May 2024, 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 doravirine / islatravir, tablet, age-appropriate oral solid dosage form, 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 MSD Europe Belgium SRL, Boulevard du Souverain 25 / Vorstlaan 25, 1170 Brussels, Belgium.

EMA/PDCO/107502/2024 Corr[1]
Amsterdam, 31 May 2024

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

EMEA-002707-PIP01-19-M02

Scope of the application

Active substance(s):

Doravirine / islatravir

Condition(s):

Treatment of human immunodeficiency virus-1 (HIV-1) infection

Pharmaceutical form(s):

Tablet

Age-appropriate oral solid dosage form

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

MSD Europe Belgium SRL

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, MSD Europe Belgium SRL submitted to the European Medicines Agency on 22 February 2024 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/0395/2020 issued on 23 October 2020 and the decision P/0073/2021 issued on 17 March 2021.

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

The procedure started on 2 April 2024.

[1] 25 June 2024

Scope of the modification

Some measures and 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.
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 human immunodeficiency virus-1 (HIV-1) infection

The waiver applies to:

- the paediatric population from birth to less than 28 days of age;
- tablet, age-appropriate oral solid dosage form, oral 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 human immunodeficiency virus-1 (HIV-1) infection

2.1.1. Indication(s) targeted by the PIP

Treatment of human immunodeficiency virus-1 (HIV-1) infection

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

From 28 days to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Tablet

Age-appropriate oral solid dosage form

2.1.4. Measures

Area	**Description**
Quality-related studies	**Study 1** Development of an age appropriate oral solid dosage form
Non-clinical studies	Not applicable
Clinical studies	**Study 2** Open label uncontrolled study to evaluate islatravir (MK-8591) pharmacokinetic and the safety and activity of doravirine (DOR)/islatravir (ISL) in paediatric participants who are less than 18 years of age and weigh ≥35 kg with HIV-1 infection (P028)

	Study 3 Open label uncontrolled pharmacokinetic safety and activity study of the fix-doe combination (FDC) of doravirin/ islatravir (age appropriate formulation) for paediatric subjects who are at least 28 days of age and weigh less than 35kg **Study 6** Study added in EMEA-002707-PIP01-19-M02 Open label uncontrolled study to evaluate the pharmacokinetics of islatravir and the safety and antiviral activity of doravirine/islatravir in paediatric patients with HIV-1 infection, who are virologically suppressed (defined as HIV-1 RNA less than 50 copies/mL) for at least 3 months prior to the screening visit on a stable anti-retroviral (ARV) regimen, without history of virologic failure, and without evidence of resistance to the individual components of the fixed-dose combination (FDC)
Extrapolation, modelling and simulation studies	**Study 4** Modelling and simulation study to support ISL dose finding in paediatric subjects weighing at least 35 kg. **Study 5** Modelling and simulation study to support ISL dose finding in paediatric subjects at least 28 days of age and weighing less than 35 kg
Other studies	Not applicable
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 December 2029
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:

The product is not authorised anywhere in the European Community.