EMA/306614/2023

European Medicines Agency decision

P/0257/2023

of 14 July 2023

on the acceptance of a modification of an agreed paediatric investigation plan for darunavir / cobicistat (Rezolsta), (EMEA-001280-PIP01-12-M06) 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/0036/2013 issued on 27 February 2013, the decision P/0256/2017 issued on 4 September 2017, the decision P/0006/2019 issued on 3 January 2019, the decision P/0049/2021 issued on 27 January 2021, the decision P/0254/2021 issued on 9 July 2021 and the decision P/0039/2023 issued on 31 January 2023,

Having regard to the application submitted by Janssen-Cilag International NV on 15 March 2023 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 26 May 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.

(2) It is therefore appropriate to adopt a decision on the acceptance of changes to the agreed paediatric investigation plan.

[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 darunavir / cobicistat (Rezolsta), film-coated tablet, dispersible tablet, oral use, 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 Janssen-Cilag International NV, Turnhoutseweg 30, 2340 - Beerse, Belgium.

EMA/PDCO/147945/2023
Amsterdam, 26 May 2023

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

EMEA-001280-PIP01-12-M06

Scope of the application

Active substance(s):

Darunavir / cobicistat

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of human immunodeficiency virus-1 infection

Pharmaceutical form(s):

Film-coated tablet

Dispersible tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Janssen-Cilag International NV

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted to the European Medicines Agency on 15 March 2023 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/0036/2013 issued on 27 February 2013, the decision P/0256/2017 issued on 4 September 2017, the decision P/0006/2019 issued on 3 January 2019, the decision P/0049/2021 issued on 27 January 2021, the decision P/0254/2021 issued on 9 July 2021 and the decision P/0039/2023 issued on 31 January 2023.

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

The procedure started on 24 April 2023.

Scope of the modification

Some 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 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 human immunodeficiency virus-1 (HIV-1) infection

The waiver applies to:

- the paediatric population from birth to less than 3 years of age;
- film-coated tablet, dispersible 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 HIV-1 infection

2.1.1. Indication(s) targeted by the PIP

Treatment of HIV-1 infection in paediatric patients from 3 years to less than 18 years of age in combination with other antiretroviral medicinal products

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

From 3 years to less than 18 years of age of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Dispersible tablet

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Acceptability assessment of adult film-coated tablets in children from 12 to less than 18 years of age. **Study 2** Development of a scored film-coated tablet for patients from 6 to less than 12 years and/or weighing at least 25 kg. ***Study 3*** Deleted in procedure EMEA-001280-PIP01-12-M03

	Study 8 Development of a dispersible tablet for children from 3 years of age and older and weighing 15 to < 25 kg with acceptability assessments. Added in the procedure EMEA-001280-PIP01-12-M02
Non-clinical studies	Not applicable
Clinical studies	**Study 4 (TMC114-228)** Phase II, open-label multiple dose trial. Part I: Pharmacokinetic study to determine the recommended paediatric dose and to evaluate short-term safety, tolerability and efficacy of darunavir. Part II: To evaluate long-term safety, tolerability and efficacy of the selected paediatric dose of darunavir. **Study 5 (TMC114-C230)** Phase II, open-label trial to investigate pharmacokinetics, long-term safety, tolerability and antiviral activity of the selected adult dose of darunavir in treatment-naïve HIV-1 infected adolescents from 12 to less than 18 years of age. **Study 6 (GS-US-216-0128)** Open-label trial to evaluate pharmacokinetics, safety and efficacy of once-daily cobicistat-boosted darunavir administered as part of a combined antiretroviral regimen in HIV-1 infected, treatment-experienced children from 3 years to less than 18 years of age.
Extrapolation, modelling and simulation studies	**Study 7 (TMC114-C0000013)** Extrapolation of pharmacokinetic, safety and efficacy data on darunavir and cobicistat from studies including at least TMC114-228, TMC114-C230 and GS-US-216-0128 (measures 4, 5 and 6) to children from 3 to less than 18 years of age for darunavir/cobicistat fixed dose combination for treatment of HIV-1 infection.
Other studies	Not applicable
Other measures	Not applicable

3. Follow-up, completion and deferral of PIP

Concerns on potential long-term safety issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	By March 2025
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 human immunodeficiency virus-1 infection

Authorised indication(s):

- Rezolsta is indicated in combination with other antiretroviral medicinal products for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults adolescents (aged 12 years and older, weighing at least 40 kg).
  - Invented name(s): Rezolsta
  - Authorised pharmaceutical form(s): Film-coated tablet
  - Authorised route(s) of administration: Oral use
  - Authorised via centralised procedure