EMA/24564/2013

# European Medicines Agency decision

P/0036/2013

of 27 February 2013

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for darunavir / cobicistat (EMEA-001280-PIP01-12) 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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# European Medicines Agency decision

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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 Janssen-Cilag International NV on 10 April 2012 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 11 January 2013, in accordance with Article 18 of Regulation (EC) No 1901/2006, and Article 21 of said Regulation 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 deferral 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 deferral.

(4) 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 darunavir / cobicistat, film-coated tablet, age-appropriate oral solid dosage forms, age-appropriate oral liquid dosage forms, 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 deferral for darunavir / cobicistat, film-coated tablet, age-appropriate oral solid dosage forms, age-appropriate oral liquid dosage forms, 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***

A waiver for darunavir / cobicistat, film-coated tablet, age-appropriate oral solid dosage forms, age-appropriate oral liquid dosage forms, 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 4***

This decision is addressed to Janssen-Cilag International NV, Turnhoutseweg 30, 2340 – Beerse, Belgium.

Done at London, 27 February 2013

For the European Medicines Agency
Guido Rasi
Executive Director
(Signature on file)

EMA/PDCO/686592/2012 Corr

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

EMEA-001280-PIP01-12

## Scope of the application

**Active substance(s):**

Darunavir / cobicistat

**Condition(s):**

Treatment of HIV-1 infection

**Pharmaceutical form(s):**

Film-coated tablet

Age-appropriate oral solid dosage form

Age-appropriate oral liquid dosage form

**Route(s) of administration:**

Oral use

**Name/corporate name of the PIP applicant:**

Janssen-Cilag International NV

## Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Janssen-Cilag International NV submitted for agreement to the European Medicines Agency on 10 April 2012 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation and a waiver under Article 13 of said Regulation.

The procedure started on 19 June 2012

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Supplementary information was provided by the applicant on 22 October 2012. 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 18 of said Regulation,
   - to grant a deferral in accordance with Article 21 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)(a) of said Regulation, on the grounds that the specific medicinal product is likely to be ineffective or unsafe in part or all of the paediatric population.

   The Icelandic and the Norwegian Paediatric Committee members agree 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.

London, 11 January 2013

On behalf of the Paediatric Committee
Dr Daniel Brasseur, Chairman
(Signature on file)

# 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

# 1. Waiver

## *1.1. Condition: treatment of HIV-1 infection*

The waiver applies to:

- The paediatric population from birth to less than 3 years of age;
- for film-coated tablet, age-appropriate oral solid dosage forms, age-appropriate oral liquid dosage forms, 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 infected paediatric subjects from the age of 3 years who are antiretroviral (ART)-naive or ART-experienced without darunavir resistant associated mutations (DRV RAMs), and with plasma HIV-1 RNA < 100,000 copies/ml and CD4+ cell count ≥ 108 cells/l.

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

From 3 to less than 18 years of age.

### 2.1.3. Pharmaceutical form(s)

Film-coated tablet

Age-appropriate oral solid dosage form

Age-appropriate oral liquid dosage form

### 2.1.4. Measures

| Area | Number of measures | Description |
|---|---|---|
| Quality | 3 | **Measure 1**<br>Acceptability assessment of adult film-coated tablets in children from 12 to less than 18 years of age.<br>**Measure 2**<br>Development of age-appropriate oral solid dosage form and age-appropriate oral liquid dosage form for children from 3 to less than 12 years of age with acceptability assessment.<br>**Measure 3**<br>Bioavailability study in healthy adult subjects with the liquid dosage form. |

| | | |
|---|---|---|
| Non-clinical | 0 | Not applicable. |
| Clinical | 4 | **Measure 4**<br><br>Phase II, open-label multiple dose trial.<br><br>Part I: Pharmacokinetic study to determine the recommended paediatric dose and to evaluate short-term safety, tolerability and efficacy of darunavir.<br><br>Part II: To evaluate long-term safety, tolerability and efficacy of the selected paediatric dose of darunavir.<br><br>**Measure 5**<br><br>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.<br><br>**Measure 6**<br><br>Open-label, multicentre, multi-cohort, 2-part study to evaluate pharmacokinetics (PK), safety, and efficacy and confirm the dose of cobicistat-boosted atazanavir (ATV) or cobicistat-boosted darunavir (DRV) in children from 3 to less than 18 years of age with HIV-1 infection.<br><br>**Measure 7**<br><br>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. |

# 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 December 2021 |
| Deferral for one or more measures contained in the paediatric investigation plan: | Yes |