EMA/585624/2019

European Medicines Agency decision

P/0362/2019

of 4 November 2019

on the acceptance of a modification of an agreed paediatric investigation plan for letermovir (Prevymis), (EMEA-001631-PIP01-14-M04) 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 European Medicines Agency's decision P/0155/2015 issued on 10 July 2015, the decision P/0090/2017 issued on 11 April 2017 and the decision P/0385/2018 issued on 7 December 2018,

Having regard to the application submitted by Merck Sharp & Dohme (Europe), Inc. on 27 June 2019 under Article 22 of Regulation (EC) No 1901/2006 proposing changes to the agreed paediatric investigation plan with a deferral,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 18 October 2019, 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.
[2] OJ L 136, 30.4.2004, p. 1.

Has adopted this decision:

Article 1

Changes to the agreed paediatric investigation plan for letermovir (Prevymis), film-coated tablet, granules, concentrate for solution for infusion, oral use, intravenous 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 Merck Sharp & Dohme (Europe), Inc., Clos du Lynx, 5, 1200 – Brussels, Belgium.

EMA/PDCO/412490/2019
Amsterdam, 18 October 2019

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

EMEA-001631-PIP01-14-M04

Scope of the application

Active substance(s):

Letermovir

Invented name:

Prevymis

Condition(s):

Prevention of cytomegalovirus infection

Authorised indication(s):

See Annex II

Pharmaceutical form(s):

Film-coated tablet

Granules

Concentrate for solution for infusion

Route(s) of administration:

Oral use

Intravenous use

Name/corporate name of the PIP applicant:

Merck Sharp & Dohme (Europe), Inc.

Information about the authorised medicinal product:

See Annex II

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Merck Sharp & Dohme (Europe), Inc. submitted to the European Medicines Agency on 27 June 2019 an application for modification of the agreed paediatric investigation plan with a deferral as set out in the European Medicines Agency's decision P/0155/2015 issued on 10 July 2015, the decision P/0090/2017 issued on 11 April 2017, and the decision P/0385/2018 issued on 7 December 2018.

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

The procedure started on 20 August 2019.

Scope of the modification

Some measures 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 Norwegian agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the paediatric investigation plan 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

Not applicable.

2. Paediatric investigation plan

2.1. Condition

Prevention of cytomegalovirus infection

2.1.1. Indication(s) targeted by the PIP

Prevention of CMV viraemia and / or disease in at-risk patients having undergone an allogeneic haematopoietic stem cell transplant (HSCT) or solid organ transplant (SOT)

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

From birth to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Film-coated tablet

Granules

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	2	*Study 1 deleted in EMEA-001631-PIP01-14-M02.* **Study 2** Development of granules. **Study 3** Development of concentrate for solution for infusion.
Non-clinical studies	0	Not applicable.
Clinical studies	2	**Study 4** Open-label, single-arm trial to evaluate pharmacokinetics, safety and acceptability/palatability of letermovir in children from birth to less than 18 years of age who are at-risk of developing CMV infection and/or disease following allogeneic haematopoietic stem cell transplantation. **Study 5**

		Open-label, randomised trial in healthy adult volunteers to determine the bioavailability of the letermovir paediatric formulation(s) relative to the adult film-coated tablet.
Extrapolation, modelling and simulation studies	2	**Study 6** Modelling and Simulation study to support dose finding and the extrapolation of efficacy of letermovir from adult haematopoietic stem cell transplant (HSCT) recipients to children from birth to less than 18 years of age who are at-risk of developing CMV infection and/or disease following HSCT. **Study 7** Extrapolation study to support the use of letermovir in children from birth to less than 18 years of age who are at-risk of developing CMV infection and/or disease following solid organ transplantation.
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:	Yes
Date of completion of the paediatric investigation plan:	By August 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes

Annex II

Information about the authorised medicinal product

Condition(s) and authorised indication(s):

1. Prevention of cytomegalovirus infection

Authorised indication:

- Prevymis is indicated for prophylaxis of cytomegalovirus (CMV) reactivation and disease in adults CMV-seropositive recipients [R+] of an allogeneic haematopoietic stem cell transplant (HSCT). Consideration should be given to official guidance on the appropriate use of antiviral agents.

Authorised pharmaceutical form(s):

Film-coated tablets

Concentrate for solution for infusion

Authorised route(s) of administration:

Oral use

Intravenous use