EMA/100919/2020

European Medicines Agency decision

P/0109/2020

of 20 March 2020

on the acceptance of a modification of an agreed paediatric investigation plan for emapalumab (EMEA-002031-PIP01-16-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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on the acceptance of a modification of an agreed paediatric investigation plan for emapalumab (EMEA-002031-PIP01-16-M03) in accordance with Regulation (EC) No 1901/2006 of the European Parliament and of the Council

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/0358/2017 issued on 1 December 2017, the decision P/0152/2018 issued on 20 May 2018 and the decision P/0306/2018 issued on 12 September 2018,

Having regard to the application submitted by Novimmune B.V. on 28 October 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 31 January 2020, 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 emapalumab, concentrate for solution for infusion, 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 Novimmune BV, Prins Bernhardplein 200, 1907 JB - Amsterdam, The Netherlands.

EMA/PDCO/601059/2019
Amsterdam, 31 January 2020

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

EMEA-002031-PIP01-16-M03

Scope of the application

Active substance(s):

Emapalumab

Condition(s):

Treatment of haemophagocytic lymphohistiocytosis

Pharmaceutical form(s):

Concentrate for solution for infusion

Route(s) of administration:

Intravenous use

Name/corporate name of the PIP applicant:

Novimmune B.V.

Basis for opinion

Pursuant to Article 22 of Regulation (EC) No 1901/2006 as amended, Novimmune B.V submitted to the European Medicines Agency on 28 October 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/0358/2017 issued on 1 December 2017, the decision P/0152/2018 issued on 20 May 2018 and the decision P/0306/2018 issued on 12 September 2018.

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

The procedure started on 3 December 2019.

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 Norwegian Paediatric Committee member 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 annex 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:

Treatment of haemophagocytic lymphohistiocytosis

2.1.1. Indication(s) targeted by the PIP

Treatment of primary haemophagocytic lymphohistiocytosis in children

Treatment of secondary haemophagocytic lymphohistiocytosis in children

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)

Concentrate for solution for infusion

2.1.4. Measures

Area	Number of measures	Description
Quality-related studies	0	Not applicable
Non-clinical studies	2	**Study 1 (20135225)** Fertility study in mice with the functional surrogate rat anti-mouse IFNγ monoclonal antibody (mAb) XMG1.2, to assess adverse effect on fertility **Study 2** Pre- and postnatal development study in mice with the functional surrogate rat anti-mouse IFNγ monoclonal antibody (mAb) XMG1.2, to assess adverse effect on pre- and post-natal development in mice
Clinical studies	6	**Study 3 (NI-0501-04)** Open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, safety, tolerability, immunogenicity and activity of emapalumab in children from birth to less than 18 years of age (and adults) with primary haemophagocytic lymphohistiocytosis (pHLH)

		Study 4 *(NI-0501-05)* Open-label, single-arm trial to evaluate patients' survival and long-term safety, elimination profile and immunogenicity of emapalumab in children from birth to less than 18 years of age (and adults) with pHLH **Study 5 *(NI-0501-06)*** Open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, safety, tolerability, immunogenicity and activity of emapalumab in children from birth to less than 18 years of age with systemic juvenile idiopathic arthritis (sJIA) developing macrophage activation syndrome/secondary HLH (MAS/sHLH) **Study 6 *(NI-0501-09)*** Open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, activity, safety, immunogenicity and impact on quality of life of emapalumab in children from birth to less than 18 years of age (and adults) with pHLH **Study 7** Open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, safety, and activity of emapalumab in children from birth to less than 18 years of age (and adults) with secondary haemophagocytic lymphohistiocytosis (sHLH) **Study 8 *(NI-0501-HC)*** Retrospective data collection in primary HLH patients who received HLH available therapies after Jan 2010 to generate an historical cohort which can serve as matching comparator for the patient population recruited in study 3 (NI-0501-04) and followed-up in study 4 (NI-0501-05)
Extrapolation, modelling and simulation studies	2	**Study 9** Modelling and simulation study using popPK and PK-PD models to predict the appropriate dose of emapalumab and PD-clinical response relationships in children from birth to less than 18 years of age with pHLH **Study 10** Extrapolation study to predict the effective doses of emapalumab for paediatric age categories that would not have been covered in studies NI-0501-04 and NI-0501-05 (e.g. patients younger than 27 days and between 12 and 18 years of age) in children with pHLH
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 March 2023
Deferral for one or more measures contained in the paediatric investigation plan:	Yes