

EMA/763260/2017

European Medicines Agency decision

P/0358/2017

of 1 December 2017

on the agreement of a paediatric investigation plan and on the granting of a deferral for emapalumab (EMA-002031-PIP01-16) 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 agreement of a paediatric investigation plan and on the granting of a deferral for emapalumab (EMA-002031-PIP01-16) 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 726/2004¹,

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 Agency²,

Having regard to the application submitted by Novimmune B.V on 16 January 2017 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a deferral under Article 20 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 13 October 2017, in accordance with Article 17 of Regulation (EC) No 1901/2006 and Article 21 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.
- (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.

Has adopted this decision:

Article 1

A paediatric investigation plan for emapalumab, concentrate for solution for infusion, intravenous 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.

¹ OJ L 378, 27.12.2006, p.1.

² OJ L 136, 30.4.2004, p. 1.

Article 2

A deferral for emapalumab, concentrate for solution for infusion, intravenous 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

This decision is addressed to Novimmune B.V, Prins Bernhardplein 200, 1907 JB - Amsterdam, The Netherlands.

EMA/PDCO/475889/2017

London, 13 October 2017

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

EMA-002031-PIP01-16

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 16(1) of Regulation (EC) No 1901/2006 as amended, Novimmune B.V submitted for agreement to the European Medicines Agency on 16 January 2017 an application for a paediatric investigation plan for the above mentioned medicinal product and a deferral under Article 20 of said Regulation.

The procedure started on 21 February 2017.

Supplementary information was provided by the applicant on 24 July 2017. 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 17(1) of said Regulation;
- to grant a deferral in accordance with Article 21 of said Regulation.

The Norwegian Paediatric Committee member agrees with the above-mentioned recommendation of the Paediatric Committee.

2. The measures and timelines of the agreed 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 Fertility study in mice with the functional surrogate rat anti-mouse IFN γ 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 IFN γ 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 between Jan 2010 and Dec 2017 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