EMA/243653/2024

European Medicines Agency decision

P/0185/2024

of 23 May 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral and on the granting of a waiver for mavorixafor (EMEA-002490-PIP01-18) 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 application submitted by X4 Pharmaceuticals (Austria) GmbH on 23 April 2019 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 26 April 2024, in accordance with Article 17 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, as amended.
[2] OJ L 136, 30.4.2004, p. 1, as amended.

Has adopted this decision:

Article 1

A paediatric investigation plan for mavorixafor, hard capsules, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, 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 mavorixafor, hard capsules, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, 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 mavorixafor, hard capsules, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, 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 X4 Pharmaceuticals (Austria) GmbH, Helmut-Qualtinger-Gasse 2, A-1030 - Vienna, Austria.

EMA/PDCO/49426/2024
Amsterdam, 26 April 2024

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

EMEA-002490-PIP01-18

Scope of the application

Active substance(s):

Mavorixafor

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome

Pharmaceutical form(s):

Hard capsules

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:

X4 Pharmaceuticals (Austria) GmbH

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, X4 Pharmaceuticals (Austria) GmbH submitted for agreement to the European Medicines Agency on 23 April 2019 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 28 May 2019.

Supplementary information was provided by the applicant on 18 January 2024. 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;
   - 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 withArticle 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 Paediatric Committee member of Norway agrees 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 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 WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome

The waiver applies to:

- the paediatric population from birth to less than 2 years of age;
- hard capsules, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form, oral use;
- on the grounds that the specific medicinal product is likely to be unsafe.

2. Paediatric investigation plan

2.1. Condition:

Treatment of WHIM (warts, hypogammaglobulinemia, infections, and myelokathexis) syndrome

2.1.1. Indication(s) targeted by the PIP

Treatment of WHIM syndrome in paediatric patients aged 2 years and above

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

From 2 years to less than 18 years of age

2.1.3. Pharmaceutical form(s)

Hard capsules, age-appropriate oral solid dosage form, age-appropriate oral liquid dosage form

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Development of an age-appropriate solid formulation for oral use in paediatric patients aged 6 years to less than 12 years **Study 2** Development of an age-appropriate liquid formulation for oral use in paediatric patients aged 2 years to less than 6 years
Non-clinical studies	**Study 3** Dose-range finding study in juvenile dogs (8528319). **Study 4** Toxicity and toxicokinetic study with mavorixafor or placebo in juvenile dogs

Clinical studies	**Study 5** Double-blind, randomised, placebo-controlled trial to evaluate efficacy of mavorixafor in children aged 12 years to less than 18 years (and adults) with WHIM syndrome (X4P-001-103 - EudraCT 2019-001153-10). **Study 6 Study** Open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, and safety of mavorixafor in children from 6 years to less than 12 years of age with WHIM syndrome (X4P-001-001-PAED). **Study 7** Open-label, single-arm trial to evaluate pharmacokinetics, pharmacodynamics, and safety of mavorixafor in children from 2 years to less than 6 years of age with WHIM syndrome (X4P-001-002-PAED).
Modelling and simulation analyses	**Study 8** Population pharmacokinetic analysis and paediatric scaling of mavorixafor in patients with WHIM syndrome (X4P-001 PPK). **Study 9** Population pharmacokinetic/pharmacodynamic model (M&S-002). **Study 10** Extrapolation of mavorixafor PK/PD to children, predictive PopPK/PD model in children developed based on study 9. Potential differences in PK and PD processes due to ontogeny and maturation will be incorporated into the model to provide predictive capacity (M&S-003/EXTRAPOL-001).
Other studies	Not applicable
Extrapolation plan	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 December 2032
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:

The product is not authorised anywhere in the European Community.