EMA/284186/2024

European Medicines Agency decision

P/0223/2024

of 20 June 2024

on the agreement of a paediatric investigation plan and on the granting of a deferral for mirdametinib (EMEA-003525-PIP01-23) 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 Springworks Therapeutics Ireland Limited on 16 October 2023 under Article 16(1) of Regulation (EC) No 1901/2006 also requesting a waiver under Article 13 of said Regulation,

Having regard to the opinion of the Paediatric Committee of the European Medicines Agency, issued on 31 May 2024, 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.

[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 mirdametinib, capsule, hard, tablet, 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 mirdametinib, capsule, hard, tablet, 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

This decision is addressed to Springworks Therapeutics Ireland Limited, 70 Sir John Rogerson's Quay, D02 R296 – Dublin, Ireland.

EMA/PDCO/90811/2024
Amsterdam, 31 May 2024

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

EMEA-003525-PIP01-23

Scope of the application

Active substance(s):

Mirdametinib

Invented name and authorisation status:

See Annex II

Condition(s):

Treatment of neurofibromatosis type 1

Pharmaceutical form(s):

Capsule, hard

Tablet

Route(s) of administration:

Oral use

Name/corporate name of the PIP applicant:

Springworks Therapeutics Ireland Limited

Basis for opinion

Pursuant to Article 16(1) of Regulation (EC) No 1901/2006 as amended, Springworks Therapeutics Ireland Limited submitted for agreement to the European Medicines Agency on 16 October 2023 an application for a paediatric investigation plan for the above mentioned medicinal product and a waiver under Article 13 of said Regulation.

The procedure started on 20 November 2023.

Supplementary information was provided by the applicant on 26 February 2024. The applicant proposed modifications to the paediatric investigation plan and requested a deferral and withdrew its request for a waiver.

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.
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 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:

Treatment of neurofibromatosis type 1

2.1.1. Indication(s) targeted by the PIP

Treatment of neurofibromatosis type 1-plexiform neurofibroma

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)

Capsule, hard

Tablet

2.1.4. Measures

Area	Description
Quality-related studies	**Study 1** Generation of data on the dosing accuracy and suitability of dispersing the tablets in water prior to administration for patients with neurofibromatosis type 1 younger than 2 years of age.
Non-clinical studies	Not applicable
Clinical studies	**Study 2 (MEK-NF-201, NCT03962543)** Open-label, multicentre, single-arm trial to evaluate the safety, pharmacokinetics (PK), and efficacy of mirdametinib in children and adolescents from 2 years to less than 18 years of age (and adults) with an inoperable neurofibromatosis type 1 (NF1)-associated plexiform neurofibroma (PN) causing significant morbidity. **Study 3** Open-label, multicentre, single-arm trial to evaluate the safety, PK and activity of mirdametinib in children from birth to less than 2 years of age with measurable neurofibromatosis type 1 (NF1)-associated plexiform neurofibroma (PN) that is asymptomatic in a high-risk location or symptomatic.

Modelling and simulation analyses	**Study 4** Population PK model to characterize the PK profile and simulate drug exposure of mirdametinib in paediatric patients from 2 years to less than 18 years of age with neurofibromatosis type 1-associated plexiform neurofibroma **Study 5** Physiologically-based pharmacokinetic (PBPK) modelling to predict age-appropriate dose recommendations for children younger than 2 years of age with neurofibromatosis type 1-plexiform neurofibroma
Other studies	Not applicable
Extrapolation plan	Studies 2, 3 and 5 are part of the extrapolation plan covering the paediatric population from birth to less than 2 years of age, as agreed by the PDCO.

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 May 2028
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.