MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

agree a paediatric investigation plan and grant a deferral

MHRA-101678-PIP01-24

Scope of the Application

Active Substance(s)

Mirdametinib

Condition(s)

Treatment of neurofibromatosis type 1

Pharmaceutical Form(s)

Tablets; Capsules, hard

Route(s) of Administration

ORAL USE

Name / Corporate name of the PIP applicant

Springworks Therapeutics Ireland Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Springworks Therapeutics Ireland Limited submitted to the licensing authority on 25/11/2024 16:49 GMT an application for a Paediatric Investigation Plan

The procedure started on 13/01/2025 13:47 GMT

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to agree a paediatric investigation plan and grant a deferral

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-101678-PIP01-24

Of 26/03/2025 18:06 GMT

On the adopted decision for Mirdametinib (MHRA-101678-PIP01-24) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on a paediatric investigation plan

This decision applies to a Paediatric Investigation Plan for Mirdametinib, Tablets; Capsules, hard , ORAL USE .

This decision is addressed to Springworks Therapeutics Ireland Limited, Hamilton House, 28 Fitzwilliam Place, Dublin 2, IRELAND, D02 P283

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of neurofibromatosis type 1

2.2 Indication(s) targeted by the PIP:

Treatment of neurofibromatosis type 1 (NF1) plexiform neurofibromas

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

All subsets of the paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Tablets; Capsule, hard

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	1	Study 1 Generation of data on the dosing accuracy and suitability of dispersing the tablets in water prior to administration for patients younger than 2 years of age.
Non-Clinical Studies	0	Not applicable.
Clinical Studies	2	Study 2 (MEK-NF-201) 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 (MEK-NF1-104) 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.
Extrapolation, Modeling & Simulation Studies	3	Study 4 Population PK model to characterise 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. 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.
Other Studies	0	Not applicable.
Other Measures	0	Not applicable.

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	31/12/2028
Deferral of one or more studies contained in the paediatric investigation plan:	Yes