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

gov.uk/mhra

Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan (MHRA-101678-PIP01-24) and to the deferral

MHRA-101678-PIP01-24-M01

Scope of the Application

Active Substance(s)

MIRDAMETINIB

Condition(s)

Treatment of neurofibromatosis type 1

Pharmaceutical Form(s)

Capsule, hard; Dispersible tablet

Route(s) of Administration

Oral use

Name / Corporate name of the PIP applicant

Merck Serono Ltd

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Merck Serono Ltd submitted to the licensing authority on 13/07/2026 15:01 BST an application for a Modification

The procedure started on 04/08/2026 14:36 BST

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 accept change(s) to the agreed paediatric investigation plan and to the 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-M01

Of 13/10/2026 16:07 BST

On the adopted decision for MIRDAMETINIB (MHRA-101678-PIP01-24-M01) 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 modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for MIRDAMETINIB, Capsule, hard; Dispersible tablet , Oral use .

This decision is addressed to Merck Serono Ltd, 5 New Square, Bedfont Lakes Business Park, Feltham, London, UNITED KINGDOM, TW14 8HA

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):

Dispersible tablet 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:	31/01/2029
Deferral of one or more studies contained in the paediatric investigation plan:	Yes