NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Mirdametinib for treating symptomatic inoperable plexiform neurofibromas in people 2 years and over with neurofibromatosis type 1 ID6618

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of mirdametinib within its marketing authorisation for for treating symptomatic inoperable plexiform neurofibromas in people 2 years and over with neurofibromatosis type 1.

Background

Neurofibromatosis (NF) refers to a group of genetic disorders that primarily affect the cell growth of neural tissues. There are two forms of NF: type 1 (NF1) and type 2 (NF2). NF1 is the more common form and caused by a defect in the gene, NF1, situated at chromosome 17q11.2 [1]. NF1 is an incurable condition with highly-variable symptoms, including cutaneous (skin), neurological (nervous system) and orthopaedic (skeletal) manifestations. There are approximately 25,000 people in the UK diagnosed with NF1[2]. While most people with NF1 may only have mild symptoms, it can cause secondary complications including learning difficulties, visual impairment, pain, disfigurement, twisting and curvature of the spine, high blood pressure and epilepsy[3,4].

Plexiform neurofibromas (PNs) are a neurological manifestation of NF1 and arise from nerve fascicles that tend to grow along the length of the nerve. PNs occur in approximately 30 to 50% of people with NF1[5]. It can cause symptoms including pain, motor dysfunction and disfigurement[4] . The location of the PN on the body can impact the severity of the symptoms experienced and the complexity of the condition. PNs can also develop into malignant peripheral nerve sheath tumours (MPNST), which are associated with poor survival[1] . Most PNs are diagnosed in early childhood and grow most rapidly during this period. Approximately half of all people with NF1 PN have inoperable PN (that is PN which cannot be completely resected without a risk of substantial morbidity because of close proximity to vital structures, invasiveness, or high vascularity). Surgery is often complicated as tumours can be intertwined with healthy tissue.

NICE highly specialised technology guidance 20 recommends targeted systemic therapy with a mitogen-activated protein kinase 1 and 2 (MEK1/2) inhibitor selumetinib for treating symptomatic and inoperable PN in children aged 3 years and over.

The technology

Mirdametinib (Ezmekly, SpringWorks Therapeutics) is a highly selective small-molecule inhibitor of mitogen-activated kinase (MEK1 and MEK2). It blocks MEK activity in the RAS-mitogen-activated protein kinase (RAS MAPK) signalling cascade, blocking the proliferation and survival of tumour cells.

Appendix B

Mirdametinib does not currently have a marketing authorisation for inoperable plexiform neurofibromas associated with neurofibromatosis type 1 in the UK. It has conditional marketing authorisation in Europe for 'the treatment of symptomatic, inoperable plexiform neurofibromas (PN) in paediatric and adult patients with neurofibromatosis type 1 (NF1) aged 2 years and above'. It is being studied in clinical trials in adults and children aged 2 years and older with symptomatic inoperable neurofibromatosis type 1-associated plexiform neurofibromas.

Intervention(s)	Mirdametinib
Population(s)	People aged 2 years and over with neurofibromatosis type 1 and symptomatic inoperable plexiform neurofibromas
Subgroups	• Children aged 2 to 17 years with neurofibromatosis type 1 and symptomatic inoperable plexiform neurofibromas • Adults aged 18 years and over with neurofibromatosis type 1 and symptomatic inoperable plexiform neurofibromas
Comparators	In children aged 3 years and over • Selumetinib • Established clinical management without mirdametinib In children aged 2 years and adults aged 18 years and over • Established clinical management without mirdametininib
Outcomes	• complete and partial response rate • growth rate of PN • disfigurement • physical functioning • visual function • airway functioning • bowel and bladder continence • pain • adverse effects of treatment • health-related quality of life

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related highly specialised technology appraisals:** Selumetinib for treating symptomatic and inoperable plexiform neurofibromas associated with type 1 neurofibromatosis in children aged 3 and over (2022) NICE Highly specialised technologies guidance HST20

Questions for consultation

How is symptomatic inoperable plexiform neurofibromas associated with type 1 neurofibromatosis defined?

Can you provide an estimate of how many people with symptomatic inoperable plexiform neurofibromas associated with type 1 neurofibromatosis would expect to be treated with mirdametinib in England?

Which treatments are considered to be established clinical practice in the NHS for symptomatic inoperable plexiform neurofibromas?

How do treatment options and managing the condition differ for children (aged 2 to 17 years) and adults (aged 18 years and over)?

Would children and adults be managed by the same treatment centres?

Is selumetinib considered standard of care for people aged 3 to 17 years?

How would mirdametinib fit into the clinical pathway for symptomatic inoperable plexiform neurofibromas associated with type 1 neurofibromatosis?

Please select from the following, will mirdametinib be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Are the outcomes listed appropriate?

Are there any subgroups of people in whom mirdametinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which mirdametinib is licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. Patient: Neurofibromatosis. Available from https://patient.info/doctor/neurofibromatosis-pro [accessed 03 October 2025]
2. Nerve Tumours UK. Available from Nerve Tumours UK | What is NF1? | Nerve Tumours UK [accessed 03 October 2025]

3. NHS. Symptoms: Neurofibromatosis type 1 https://www.nhs.uk/conditions/neurofibromatosis-type-1/symptoms/ [accessed 03 October 2025]

4. Varni JW, Nutakki K, Swigonski NL. Speech difficulties and patient health communication mediating effects on worry and health-related quality of life in children, adolescents, and young adults with Neurofibromatosis Type 1. Am J Med Genet A. 2019; 179(8):1476-1482.

5. Yoo, H.K, Porteous, A, Ng, A. *et al.* Impact of neurofibromatosis type 1 with plexiform neurofibromas on the health-related quality of life and work productivity of adult patients and caregivers in the UK: a cross-sectional survey. BMC Neurol 2023; 23(1):419