NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Tovorafenib for treating relapsed or refractory paediatric low-grade glioma with BRAF fusion or rearrangement or BRAF V600 mutation in people 6 months and over ID6557

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness tovorafenib within its marketing authorisation treating people aged 6 months and over with relapsed or refractory paediatric low-grade glioma (LGG) with a BRAF fusion or rearrangement or BRAF V600 mutation.

Background

Gliomas are the most common type of primary brain tumour. They develop from the glial cells that support the nerve cells of the brain and spinal cord. In the NHS gliomas are graded according to the most recent World Health Organisation (WHO) categories which take account of likely growth rate. Grade 1 or 2 tumours are considered 'low-grade', are slow growing and may rarely spread to other areas of the brain. Grade 3 and 4 tumours, known as 'high-grade', are malignant and have a worse prognosis. The types of glioma are further identified by the cells they develop from (astrocytoma, ependymoma and oligodendroglioma) and increasingly, by a range of genetic markers including BRAF mutation status.[1]

Symptoms of glioma in children and young people are often general and nonspecific and may include headaches, nausea or vomiting, double vision and seizures. Other symptoms depend on where the glioma is in the brain.[2] Glioma is associated with wide reaching impacts on quality of life, including loneliness, difficulty doing activities outside the house and difficulty concentrating and processing information.[3] Astrocytomas are the most common type of glioma and more than 80% of astrocytomas in children are low grade.[2,4] There are around 150 cases of childhood low-grade glioma a year in the UK.[4] BRAF genomic alterations are common in paedatric low-grade glioma and the BRAF V600E mutation occurs in 7-20% of cases.[1,5,6]

Low-grade glioma is usually treated with surgery if possible, which may achieve either complete or partial macroscopic resection of the tumour. After surgery, radiotherapy or proton beam therapy, with or without chemotherapy may be used. Chemotherapy may also be used alone. NICE Technology Appraisal Guidance TA977 recommends dabrafenib with trametinib as an option for treating low-grade glioma with a BRAF V600E mutation in children and young people aged 1 year and over who need systemic treatment.

The technology

Tovorafenib (Ojemda, Ipsen) does not currently have a marketing authorisation in the UK for treating relapsed or refractory paediatric low-grade glioma.It has been studied in an open-label clinical trial alone in people aged 6 months to 25 years with relapsed or refractory low-grade glioma with documented activating BRAF alteration.

Intervention(s)	Tovorafenib
Population(s)	People 6 months and over with relapsed or refractory paediatric low-grade glioma with a BRAF fusion or rearrangement, or BRAF V600 mutation
Subgroups	If the evidence allows, the following subgroups will be considered: • BRAF V600E mutation status • BRAF fusion or rearrangement
Comparators	Established clinical management including but limited to: • Dabrafenib with trametinib, for glioma with BRAF V600 mutation • Chemotherapy (including but not limited to vinblastine monotherapy) • Best supportive care • Vorasidenib (subject to NICE evaluation)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • duration of response • 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The use of tovorafenib is conditional on the presence of BRAF fusion or rearrangement, or BRAF V600E mutation. The economic modelling should include the costs associated with diagnostic testing for BRAF fusion or rearrangement, or BRAF V600E in people with glioma who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation)
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 technology appraisals:** Dabrafenib with trametinib for treating BRAF V600E mutation-positive glioma in children and young people aged 1 year and over (2024) NICE technology appraisal guidance 977 Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer) (2001; last updated 2016) NICE technology appraisal guidance 23 Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma (2007) NICE technology appraisal guidance 121 reviewed March 2016 **Related technology appraisals in development:** Vorasidenib for treating astrocytoma or oligodendroglioma with IDH1 or IDH2 mutations after surgery in people 12 years and over NICE technology appraisal guidance [ID6407] publication expected September 2025

	MTX110 for untreated diffuse intrinsic pontine glioma NICE technology appraisal guidance [ID2695] publication date to be confirmed Vocimagene amiretrorepvec with extended-release 5-fluorocytosine for treating recurrent high-grade glioma NICE technology appraisal guidance [ID1425] publication date to be confirmed DCVax-L for treating glioblastoma NICE technology appraisal guidance [ID836] publication date to be confirmed Asunercept for treating glioblastoma NICE technology appraisal guidance [1301] publication date to be confirmed **Related NICE guidelines:** Brain tumours (primary) and brain metastases in over 16s (2018; last updated 2021) NICE Guideline NG99 reviewed 2021 **Related interventional procedures:** Photodynamic therapy for brain tumours (2009) NICE Interventional Procedures Guidance 290 **Related quality standards:** Brain tumours (primary) and brain metastases in over 16s (2021) NICE quality standard 203

Questions for consultation

What is considered established clinical management for relapsed or refractory low-grade glioma with a BRAF fusion or rearrangement, or BRAF V600 mutation?

If chemotherapy is an option for treating relapsed or refractory low-grade glioma with BRAF fusion or rearrangement, or BRAF V600 mutation, which chemotherapy regimens are used in this population?

Would vorasidenib be a relevant comparator in this evaluation if it receives a NICE recommendation for treating astrocytoma or oligodendroglioma with IDH1 or IDH2 mutations after surgery in people 12 years and over?

Do all people with low grade glioma currently receive testing for BRAF V600E mutation?

Do all people with low grade glioma currently receive testing for BRAF fusion or rearrangement?

Where do you consider tovorafenib will fit into the existing care pathway for relapsed or refractory low-grade glioma?

Please select from the following, will tovorafenib 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.

Would tovorafenib be a candidate for managed access?

Do you consider that the use of tovorafenib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.

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 tovorafenib will be 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).

References

1. Andrews, Lily J., et al. Prevalence of BRAF V600 in glioma and use of BRAF Inhibitors in patients with BRAF V600 mutation-positive glioma: systematic review. Neuro-oncology 24.4 (2022): 528-540

2. Cancer Research UK; Astrocytoma in children. Accessed May 2025

3. The Brain Tumour Charity; Losing my place: the reality of childhood with a brain tumour. Accessed May 2025

4. The Royal Marsden NHS Foundation Trust; Low grade glioma. Accessed May 2025

5. Di Nunno V, Gatto L, Tosoni A, Bartolini S, Franceschi E. Implications of BRAF V600E mutation in gliomas: Molecular considerations, prognostic value and treatment evolution. Front Oncol. (2023) Jan 4

6. Nobre L, et al. Outcomes of BRAF V600E Pediatric Gliomas Treated With Targeted BRAF Inhibition. JCO Precis Oncol. (2020) May 20