NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Depatuxizumab mafodotin for treating recurrent EGFR-amplified glioblastoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of depatuxizumab mafodotin within its marketing authorisation for treating recurrent EGFR-amplified glioblastoma.

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. The main types of gliomas are named according to the cells they develop from: astrocytoma, ependymoma and oligliodendroglioma. Gliomas are graded according to their likely growth rate, from grade 1 (slowest growing) to grade 4 (fastest growing). Grade 1 or 2 tumours are considered 'low-grade' and usually classed as benign or non-cancerous. Grade 3 and 4 tumours, known as 'high-grade', are malignant and have a worse prognosis. Glioblastoma, a grade 4 glioma, is the most common type of astrocytoma and is the most aggressive type of brain tumour. Epidermal growth factor receptor (EGFR) is known to be over-expressed in a wide variety of tumours and is associated with increased metastasis, decreased survival and a poor prognosis. About 40% of glioblastomas are EGFR-amplified[1].

Symptoms of glioblastoma depend on the size, location, and degree of infiltration of the tumour. They include headache, nausea, vomiting, seizure, visual disturbance, speech and language problems and changes in cognitive or functional ability. Scales of performance status, such as the World Health Organisation (WHO) performance status, can be used to categorise functional ability with glioblastoma.

In 2014, about 2,000 people were diagnosed with glioblastoma in England[2]. The average age of diagnosis is 55 years[3]. Between 2010 and 2011, 40% of adults with brain cancer in England and Wales survived for 1 year or more and 19% survived for 5 years or more[4].

Treatment of glioblastoma usually consists of surgical resection if possible, which may achieve either complete or partial resection of the tumour, although complete resection is rare. After surgery, radiotherapy with or without chemotherapy is used. If the size or position of the tumour means surgery is not possible without damaging surrounding tissue, radiotherapy and/or chemotherapy is offered.

NICE technology appraisal guidance 121 recommends temozolomide as an option for treating newly diagnosed glioblastoma in people with a WHO performance status or 0 or 1. It also recommends carmustine implants for newly diagnosed high-grade glioma, but only for people in whom 90% or more of the tumour has been resected. Both temozolomide and carmustine implants are licensed in combination with radiotherapy.

For people with glioblastoma which has recurred or progressed after standard therapy, people may be offered more surgery, radiotherapy, or chemotherapy such as lomustine alone or in combination with procarbazine and vincristine (PCV). NICE technology appraisal guidance 23 recommends temozolomide only if the person has a Karnofsky performance status score greater than or equal to 70 and a life expectancy of 12 weeks or more.

The technology

Depatuxizumab mafodotin (brand name unknown, AbbVie) is a monoclonal antibody-drug conjugate that targets the epidermal growth factor receptor (EGFR). It is administered intravenously.

Depatuxizumab mafodotin does not currently have a marketing authorisation in the UK for treating recurrent EGFR-amplified glioblastoma. It has been studied in clinical trials alone and in combination with temozolomide in adults with recurrent glioblastoma, compared with temozolomide or lomustine alone.

Intervention(s)	Depatuxizumab mafodotin (alone or in combination with temozolomide)
Population(s)	People with recurrent EGFR-amplified glioblastoma
Comparators	• Temozolomide • Lomustine • Procarbazine, lomustine and vincristine
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • 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 and NICE Pathways	Related Technology Appraisals: 'Guidance on the use of temozolomide for the treatment of recurrent malignant glioma (brain cancer)' (2001). NICE Technology Appraisal 23. Static list. Related Guidelines: 'Improving outcomes for people with brain and other central nervous system tumours' (2006). NICE cancer service guideline 10. Static list. Guidelines in development: 'Brain tumours (primary) and brain metastases in adults'. Publication expected July 2018 Related Interventional Procedures: 'Photodynamic therapy for brain tumours' (2009). NICE interventional procedures guidance 290. Related Quality Standards: 'Suspected cancer' (2016). NICE quality standard 124. Related NICE Pathways: Brain cancers (2017) NICE pathway http://pathways.nice.org.uk/pathways/brain-cancers
Related National Policy	NHS England (2016/17) Manual for prescribed specialised services. Chapter 105: specialist cancer services (adults) and Chapter 106: specialist cancer services for children and young people. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-

	may16.pdf Department of Health (2014) Improving outcomes: a strategy for cancer fourth annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report NHS England (2013/14) B13/S/a NHS Standard Contract for Cancer: Brain/Central Nervous System (adult) https://www.england.nhs.uk/wp-content/uploads/2013/06/b13-cancr-brain-cent-nervous.pdf NHS England (2013/14) B01/S/a NHS Standard Contract for Radiotherapy (all ages) https://www.england.nhs.uk/wp-content/uploads/2013/06/b01-radiotherapy.pdf NHS England (2013/14) B15/S/b NHS Standard Contract for Cancer: Chemotherapy (children, teenagers and young adults) https://www.england.nhs.uk/wp-content/uploads/2013/06/b15-cancr-chemoth-child-teen-yng-adul.pdf NHS England (2011) Improving outcomes: a strategy for cancer https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213785/dh_123394.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 3. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

How would depatuxizumab mafodotin be used in practice: alone or in combination with temozolomide?

Have all relevant comparators for depatuxizumab mafodotin been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for treating recurrent EGFR-amplified glioblastoma?

Would temozolomide retreatment be considered for people with recurrent glioblastoma who had previously received temozolomide for newly diagnosed disease?

Are the outcomes listed appropriate?

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

Where do you consider depatuxizumab mafodotin will fit into the existing NICE pathway for brain cancers?

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 depatuxizumab mafodotin 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.

Do you consider depatuxizumab mafodotin to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of depatuxizumab mafodotin can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made. We welcome comments on the appropriateness and suitability of the cost comparison methodology to this topic.

- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?

- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?

- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

[1] Furnari et al (2007) Malignant astrocytic glioma: genetics, biology, and paths to treatment. Genes and Development. 21: 2683-2710
[2] Cancer Research UK Brain, other CNS and intracranial tumours incidence statistics. Accessed August 2017.
[3] Patient UK. Gliomas and glioblastoma multiforme. Accessed August 2017.
[4] Cancer Research UK Brain, other CNS and intracranial tumours survival statistics. Accessed August 2017.