NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Bevacizumab for the treatment of recurrent glioblastoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of bevacizumab within its licensed indication for the treatment of recurrent glioblastoma.

Background

Gliomas are the most common type of malignant brain tumour. They develop from the glial cells that support the nerve cells of the brain and spinal cord. There are four main types: astrocytoma, ependyoma, oligliodendroglioma, and mixed tumours. Gliomas are graded according to their proliferative potential, from grade 1 to grade 4. Grades 3 and 4 – collectively referred to as glioblastoma – are considered high-grade gliomas. Grade 4 gliomas are called glioblastoma multiforme (GBM).

Symptoms of high-grade glioma 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 and/or functional ability. Functional ability of patients can be categorised using scales of performance status, such as the WHO performance status.

Brain tumours account for less than 2% of all primary cancers. The annual incidence of malignant brain tumours in those aged 15 years and over is 8.5 per 100 000, corresponding to approximately 3500 cases each year. The incidence of high-grade glioma increases with age; people diagnosed with GBM are, on average, older than people diagnosed with grade 3 gliomas. Approximately 30% of adults with high-grade tumours survive 1 year, and 13% survive 5 years from initial diagnosis.

Treatment usually consists of surgical resection (where possible), followed by radiotherapy. Complete surgical resection of these tumours is rarely possible; expert opinion suggests a large proportion of cases will go on to relapse after first- and second-line treatment. Palliative care aims to improve function and quality of life for those in whom the disease recurs.

NICE technology appraisal TA121 recommends the use of temozolomide for the treatment of newly-diagnosed GBM in patients with a WHO performance score of 0 or 1, and carmustine implants for use in patients with newly-diagnosed high-grade glioma in whom 90% or more of the tumour has been resected. NICE technology appraisal TA23 recommends temozolomide for the treatment of recurrent malignant glioma in patients with a Karnofsky

performance status greater than or equal to 70 and a projected life expectancy of 12 weeks or more at the initiation of temozolomide treatment.

The technology

Bevacizumab (Avastin, Roche) is a humanised anti-vascular endothelial growth factor (VEGF) monoclonal antibody that inhibits VEGF-induced signalling and inhibits VEGF-driven angiogenesis. This reduces vascularisation of tumours, thereby inhibiting tumour growth. Bevacizumab is administered by intravenous infusion.

Bevacizumab does not currently hold a UK marketing authorisation for the treatment of recurrent glioblastoma. It has been studied in clinical trials compared with lomustine in people with recurrent glioblastoma.

Intervention(s)	Bevacizumab
Population(s)	People with recurrent glioblastoma.
Comparators	Chemotherapy regimens including: • combination therapy with procarbazine, carmustine and vincristine • carmustine monotherapy • lomustine • temozolomide
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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. If the evidence allows, the appraisal will consider subgroups of people defined by their: • performance status • tumour grade at presentation • MGMT biomarker status
Related NICE recommendations	Related Technology Appraisals: Technology Appraisal No.23, Apr 2001, 'Temozolomide for the treatment of recurrent malignant glioma' (Review date to be confirmed) Technology Appraisal No. 121, Jun 2007, 'Carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma' (To be reviewed August 2010) Technology Appraisal No. 149, Jun 2008, 'Carmustine implants for the treatment of recurrent glioblastoma multiforme' (Terminated Appraisal) Related Guidelines: Cancer Service Guidance, Jun 2006, 'Service guidance for improving outcomes for people with brain and other central nervous system tumours'

Appendix A