NATIONAL INSTITUTE FOR CLINICAL EXCELLENCE

Health Technology Appraisal

Carmustine implants and temozolomide for the treatment of newly diagnosed glioblastoma multiforme

Draft scope

Appraisal objective

To appraise the clinical and cost effectiveness of carmustine implants (Gliadel Wafers, Link Pharmaceuticals) and temozolomide (Temodal, Schering-Plough) for the treatment of newly diagnosed glioblastoma multiforme (GBM) as an adjunct to surgery and radiation, and to provide guidance to the NHS in England and Wales[1].

Background

Brain tumours account for 1.6% of all primary cancers. The majority of brain tumours are gliomas, so called because they develop from the glial cells that support the nerve cells of the brain. There are three main types of gliomas – astrocytoma, ependymoma and oligodendroglioma. Brain tumours are graded according to their likely rate of growth, from grade 1 (slowest growing) to grade 4 (fastest growing). Grade 4 astrocytoma is also known as glioblastoma multiforme (GBM).

The annual incidence of malignant brain tumours in the England and Wales is 7 per 100,000 population, corresponding to about 3,500 new cases each year. GBM accounts for approximately 22% of these new cases. GBM is more common in males, with a male: female ratio of around 3:2. Approximately 30% of adults with high-grade tumours (grades 3 and 4) survive one year, and 13% survive 5 years. The median survival of patients with GBM is 10 to 12 months.

Treatment usually consists of surgical resection followed by radiotherapy and sometimes systemic chemotherapy. Complete surgical resection of these tumours is difficult, and patients with malignant glioma usually experience more than one operation due to recurrence of the disease.

The technology

Carmustine implants are biodegradable polymer wafers that are implanted in the cavity created by the partial or complete resection of the brain tumour. Each wafer contains 7.7mg of carmustine. The wafers release carmustine directly to the tumour site and slowly dissolve over two to three weeks. A maximum of eight wafers may be used at any one time. Gliadel is indicated as an adjunct to surgery in patients with recurrent histologically proved GBM. Gliadel has recently received UK approval for newly diagnosed high grade

[1] The Department of Health and Welsh Assembly government remit to the Institute: to appraise the clinical and cost effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed glioblastoma multiforme as an adjunct to surgery and radiation.

malignant glioma through the EU mutual recognition scheme. It is anticipated that a revised Summary of Product Characteristics will be available shortly.

Temozolomide is an alkylating agent derived from dacarbazine. It is administered orally once a day for 5 days in a 28-day cycle. Temozolomide is indicated for the treatment of patients with malignant glioma showing recurrence or progression after standard therapy. The manufacturer also has a licence application pending for the treatment of patients with newly diagnosed high-grade malignant glioma concomitantly with radiotherapy or after radiotherapy, as adjuvant treatment.

Intervention(s)	• Carmustine implants • Temozolomide Both are used as adjuncts to surgery and radiotherapy
Population(s)	Adults with newly diagnosed GBM for whom surgery is indicated.
Standard comparators	Comparators may include: • surgery and radiotherapy alone • surgery, radiotherapy combined with antineoplastic agents other than those listed under interventions (for example nitrosourea-based regimens such as procarbazine, carmustine, and vincristine [PCV]) .
Outcomes	The outcome measures to be considered include: • survival • progression-free survival • adverse effects of treatment • health-related quality of life.
Economic analysis	Ideally, the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. Costs will be considered from an NHS and Personal Social Services perspective.

Other considerations	The technologies will be considered as adjunct to standard therapies such as surgery and radiotherapy. If the evidence allows, the appraisal will identify subgroups for whom treatment may be particularly appropriate. For example, subgroups may be defined according to the extent of surgery (biopsy, partial resection or complete resection). If the evidence allows, treatment strategies using carmustine implants or temozolamide will be compared with each other. The manufacturers of both technologies currently have a licence application pending for the treatment of patients with newly diagnosed high-grade malignant glioma. The interventions will be appraised according to the anticipated licensed indication. Guidance will only be issued in accordance with the marketing authorisations.
Related NICE recommendations	Related Technology Appraisals: NICE Technology Appraisal Guidance No.23: temozolomide for the treatment of recurrent malignant glioma (brain cancer). Related Guidelines: Cancer Service Guideline on brain tumours. Expected publication date is September 2005.

Question for consultation

The Institute would welcome views as to the appropriate comparators for this appraisal.