NICE submission for clinical and cost effectiveness of biodegradable carmustine (BCNU) implants (Gliadel Implants) for the treatment of newly-diagnosed high-grade (malignant) glioma

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Executive summary

High-grade glioma is a rare condition with an annual incidence in England and Wales between 4 and 6 per 100,000 population. In 2001 there were around 3,800 new cases of malignant neoplasms of the brain in England and Wales. It is estimated that 55% to 85% (2,100 to 3,246 cases in England and Wales) of these are grade III or IV glioma.

The prognosis for patients diagnosed with high-grade glioma is extremely poor and morbidity is high. Without any intervention death is likely to occur within weeks although surgery and radiotherapy can prolong survival to a median of approximately 1 year. Even with treatment, most patients will experience tumour regrowth.

There has been little improvement on this survival over the past 2 decades although studies have shown incremental benefit for the multi-modal approach where one treatment modality is supplemented with another i.e. surgical resection followed by radiotherapy and adjuvant chemotherapy. Importantly there may be an increase in the proportion of long-term survivors that occurs with this combination of treatments. A multi-modal treatment approach is likely to provide the greatest clinical and thereby patient benefits of both median and long term survival.

For a condition with a devastating, 12 month prognosis, an increase in survival of 20% with sustained quality of life represents a really valuable and meaningful advance for patients, carers and clinicians.

Carmustine implants have been shown to provide just such an advance. In patients with newly-diagnosed high-grade glioma, surgical resection with the placement of carmustine implants and radiotherapy has shown a statistically significant improvement in median survival compared to placebo (2.3 months p=0.03). Long term survival benefits were also seen at 12, 24 and 36 months.

Carmustine implants sustain patients functionality by delaying deterioration of both Karnofsky Performance Status and neuroperformance.

Carmustine implants are single use, biodegradable discs inserted into the cavity in the brain at the time of surgical resection. Their use can easily be included in the current treatment pathway for this disease and their use does not preclude or delay subsequent chemotherapy treatment. Failure to use carmustine implants at the time of resection represents a missed opportunity for effective treatment of patients with high-grade glioma.

Additionally, the use of a local delivery of chemotherapy, such as carmustine implants, provides an effective means to bypass the blood brain barrier producing a high concentration of drug directly in the region of the tumour and minimising systemic toxicity.

Radiotherapy waiting times are common in England and Wales and carmustine implants allow active treatment at the time of surgery which may help to lessen any negative impact caused by delays in receiving radiotherapy.

In determining cost-effectiveness, progression free survival is widely used as an indicator of the time at which there is a decrease in utility. However progression free survival is difficult to assess in patients with high-grade glioma. PFS as measured by imaging techniques may be confounded by necrosis, timing of scans, as well as the effects of surgery and other treatments. This is further complicated in patients who have received carmustine implants as the implants themselves may cause enhancement. For this reason, PFS in these patients is better determined by the use of less direct, but nevertheless appropriate, measures of tumour activity such as decline in neurological status and functional impairment.

Using the cost effectiveness model detailed in the submission, carmustine implants have been shown to be a cost effective intervention in the management of high-grade glioma in terms of the cost per QALY. Moreover they have been shown to be cost effective compared to other interventions used in this indication.

Intervention	Average cost of intervention (£ per patient)	Cost per LYG (£)	Cost per QALY (£)
Carmustine implants	4,252	19,200	28,000
Temozolomide	7,879	37,800	53,700
PCV	2,483	14,900	34,150

As carmustine implants can only be used at the time of routine surgical resection, requiring no additional surgery or intervention, they represent a one-off fixed cost and require few if any of the additional ancillary costs commonly associated with the use of conventional chemotherapies.

Based on an average cost per patient of £4,252 and given the relatively low incidence of

high-grade glioma coupled with the specific criteria of patients likely to benefit from the use of carmustine implants, the impact on the NHS in England and Wales is estimated to be between £2.2 and £3.4 million (+ VAT) per annum.