NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma

Summaries of issues arising from consultation with the public

The table contains summaries of comments received in response to consultation on the ACD received via the NICE website and in writing from the public. The key issues are organised into the following subject headings:

1. **Impact of glioma on quality of life/ impact of treatments upon quality of life**
2. **Consideration of the data on effectiveness**
3. **Criticisms of the cost effectiveness analyses**
4. **Agreement with the preliminary recommendations**
5. **Consideration of subgroups**
6. **Use of temozolomide for the second-line treatment of high-grade glioma**
7. **Lack of alternative therapies and advancement in treatment**
8. **The technologies have been approved by other countries/organisations**
9. **Criticisms of the Institute's methods and processes**
10. **Description of the disease**
11. **Equity and special considerations**
12. **Evidence relating to children with high-grade glioma**
13. **Future research**
14. **The proposed review date for the appraisal**
15. **The guidance in relation to other technologies**

1. Impact of glioma on quality of life/ impact of treatments upon quality of life

Comment from	Nature of comment	Response
• Association of neuro-oncology nurses, • Patient	The impact on quality of life should be considered in addition to the impact on length of life.	The Committee agreed that the impact on quality of life was important and this contributed to the recommendations (see FAD section 4.3.3 and 4.3.26).
• IBTA, • Diana Ford Trust	Brain tumours have a considerable emotional and physical impact on the family and carers of people with brain tumours.	The Committee acknowledged that the quality of life of patients with high grade glioma was important (see FAD section 4.3.3).
• NHS Professional	Temozolomide enhances quality of life.	The Committee agreed that the impact of glioma on quality of life was important and acknowledged the quality of life data from the EORTC trial which demonstrated that the side effects of temozolomide are usually well tolerated (see FAD section 4.3.3, 4.3.20 and 4.3.26).
• Charlie's Challenge (Brain Tumour Charity) • Brain Tumour Action, IBTA, • Diana Ford Trust, • Patient • NHS Professional, • Wife of patient, • Ali's Dream (brain tumour research charity)	Temozolomide does not have a detrimental effect on quality of life. Adverse events of temozolomide are well tolerated.	The Committee considered the quality of life data from the EORTC trial which demonstrated that the side effects of temozolomide are usually well tolerated (see FAD section 4.3.3, 4.3.20 and 4.3.26).

Comment from	Nature of comment	Response
• EORTC Brain Tumour Group	Deterioration of quality of life from time of disease progression is frequently delayed.	The Assessment Group's economic analysis assumed a reduction in quality of life of 0.5% per week. For example, based on the estimates of utility included in the analysis, the quality of life of a patient whose disease has progressed for 6 months, is be estimated to be approximately 65% of a person without the disease and who is in full health at the end of that 6 month period.
• British Neuro-oncology Society	The assumption in the economic analysis that quality of life constantly deteriorates is inappropriate.	The deterioration in quality of life employed in the analysis applies only to the progressive disease state. It is not employed for patients whose disease is stable. The Committee considered that most patients would experience a decline in quality of life following disease progression (see FAD section 4.3.3).
• EORTC Brain Tumour Group	Section 4.1.13 presents data on adverse events from the RCT of temozolomide but does not recognise that these events are not clinically significant. Data on quality of life from the RCT of temozolomide were not appropriately considered.	It is standard practice to report in the guidance documents the details of side effects reported in clinical trials. In addition, the Committee considered the quality of life data from the EORTC study of temozolomide (see FAD sections 4.1.15 and 4.3.20.) The Committee considered the quality of life data from the EORTC study of temozolomide (see FAD sections 4.1.15 and 4.3.20.)
• Brain Tumour Action	Carmustine implants do not have aggressive side effects	Comments noted. The Committee considered the data on adverse events from the RCTs of carmustine implants and the evidence from representatives of patients and carers (see FAD section 4.1.7).

2. Consideration of the data on effectiveness

Comment from	Nature of comment	Response
• Sussex Cancer Network • Ali's Dream (brain tumour research charity) • Charlie's Challenge (Brain Tumour Charity) • Way Ahead (brain tumour research charity) • Patients (2 comments) • Chairperson of charity	The appraisal should recognise that patients with high-grade glioma have a poor prognosis. Relatively modest gains in life expectancy are particularly significant to patients because they only have a few months to live.	The Committee noted that people with high grade glioma have a relatively short life expectancy – see FAD section 4.3.26.
• SELCN Brain tumour working group • Ali's Dream (brain tumour research charity) • Charlie's Challenge • Way Ahead • IBTA • EORTC Brain Tumour Group	The two-year survival data are the most significant. The 2 year data from the EORTC trial of temozolomide should be considered rather than focusing on median survival. Long-term data on survival from the EORTC trial of temozolomide has not been adequately considered.	The Committee carefully considered the survival data from this trial, including the long term data. See FAD section 4.1.10.
• Patient	5 year survival data is available from the US.	Data from the RCTs of temozolomide in patients with newly diagnosed high-grade glioma are not available to 5 years.
• Patients (2 comments) • Brain Tumour Action • Carer (wife of person with glioma)	Costs should not be considered if treatments extend survival, regardless of length of survival.	NICE is directed by the Secretary of State for Health and the Welsh Assembly Government to appraise the health benefits and the costs of specific technologies and to make recommendations to the NHS in England and Wales.

Comment from	Nature of comment	Response
• Brain Tumour Charity • Diana Ford Trust	Data on person life years lost have not been considered	The Committee considered that it was important to consider the impact of the disease and treatments upon quality as well as quantity of life. Furthermore, the reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. See Guide to the Methods of Technology Appraisal section 5.3.4 (Available from URL http://www.nice.org.uk/page.aspx?o=201974).
• Chairperson of charity (parent of child who died from glioma) • Carer (wife of person who died from a glioma) • NHS Professional • Wife of patient, • 2 patients (USA)	Research has shown that these drugs have an impact on glioma. Temozolomide has a positive impact	Comments noted. The Committee considered the evidence on the effectiveness of the technologies from the RCTs and provided by the clinical experts and patient\carer representatives.
• Charlie's Challenge • Diana Ford Trust, Chairman of brain tumour charity • Way Ahead • IBTA	The preliminary guidance doesn't allow hope for patients. The preliminary guidance disregards the emotional impact of the disease on people with glioma.	The Committee was mindful that people with high-grade glioma have a relatively short life expectancy and that previously used chemotherapy regimens for this disease have not demonstrated a benefit in survival when making its recommendations. Temozolomide is recommended for patients with performance status of 0.
• EORTC Brain Tumour Group	The observation that length of survival was better in the control arm of the EORTC trial of temozolomide does not reflect conduct of the trial, but should raise concerns about current UK practice.	This is a factual comment and not intended to be a criticism of the trial. The Committee noted the importance of optimising the extent and timing of radiotherapy, irrespective of the use of other therapies (see FAD section 4.3.5).

Comment from	Nature of comment	Response
• Charlie's Challenge	The availability of radiotherapy should not be used as an excuse to withhold these treatments	The Committee noted the importance of optimising the extent and timing of radiotherapy, irrespective of the use of other therapies (see FAD section 4.3.5).
• Nottingham, Swansea and Cardiff neuro-oncology MDTs	The small increase in median time to recurrence should not be relied on as the sole reason for not recommending temozolomide.	The recommendations are based on a consideration of the clinical and cost effectiveness. Temozolomide is recommended for patients with performance status of 0.
• EORTC Brain Tumour Group	The grading of tumours is arbitrary and irrelevant to the discussion (in reference to section 4.3.8 of the ACD).	The FAD has been amended to clarify this consideration in the context of the trial of carmustine implants. The Committee accepted the difficulty of making a definitive pathological diagnosis and accepted the pragmatic evidence from the RCT as a reflection of this issue in clinical practice (see FAD section 4.3.10).
• Sussex Cancer Network	The post hoc analysis of the pathology results conducted by the FDA is flawed.	The Committee accepted the difficulty of making a definitive pathological diagnosis and accepted the pragmatic evidence from the RCT as a reflection of this issue in clinical practice (see FAD section 4.3.10).
• NHS professional • Charlie's Challenge • Way Ahead • IBTA	The data on MGMT promoter methylation are not yet validated and should be seen as hypothesis generating.	The Committee considered these data. The Committee rejected the notion of patient selection on the basis of this marker (see FAD section 4.3.25).
• NHS Professional	The data on the proportions of people who underwent complete and partial resection in the EORTC trial of temozolomide is incorrectly presented in Section 4.1.9.	This has been amended.
• IBTA	The study by Beresford et al. ([Abstract] European Cancer Conference ECCO 13, Paris 2005) is not mentioned.	This study did not meet the Assessment Group's inclusion criteria for review.

3. Criticisms of the cost effectiveness analyses

Comment from	Nature of comment	Response
• British Neuro-oncology Society	The assumption that survival is dependent on time rather than health state is over-simplistic.	The Committee carefully considered this assumption and the results of a sensitivity analysis. It concluded that the sensitivity analysis demonstrated that the results of the analysis were not sensitive to this time dependency assumption (see FAD section 4.3.12 and AR pages 115 and 127).
• EORTC Brain Tumour Group	The economic analysis submitted by the manufacturer of temozolomide was not appropriately considered.	The Committee carefully considered the analysis submitted by Schering-Plough. It concluded that the Assessment Group's analysis was the most appropriate analysis on which to base its decisions as it incorporated the effects of glioma on quality of life and presented health outcomes in QALYs (see FAD sections 4.2.8, 4.2.9 and 4.3.20). Further consideration of this analysis was also provided by the assessment group (see AR pages 83 to 88).
• NHS Professional	The economic analysis has not appropriately considered subsequent chemotherapy, in particular that if temozolomide was used as adjuvant therapy, patients would be offered cheaper PCV second-line.	Additional analyses were performed using different assumptions about second-line treatment. The Committee carefully considered the evidence and existing NICE guidance regarding appropriate treatment at relapse (see FAD sections 4.2.12, 4.2.13 and 4.3.22).
• NHS Professional	The economic analysis has not appropriately considered current temozolomide usage.	
• NHS Professional	Did the AG analysis include the costs of 3 cycles of temozolomide therapy or was it based on 6 cycles?	The Assessment Group's economic analysis does not assume all patients receive 6 cycles of chemotherapy. The median number of cycles included in the analysis is 4.

Comment from	Nature of comment	Response
• Nottingham, Swansea and Cardiff neuro-oncology MDTs • NHS Professional	The utility estimates included in the economic analysis were derived from small samples of both patient and normal populations. The utility values used were not validated.	Published utility data for patients with high grade glioma were not available. The Committee carefully considered the utility data included in the analyses and the results of sensitivity analyses (see AR Figures 16, 19, 20, 28, 31 and 32).
• Nottingham, Swansea and Cardiff neuro-oncology MDTs, • International Brain Tumour Association (IBTA)	Measurement of benefits to the carers and families of people with high grade glioma was not considered.	The Guide to methods for technology appraisal states that the reference case analysis should include all direct health benefits from treatment, but that wider sets of outcomes may be included as a sensitivity analysis where these are expected to influence the results significantly. The Committee carefully considered the evidence provided by representatives of people with high grade glioma and their carers, and was mindful that people with high grade glioma have a short life expectancy when formulating its recommendations.
• NHS Professionals (2 comments)	As the number of people with high-grade glioma who would be likely to receive treatment is small, the overall budget impact will be small.	Commonness or rarity of the condition is not considered by the Committee.
• Ali's Dream • Charlie's Challenge • Way Ahead	The recommendations are based on an economic model that is applied to other disease areas. The model is not designed for rare diseases.	The general methods, processes and principles of conducting technology appraisals are consistent across disease areas and described in process guides available from URL http://www.nice.org.uk/page.aspx?o=taprocess. The economic model developed by the Assessment Group was specifically designed to assess the cost effectiveness of carmustine implants and temozolomide for the treatment of newly diagnosed high grade glioma.

Comment from	Nature of comment	Response
• Way Ahead	The sensitivity of the economic analysis to slight changes in parameters raises questions about its validity.	The Committee considered the results of the extensive sensitivity analyses and concluded that their conclusions regarding the cost effectiveness of the treatments were robust to slight changes in the parameter estimates.
• IBTA • Diana Ford Trust	Average Years of Life Lost (AYLL) should be used as an outcome measure	The Committee considered that it was important to consider the impact of the disease and treatments upon quality as well as quantity of life. Furthermore, the reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. See Guide to the Methods of Technology Appraisal section 5.3.4 (Available from URL http://www.nice.org.uk/page.aspx?o=201974).
IBTA	It is not appropriate to consider the cost per QALY as treatment may extend survival long enough for the patient to benefit from new medical developments.	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. See Guide to the Methods of Technology Appraisal section 5.3.4 (Available from URL http://www.nice.org.uk/page.aspx?o=201974).
• IBTA, • Diana Ford Trust	Temozolomide is cheaper to administer as it does not incur the capital and staff costs of a day at a clinic.	This is reflected in the economic analysis (see AR section 5.5.3).

4. Agreement with the preliminary recommendations

Comment from	Nature of comment	Response
• NHS Professional	Agrees with the preliminary recommendations. The NHS should not fund experimental treatments routinely.	Comments noted.
• NHS Professional	Agrees with preliminary recommendations. Also notes that the primary analysis of the trial of carmustine implants was specified without stratification of the data.	Comments noted.
• NHS Professional	Agrees with preliminary recommendations related to carmustine implants. The phase 1 and 2 studies were not rigorous. The results of the phase 3 study are questionable. [Note. The person disagrees with the guidance relating to temozolomide. Specific comments related to temozolomide are detailed under the appropriate subject headings below.]	Comments noted.
• Nottingham, Swansea and Cardiff neuro-oncology MDTs	Agree with preliminary recommendations related to carmustine implants. [Note. The group disagree with the guidance relating to temozolomide. Specific comments related to temozolomide are detailed under the appropriate subject headings below.]	Comments noted.
• NHS Professional	Agrees with preliminary recommendations related to carmustine implants. [Note. The person disagrees with the guidance relating to temozolomide. Specific comments related to temozolomide are detailed under the appropriate subject headings below.]	Comments noted.
• UK Specialised Services Public Health Network	Agrees with the preliminary recommendations. Supports the request for further research in the preliminary recommendations.	Comments noted.

5. Consideration of subgroups

Comment from	Nature of comment	Response
• EORTC Brain Tumour Group, • Nottingham, Swansea and Cardiff neuro-oncology MDTs, • NHS Professional • Way Ahead	Subgroups of patients for whom the treatments may be more appropriate should be considered.	The data regarding subgroups has been considered by the Committee – see FAD sections 4.1.6, 4.1.11, 4.12, 4.1.13, 4.2.7, 4.2.13, 4.3.14, 4.3.16, 4.3.23, 4.3.24, 4.3.26. Temozolomide is recommended for patients with performance status of 0.
• EORTC Brain Tumour Group • NHS professional (2 comments), • Nottingham, Swansea and Cardiff neuro-oncology MDTs • NHS professional	Information on the impact of methylation status of the MGMT promoter has not been given enough weight. Patients with reduced MGMT activity should be considered for treatment with temozolomide and radiotherapy. Information on the methylation status of MGMT promoter of patients is currently being collected.	The Committee considered these data. Therefore the Committee rejected the notion of patient selection on the basis of this marker – see FAD section 4.3.25. Temozolomide is recommended for patients with performance status of 0.
NHS Professional	Only patients with good performance status would be offered treatment with temozolomide anyway.	Temozolomide is recommended for patients with performance status of 0.

Comment from	Nature of comment	Response
• IBTA • Diana Ford Trust	The treatments should not be restricted to subgroups of patients defined by: – Gender – Age – Extent of resection – methylation status of the MGMT promoter	The Committee did not consider it appropriate to recommend the treatments for subgroups of patients according to their gender, age, extent of resection and methylation status of the MGMT promoter – see FAD sections 4.3.14 to 4.3.47 and 4.3.23 to 4.3.26. Temozolomide is recommended for patients with performance status of 0.

6. Use of temozolomide second-line

Comment from	Nature of comment	Response
• NHS Professional	It is reasonable to recommend that if treatment with temozolomide is used at presentation it should not be funded again.	The Committee recommended that temozolomide is not used for the subsequent treatment of patients who have received it as part of first line treatment (see FAD sections 1.2 and 4.3.27).

7. Lack of alternative therapies and advancement in treatment

Comment from	Nature of comment	Response
• Association of neuro-oncology nurses • EORTC Brain Tumour Group • NHS Professionals (2 comments) • Nottingham, Swansea and Cardiff neuro-oncology MDTs • Ali's Dream • Charlie's Challenge • Patient • Brain Tumour Charity • Diana Ford Trust	The technologies represent a significant advancement in treatment in a disease area where there have been no significant breakthroughs for some time.	The Committee acknowledged this when making its recommendations (see FAD section 4.3.26). Temozolomide is recommended for patients with performance status of 0.
• Diana Ford Trust • IBTA	Carmustine implants represent an advance in treatment because of the anticipated anti-tumour activity in the period between surgery and radiotherapy.	Comments noted. The Committee carefully considered the effectiveness data from the RCTs of carmustine implants.
• Sussex Cancer Network • NHS Professional	There are few other treatment options available to patients with high grade glioma.	The Committee acknowledged this when making its recommendations (see FAD section 4.3.26).

Comment from	Nature of comment	Response
• NHS Professional	Decline is rapid when no further treatment is available.	The Committee considered that most patients' health would deteriorate once progression of the disease had occurred – see FAD section 4.3.3. Temozolomide is recommended for patients with performance status of 0.

8. The technologies have been approved by other countries/organisations

Comment from	Nature of comment	Response
• British Neuro-oncology Society • EORTC Brain Tumour Group • SELCN Brain tumour working group • NHS Professionals (2 comments) • Ali's Dream • Patient • Brain Tumour Charity • Charlie's Challenge • Way Ahead • Brain Tumour Action • SDRT Astro Fund • Diana Ford Trust • IBTA	The technologies have been approved in other countries.	Noted. NICE is directed by the Secretary of State for Health and the Welsh Assembly Government to appraise the health benefits and the costs of specific technologies and to make recommendations to the NHS in England and Wales. Temozolomide is recommended for patients with performance status of 0.

Comment from	Nature of comment	Response
• NHS Professional	The guidance will undermine the credibility of the UK neuro-oncology community.	Comments noted. NICE is directed by the Secretary of State for Health and the Welsh Assembly Government to appraise the health benefits and the costs of specific technologies and to make recommendations to the NHS in England and Wales. Temozolomide is recommended for patients with performance status of 0.
• London Cancer New Drugs Groups, • SELCN Brain tumour working group.	The London Cancer New Drugs Groups has supported the use of temozolomide as first-line treatment in patients with newly diagnosed GBM.	Comments noted. NICE is directed by the Secretary of State for Health and the Welsh Assembly Government to appraise the health benefits and the costs of specific technologies and to make recommendations to the NHS in England and Wales. Temozolomide is recommended for patients with performance status of 0.
• Ali's Dream • Charlie's Challenge • Way Ahead	The preliminary recommendations go against the objectives of the National Cancer Plan	Comments noted. NICE is directed by the Secretary of State for Health and the Welsh Assembly Government to appraise the health benefits and the costs of specific technologies and to make recommendations to the NHS in England and Wales. Temozolomide is recommended for patients with performance status of 0.

9. Criticisms of the NICE methods and process

Comment from	Nature of comment	Response
• EORTC Brain Tumour Group	The use of a threshold of £30,000 is confusing.	Considerations about cost effectiveness are explained in the Guide to the Methods of Technology Appraisal section 6.2.6.10 and 6.2.6.11(Available from URL http://www.nice.org.uk/page.aspx?o=201974)
• Nottingham, Swansea and Cardiff neuro-oncology MDTs	No provision of alternative health economic assessment was supported by the consultation process.	The Committee considered the results of economic analyses provided by the manufacturer of carmustine implants, the manufacturer of temozolomide and the Assessment Group. The Committee considered the analysis conducted by the Assessment Group to be the most appropriate (see FAD sections 4.3.11, 4.3.12, 4.3.13 and 4.3.20). In addition, the Committee considered the results of additional analyses conducted in response to comments on the assessment report and ACD.
• NHS Professional	The Committee have accepted the economic model without providing criticisms.	The Committee carefully considered the economic analyses submitted to it, including the results of extensive sensitivity analyses around the results of the Assessment Group's economic analysis and the results of additional analyses conducted in response to comments on the assessment report and ACD.

Comment from	Nature of comment	Response
• NHS Professional • Patient, • Carer (wife of person who died from a glioma), • Way Ahead	The ACD had been written without direct input from an oncologist and patient representative. There was no brain tumour specialist or other neuro-oncological expertise on the Committee	The ACD has been written in accordance with standard NICE procedures. The Appraisal Committee is a standing committee made up of people from a mix of backgrounds and specialist expertise. The Committee considered evidence provided by clinical experts who are specialist in treating people with high grade gliomas, and representatives of patients with high-grade glioma and their carers.
• NHS Professional, • Patient	Much of the NICE methodology use in the appraisal has not been subject to open review. The Committee's deliberations are not available under the Freedom of Information Act.	The documents considered by the Appraisal Committee have been circulated to consultees and commentators, and are publicly available from the NICE website. See URL http://www.nice.org.uk/page.aspx?o=285589#keydocs The Committee's considerations in formulating its recommendations are described in the Appraisal Consultation Document, which is also publicly available from the NICE website.
• NHS Professional Ali's Dream • Charlie's Challenge	The experts who advised the Committee disagreed with the preliminary recommendations. It appears that the evidence from charities and clinical experts has been ignored.	Comments noted. The Committee carefully considered a range of evidence including that from the RCTs of the technologies, the economic analyses submitted and the evidence provided by clinical experts and representatives of patients with high-grade glioma and their carers.

Comment from	Nature of comment	Response
• IBTA	The perspective of patient and carers is not sufficiently prominent in the ACD. NICE should have undertaken specific activities to solicit submissions from actual patients/carers.	The Institute solicited submissions from a range of stakeholders representing patients and their carers. See Appendix B of the FAD. These organisations were also invited to comment on the draft scope, Assessment Report and Appraisal Consultation Document.

10. Description of the disease

Comment from	Nature of comment	Response
• Carer (wife of person who died from a glioma)	Disagrees with comments regarding the age of people with glioma.	Comments noted. These data refer to the average ages of people with glioma, however it is noted that glioma can affect people of all ages.
• SDRT Astro Fund • Diana Ford Trust • IBTA	The guidance should reflect that low-grade tumours can progress to become high-grade tumours.	Comments noted. The guidance applies specifically to the use of the technologies for the treatment of high-grade glioma in accordance with their UK marketing authorisations.

11. Equity and special considerations

Comment from	Nature of comment	Response
• Way Ahead	Special consideration should be given to these treatments as glioma is a rare disease.	Commonness or rarity of the condition is not considered by the Committee.
• IBTA, • Patients (2 comments) • Brain Tumour Charity • SDRT Astro Fund	If treatment is only made available in clinical trials, there will be unequal access depending on where in the country patients live	Temozolomide is recommended for patients with performance status of 0.
• Brain Tumour Charity • Patient	If the treatments are not recommended patients will have to fund treatment privately creating inequity	Temozolomide is recommended for patients with performance status of 0. NICE is directed by the Secretary of State for Health and the Welsh Assembly Government to make recommendations to the NHS in England and Wales.

Comment from	Nature of comment	Response
• IBTA	The introduction of a risk-sharing scheme similar to that launched for disease modifying drug therapies for MS would require careful examination if such a scheme was considered for these treatments.	Comments noted

12. Evidence relating to children with high-grade glioma

Comment from	Nature of comment	Response
• British Neuro-oncology Society	Childhood brain tumours should not be considered alongside gliomas in adults as they differ in site, histological type and molecular tumour genetics	Following consideration of all the available evidence, including testimonies from the clinical experts, the Committee considered that the issues outlined in the FAD would also apply to children (see FAD section 4.3.28).

13. Future research

Comment from	Nature of comment	Response
• British Neuro-oncology Society • Ali's Dream, • Way Ahead • Ali's Dream • Charlie's Challenge	The guidance will prevent future research – The control arm will be limited to outdated methods. – Funds for trials will not be made available – The UK would have to pull out of ongoing trials	Temozolomide is recommended for patients with performance status of 0. The guidance does not prevent the use of the technologies in clinical trials.
NHS Professional	Further research into relating to MGMT status is required.	Comments noted.

Comment from	Nature of comment	Response
• Chairperson of charity (parent of child who died from a glioma) • Patient • SDRT Astro Fund	Further research into all aspects of malignant glioma is needed. This disease area receives little funding. Further research into low grade glioma is needed. This disease area is seen as lower priority. Further research is welcomed but should be acted upon quickly.	Comments noted.
• EORTC Brain Tumour Group, • NHS Professional • NHS Professional (4 comments) • NHS Professional (3 comments) • NHS Professionals (2 comments) • NHS Professional • Nottingham, Swansea and Cardiff neuro-oncology MDTs, • NHS Professionals (2 comments) • NHS Professional • NHS Professional	The research recommendations are inappropriate – because an MRC trial of PCV as adjuvant treatment for astrocytoma demonstrated no increase in survival. – PCV is not effective – Because ethics approval would not be granted – Because quality of life data for temozolomide exist – Another large trial of temozolomide would not be conducted – A well designed trial of temozolomide has already been conducted (the EORTC trial) – Subgroup analyses for with respect to MGMT status have already been conducted for temozolomide – Long term data from the EORTC trial of temozolomide are available	The research recommendations have been amended (see FAD section 5). Temozolomide is recommended for patients with performance status of 0.

14. The proposed review date for the appraisal

Comment from	Nature of comment	Response
• NHS Professional • (2 comments), • Ali's Dream • Charlie's Challenge, • Brain Tumour Charity, • Patient, • Way Ahead • SDRT Astro Fund	2009 is too late for a review.	The review date has been set according to the standard processes. See Section 5 of the Guide to Technology Appraisal Process available from URL http://www.nice.org.uk/page.aspx?o=201972 If significant new evidence becomes available in the interim, consultees can request an early review.

15. The guidance in relation to other technologies

Comment from	Nature of comment	Response
• NHS Professionals (2 comments)	Consideration of cost effectiveness was not required for governmental approval of Herceptin. The Secretary of State for Health has approved Herceptin before NICE has assessed it, even when it hasn't received a license.	An appraisal of trastuzumab (Herceptin) for the treatment of early stage breast cancer is ongoing (the expected date of publication is July 2006, providing the drug receives a licence from the European licensing authority).
• NHS Professional	The cost of temozolomide is similar to many other expensive new agents.	The Appraisal Committee considered the evidence relating to the clinical and cost effectiveness of temozolomide.

Comment from	Nature of comment	Response
• IBTA	If NICE rejects these treatments for brain cancer, it will turn its back on a number of other new treatments (e.g. Gleevec, Cintredekin Besudotox, Avastin, Tarceva, Tykerb, Iressa and Enzastaurin).	NICE has issued guidance on the use of imatinib (Glivec) for the treatment of chronic myeloid leukaemia and gastro-intestinal stromal tumours– see Technology Appraisal Guidance Nos. 70 and 86. NICE guidance on the use of erlotinib (Tarceva) for the treatment of non-small cell lung cancer and bevacizumab (Avastin) for the treatment of advanced colorectal cancer are currently in development. An appraisal of gefitinib (Iressa) for the treatment of non-small cell lung cancer has been suspended pending regulatory approval. Further details of these appraisals are available from the NICE website (www.nice.org.uk).