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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

ERC1671 for treating progressed or recurrent grade IV glioma (glioblastoma or gliosarcoma)

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of ERC1671 within its marketing authorisation for treating grade IV glioma (glioblastoma or gliosarcoma) in adults with disease that has progressed or recurred following treatment with radiotherapy and temozolomide.

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. In the NHS gliomas are graded according to the most recent World Health Organisation (WHO) categories which take account of likely growth rate, from grade I (slowest growing) to grade IV (fastest growing). Glioblastoma is a diagnostic term that is used synonymously with grade IV glioma. About 90% of glioblastomas are detected as primary tumours. The remaining approximately 10% are described as secondary tumours, having transformed from lower grade gliomas to become malignant. The types of glioma are further identified by the cells they develop from (astrocytoma, ependymoma and oligodendroglioma) and increasingly, by molecular genetics such as isocitrate dehydrogenase (IDH) mutation status and 1p/19q codeletions. Gliosarcoma is a type of IDH-wildtype glioblastoma.

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.

In 2015, about 2,500 people were diagnosed with glioblastoma in England[1]. The average age of diagnosis is 55 years[2]. 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[3].

Glioblastoma is usually treated by surgical resection if possible, which may achieve either complete or partial resection of the tumour, although complete resection is rare. Treatment decisions take into account Karnofsky performance status, time from last treatment and tumour molecular markers, for example, MGMT methylation.

For people with newly diagnosed glioblastoma, following surgery or if surgery is not possible, NICE's guideline for brain tumours (primary) and brain

metastasis in adults recommends radiotherapy with temozolomide, temozolomide alone, radiotherapy alone, hypofractionated radiotherapy or best supportive care alone.

For people with recurrent glioblastoma, NICE's guideline for brain tumours (primary) and brain metastasis in adults recommends that the following treatment options are considered:

- temozolomide in line with NICE technology appraisal guidance 23
- procarbazine, lomustine and vincristine (PCV) or single agent lomustine as an alternative to temozolomide
- further surgery and radiotherapy for people with focally recurrent high-grade glioma
- best supportive care.

The technology

ERC1671 (SITOIGANAP, Epitopoietic Research Corporation) is an immunotherapy that contains a combination of autologous tumour cells and allogeneic tumour cells (generated from the glioma tumour tissues of three different donor cancer patients), and the lysates of all of these cells. It works by stimulating the patient's immune system to recognise and reject cancer cells, which may lead to their destruction. An operation is required to obtain the autologous tumour cells. ERC1671 is delivered by intradermal injection.

ERC1671 does not currently have a marketing authorisation in the UK for patients with progressed or recurrent glioblastoma. It is being studied in a clinical trial in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), cyclophosphamide and bevacizumab in adults with recurrent glioblastoma who have not previously received treatment with bevacizumab.

Intervention(s)	ERC1671
Population(s)	Adults with grade IV glioma (glioblastoma or gliosarcoma) that has progressed or recurred following treatment with radiotherapy and temozolomide

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Comparators	The following alone or in combination: • procarbazine, lomustine and vincristine (PCV) • lomustine • temozolomide • radiotherapy • surgery with or without carmustine implants • best supportive care
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 all direct health effects, whether for patients or, when relevant, carers should be considered 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) (2016). NICE Technology Appraisal 23. Review date to be confirmed

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	Related Guidelines: Brain tumours (primary) and brain metastases in adults (2018). NICE guideline 99. Review date to be confirmed Related Interventional Procedures: Photodynamic therapy for brain tumours (2009). NICE interventional procedures guidance 290 Related NICE Pathways: Brain cancer: glioma NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019). Chapter 105: Specialist cancer services (adults) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

References

1. Cancer Research UK Brain, other CNS and intracranial tumours incidence statistics. Accessed July 2019.
2. Patient UK. Gliomas and glioblastoma multiforme. Accessed July 2019.
3. Cancer Research UK Brain, other CNS and intracranial tumours survival statistics. Accessed July 2019.