# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Appraisal

## DCVax-L for treating newly diagnosed glioblastoma

## Draft scope (pre-referral)

### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of DCVax-L for newly diagnosed glioblastoma multiforme.

### 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. There are 4 main types of gliomas, named according to the cells they develop from: astrocytoma, ependymoma, oligliodendroglioma, and mixed tumours. Gliomas are graded according to their likely growth rate, from grade 1 (slowest growing) to grade 4 (fastest growing). Grade 1 or 2 tumours are considered 'low-grade' and usually classed as benign or non-cancerous. Grade 3 and 4 tumours, known as 'high-grade', are malignant and have a worse prognosis. Glioblastoma multiforme, a grade 4 glioma, is the most common type of astrocytoma and is the most aggressive type of brain tumour. Glioblastomas can be classed according how they present. High grade (grade 4) is more common and accounts for 90% of all GBMs whereas secondary GMBs develop from lower grade astrocytomas.

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. Scales of performance status, such as the World Health Organisation (WHO) performance status, can be used to categorise functional ability with glioblastoma.

In 2014, approximately 2600 people were diagnosed with glioblastoma multiforme in England and Wales, with people aged 65 and over accounting for roughly 46% of new cases[1]. 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[2].

Treatment usually consists of surgical resection if possible, which may achieve either complete or partial resection of the tumour, although complete resection is rare. After surgery, radiotherapy with or without chemotherapy is used. If the size or position of the tumour mean surgery is not possible without damaging surrounding tissue, radiotherapy and/or chemotherapy is offered. NICE technology appraisal guidance 121 recommends temozolomide as an option for treating newly diagnosed glioblastoma multiforme in people with a WHO performance status of 0 or 1. It also recommends carmustine implants

for newly diagnosed high-grade glioma, but only for people in whom 90% or more of the tumour has been resected. Both temozolomide and carmustine implants are licensed in combination with radiotherapy. Nitrosourea-based chemotherapy, such as a combination of procarbazine, lomustine and vincristine (PCV), is also routinely used in the UK for newly diagnosed glioblastomas.

### The technology

DCVax-L (Northwest Biotherapeutics) is a cancer vaccine that stimulates the immune system and enables patients T-cells and antibodies to recognise and destroy the tumour. The vaccine is derived from the patient's own tumour tissue (which provides the antigenic component of the vaccine) and precursor dendritic cells which are cultured into mature dendritic cells. DCVax-L is administered by intra-dermal injection.

DCVax-L does not currently have a UK marketing authorisation for treating glioblastoma. It is being studied in a placebo-controlled phase III clinical trial in adults with newly diagnosed glioblastoma who have had surgical resection followed by radiotherapy and temozolomide. It is also being studied in phase I/II clinical trials for treating people with both low and high grade gliomas.

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| **Intervention(s)** | DCVax-L treatment |
| **Population(s)** | People with newly diagnosed glioblastoma who have had surgical resection and radiotherapy and are currently receiving temozolomide |
| **Comparators** | Standard of care without DCVax-L |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rate<br>• adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective. |

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| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation. |
| **Related NICE recommendations and NICE Pathways** | **Related Technology Appraisals:**<br>'Carmustine implants and temozolomide for the treatment of newly diagnosed high-grade glioma' (2007) NICE technology appraisal 121. Added to static list March 2016.<br>**Related guidelines**:<br>'Improving outcomes for people with brain and other central nervous system tumours' (2006). Cancer service guideline 10. Review date to be confirmed.<br>*Guideline in development*<br>Primary brain tumours and cerebral metastases. NICE clinical guideline. Publication expected July 2018.<br>**Related Interventional Procedures:**<br>'Photodynamic therapy for brain tumours' (2009) NICE interventional procedures guidance 290.<br>**Related NICE Pathways**:<br>Brain cancers (2016) NICE Pathway http://pathways.nice.org.uk/pathways/brain-cancers |
| **Related National Policy** | National Service Frameworks: Cancer<br>NHS England (2013) Cancer: Brain and Central Nervous System Service Specifications<br>Department of Health (2014) NHS outcomes framework 2015-2016<br>Department of Health (2011) Improving outcomes: a strategy for cancer<br>Department of Health (2009) Cancer commissioning guidance<br>Department of Health (2007) Cancer reform strategy |

**Questions for consultation**

Which treatments are considered to be established clinical practice in the NHS for newly diagnosed glioblastoma?

Are there alternative treatment strategies that should be considered as comparators to DCVax-L treatment?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom DCVax-L is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider DCVax-L will fit into the existing NICE pathway, Brain cancers?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which DCVax-L will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider DCVax-L to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of DCVax-L can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

## References

1. Cancer Research UK 'Brain, other CNS and intracranial tumours incidence statistics'. Accessed December 2016.

2. Cancer Research UK 'Brain, other CNS and intracranial tumours survival statistics'. Accessed December 2016.

3. Stupp et al (2005); N Engl J Med;352(10):987-96