NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Omburtamab I-131 for treating relapsed neuroblastoma

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of omburtamab I-131 within its marketing authorisation for treating relapsed neuroblastoma with central nervous system or leptomeningeal metastasis in children and young people.

Background

Neuroblastoma is a solid cancer of embryonic nerve cells called neural crest cells. It commonly occurs in the adrenal glands or in the nerve tissue of the sympathetic nervous system. Neuroblastoma usually occurs in young children and rarely in adolescents, with most children diagnosed by 5 years of age.[1]

Neuroblastoma most commonly occurs in one of the adrenal glands above the kidneys, or in the nerve tissue that runs alongside the spinal cord in the neck, chest, abdomen or pelvis. It can spread to other sites, including the bone marrow, bone, lymph nodes, liver, skin and central nervous system.[2]

The initial symptoms are usually vague, such as tiredness, fever and loss of appetite. Specific symptoms depend on the location of the tumour. Because neuroblastoma usually develops in the abdomen, the most common symptom is an abdominal lump and children may also experience constipation or difficulty in passing urine. The tumour may affect the chest or neck region and may cause breathlessness and difficulty in swallowing or a visible lump in the neck. Occasionally it can press on the spinal cord causing numbness, weakness and loss of movement in the lower part of the body. Neuroblastoma often spreads to other parts of the body before any symptoms are apparent; approximately half of all neuroblastoma patients have metastatic disease when they are diagnosed.[3] Disease can also relapse after initial treatment, with up to up to 60% of children with high-risk neuroblastoma experiencing relapse with current therapies.[4]

Relapse to the central nervous system is rare, with approximately 5% of people with stage 4 neuroblastoma experiencing relapse to the central nervous system including relapse to the leptomeninges (the leptomeninges are the two innermost layers of the membranes that envelop the brain and spinal cord). The spread of neuroblastoma to the central nervous system or leptomeninges is associated with significant mortality.[3]

Based on various prognostic factors and international staging systems children are classified into different risk groups. High-risk neuroblastoma can be characterised by age (>18 months), metastatic disease, and amplification or overexpression of the type of gene involved.

Around 100 children are diagnosed with neuroblastoma each year in the UK.[5] The estimated risk for central nervous system relapse following treatment for stage 4 neuroblastoma (when cancer has spread to distant sites) is approximately 8% at 3 years.[6]

Treatment options are limited for relapsed neuroblastoma with central nervous system or leptomeningeal metastasis. Treatment options include neurosurgical resection of central nervous system disease, craniospinal radiotherapy and temozolomide with or without irinotecan.[6] Treatment with myeloablative therapy (busulfan/melphalan) and systemic immunotherapy with anti-GD2 monoclonal antibodies (dintuximab, TA538) plus oral cis-retinoic acid may follow if suitable.

The technology

Omburtamab I-131 (Omblastys, Y-mAb therapeutics) is an immunoglobulin G1 (IgG1) monoclonal antibody with an iodine (131I) radiolabel. It binds to cancer cells, allowing the iodine radiolabel to damage these cells. It is administered into the fluid that surrounds the brain and spinal cord by intracerebroventricular injection via a specialist access device.

It currently does not have a marketing authorisation in the UK for treating neuroblastoma. It has been studied in a single arm clinical trial in children who had neuroblastoma with relapse in the central nervous system or in the leptomeninges.

Intervention(s)	Omburtamab I-131
Population(s)	Children and young people with histologically confirmed diagnosis of neuroblastoma with relapse in the central nervous system or in the leptomeninges
Comparators	Established clinical management without omburtamab I-131.
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • adverse effects of treatment • health-related quality of life (for patients and carers).
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. Consideration should be given to alternative standardised and validated preference-based measures of health-related quality of life that have been designed specifically for use in children. 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. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.

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: Dinutuximab beta for treating neuroblastoma (2018) NICE Technology appraisal guidance 538 Appraisals in development (including suspended appraisals) Naxitamab with GM-CSF for treating relapsed or refractory high-risk neuroblastoma. Proposed NICE technology appraisal [ID 3769]. Publication date to be confirmed. Dinutuximab for treating high risk neuroblastoma. NICE technology appraisal [ID799]. Suspended. Related Guidelines: 'Improving outcomes in children and young people with cancer' NICE guideline (2005) Review proposal date: TBC Related Quality Standards: Children and young people with cancer (2014) Quality Standard No 55. Review proposal date TBC http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp Related NICE Pathways: Neurological conditions (2019) NICE pathway http://pathways.nice.org.uk/
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Specialist cancer services for children and young people, Chapter 106. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1,2 and 4 https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

What are the expected number of patients who would be eligible for omburtamab I-131 in the treatment of neuroblastoma with relapse in the central nervous system /leptomeninges per year?

How are people with neuroblastoma with relapse in the central nervous system or in the leptomeninges identified in NHS clinical practice?

Which method of administration for omburtamab I-131 would be used in NHS clinical practice? Is this generalisable to the method of administration used in the clinical trial?

Have any relevant comparators for omburtamab I-131 not been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for neuroblastoma with relapse in the central nervous system or in the leptomeninges?

How should established clinical management without omburtamab I-131 be defined?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom omburtamab I-131 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider omburtamab I-131 will fit into the existing NICE pathway? (See link to neurological conditions (2019) pathway)

Will treatment with omburtamab I-131 for neuroblastoma with CNS or leptomeninges relapse be delivered in highly specialised centres?

Does the technology have the potential for life-long use?

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 omburtamab I-131 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 omburtamab I-131 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 omburtamab I-131 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

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. BMJ (2017) Neuroblastoma. [online accessed June 2021]

2. NHS (2016) Neuroblastoma. [online accessed June 2021]

3. Matthay KK, et.al. (2003) Central nervous system metastases in neuroblastoma. *Cancer*. 98(1):155-65.

4. Morgenstern, DA et.al. (2015) Options for the Treatment of Patients with Relapsed/Progressive High-Risk Neuroblastoma.

5. Neuroblastoma UK. About Neuroblastoma. [online accessed June 2021]

6. Children's Cancer and Leukaemia Group (2015): Neuroblastoma Special Interest Group. *Options for the Treatment of Patients with Relapsed/Progressive High-Risk Neuroblastoma*. [online accessed June 2021]