NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Dinutuximab for treating high-risk neuroblastoma

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of dinutuximab within its marketing authorisation for treating high-risk neuroblastoma following myeloablative therapy and autologous stem cell transplant.

Background

Neuroblastoma is a cancer of embryonic nerve cells called neural crest cells. It commonly occurs either in the adrenal glands located above each kidney or nerve tissue that runs alongside the spinal cord, in the neck, chest, abdomen or pelvis. It usually affects children under the age of 5 years.

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 a lump in the tummy 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 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 therefore more than half of all patients present with metastases. It commonly spreads to the bones and can cause pain and difficulty in walking. If it spreads to bone marrow it may cause anaemia, bruising, bleeding and infections. It may also spread to the liver or the skin causing small blue-coloured lumps.

Based on various prognostic factors and International staging systems children are classified into different risk groups. High-risk neuroblastoma can be characterised by age (>1 year), disease which has spread, MYCN oncogene amplification, and unfavourable histopathologic findings.

Around 90 children are diagnosed with neuroblastoma each year in the UK. Approximately 40% of children with neuroblastoma are classified as high-risk. High-risk neuroblastoma is associated with a 5-year survival rate of 30-50%.

Treatment for high-risk disease is generally divided into three phases; induction, consolidation and maintenance. Children in the high-risk category are initially treated with multi-agent chemotherapy, surgery and radiotherapy, followed by consolidation therapy with high-dose chemotherapy (which may cause severe or complete depletion of bone marrow cells, also known as myeloablative therapy) and autologous stem cell transplant. In the

maintenance phase children are treated with isotretinoin for minimal residual disease.

The technology

Dinutuximab (Unituxin, United Therapeutics) is a chimeric monoclonal antibody that targets GD2, a glycolipid overexpressed in certain tumours such as neuroblastoma. It induces antibody-dependent cell-mediated cytotoxicity and complement-dependent cytotoxicity against tumour cells. It is administered intravenously.

Dinutuximab does not currently have a marketing authorisation in the UK for treating neuroblastoma. It has been studied in clinical trials in combination with isotretinoin, aldesleukin (interleukin -2), and sargramostim (granulocyte macrophage colony-stimulating factor) compared with isotretinoin in people less than 30 years of age with high-risk neuroblastoma who had received myeloablative therapy and autologous stem cell transplant.

Intervention(s)	Dinutuximab in combination with isotretinoin, aldesleukin (interleukin -2), and sargramostim (granulocyte macrophage colony-stimulating factor)
Population(s)	People with high-risk neuroblastoma who have received myeloablative therapy and autologous stem cell transplant
Comparators	Established clinical management without dinutuximab in combination with isotretinoin, aldesleukin (interleukin -2), and sargramostim (granulocyte macrophage colony-stimulating factor) (such as isotretinoin)
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • response rate • 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 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 Guidelines: Cancer Service Guideline, 'Improving outcomes in children and young people with cancer', August 2005, Review proposal date: June 2016 Related Quality Standards: Quality Standard No. 55, February 2014, 'Children and young people with cancer'. Review proposal date TBC http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp
Related National Policy	Department of Health (2013): NHS Outcomes Framework 2014–2015 Specialist cancer services for children and young people, Chapter 106, 'Manual for prescribed services'. November 2012. http://www.england.nhs.uk/wp-content/uploads/2012/12/pss-manual.pdf

Questions for consultation

How is high-risk neuroblastoma identified in the clinical practice?

Which treatments are considered to be established clinical practice in the NHS for maintenance therapy in people with high-risk neuroblastoma who have received myeloablative therapy and autologous stem cell transplant?

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

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 dinutuximab 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 dinutuximab 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 dinutuximab 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)