NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Dinutuximab for treating high-risk neuroblastoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of dinutuximab in combination with sargramostim, aldesleukin and isotretinoin 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 in any nerve tissue of the sympathetic nervous system, which runs alongside the spinal cord, from the neck through the chest and the abdomen to the pelvis. Neuroblastoma 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 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 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 (>18 months), metastatic disease, and MYCN oncogene amplification and overexpression. However, ‘high risk’ is not rigidly defined in clinical practice because the definition tends to be driven by the criteria used for including participants in clinical trials for high-risk neuroblastoma.

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 3 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. Radiotherapy may also be given after stem cell transplant. In the maintenance phase, standard of care is to treat the child for minimal residual disease with an immunotherapy-based regimen as part of a clinical trial. Children who are ineligible to participate in a trial, or who participate but subsequently withdraw, are normally treated with isotretinoin alone.

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 (also known as interleukin -2, as referred to in clinical trials), and sargramostim (also known as granulocyte macrophage colony-stimulating factor, as referred to in clinical trials) 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 sargramostim, aldesleukin, and isotretinoin
Population(s)	People with high-risk neuroblastoma who have received myeloablative therapy and autologous stem cell transplant
Comparators	Isotretinoin
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • 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. 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.
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. If the evidence allows the following subgroups will be considered. These include: • people with relapsed disease • people with refractory disease. If no evidence is available for these subgroups, this should be stated, and the Appraisal Committee would then decide if the available evidence could be extrapolated to people with relapsed or refractory disease.
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