NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

APN311 for treating high-risk neuroblastoma

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of APN311 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 in the adrenal glands or in nerve tissue of the sympathetic nervous system. 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; approximately half of all neuroblastoma patients have metastatic disease. 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.

Around 90 children are diagnosed with neuroblastoma each year in the UK.[1] Approximately 40% of children with neuroblastoma are classified as high-risk.[2] High-risk neuroblastoma is associated with a 5-year survival rate of 40-50%.[3]

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 isotretinoin.[2]

The technology

APN311 (brand name unknown, Apeiron) is a chimeric monoclonal antibody produced in the Chinese hamster ovary cell line that targets GD2, a glycolipid overexpressed in certain tumours such as neuroblastoma. Once the antibody binds to the neuroblastoma cells, the body mounts an immune response against those cells triggering their destruction. It is administered intravenously.

APN311 does not currently have a marketing authorisation in UK for treating neuroblastoma. It has been studied in clinical trials as a single agent, as well as in combination with isotretinoin with or without aldesleukin (also known as interleukin-2) in people between the ages of 1 month and 21 years with high-risk neuroblastoma who had received myeloablative therapy and autologous stem cell transplant.

Intervention(s)	APN311
Population(s)	People with high-risk neuroblastoma who have had myeloablative therapy and autologous stem cell transplant
Comparators	• Isotretinoin • Dinutuximab (subject to NICE guidance)
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 Technology Appraisals: Appraisals in development (including suspended appraisals) 'Dinutuximab for treating high risk neuroblastoma' NICE technology appraisal guidance [ID799]. Publication date September 2016. Related Guidelines: Cancer Service Guideline, 'Improving outcomes in children and young people with cancer', August 2005, Review proposal date: June 2018 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 specialised services 2016/17'. May 2016. http://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf

References

[1] Lennox Children's Cancer Fund UK (2015) Neuroblastoma. http://www.lennoxccf.org.uk/neuroblastoma.html (accessed October 2015)

[2] Kahan S, Teitelbaum J et al. (2007) In a Page: Pediatrics. 8:238.

[3] American Cancer Society (2015) Neuroblastoma: Early detection, diagnosis and staging topics – survival rates for neuroblastoma based on risk groups. http://www.cancer.org/cancer/neuroblastoma/detailedguide/neuroblastoma-survival-rates (accessed October 2015)