NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Eflornithine maintenance treatment after first-line therapy for high-risk neuroblastoma

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of eflornithine within its marketing authorisation for maintenance treatment of high-risk neuroblastoma that is in remission after first-line therapy.

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. People are classified as having high-risk when they are older than 18 months of age, have metastatic disease and have MYCN oncogene amplification and overexpression. [1,2]

The initial symptoms of neuroblastoma 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.

Neuroblastoma usually affects children under the age of 5 years. Approximately 90 children are diagnosed with neuroblastoma in the UK each year. Of these, 40% may be considered high-risk. High-risk neuroblastoma is associated with a 5-year survival rate of approximately 30-50% [3,4].

Treatment for high-risk disease is generally divided into 3 phases; induction, consolidation and maintenance. During induction and consolidation phases, people in the high-risk category are initially treated with multi-agent chemotherapy, surgery and radiotherapy, followed by 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. Following full treatment, the maintenance phase aims to stop the cancer from coming back. Standard of care in the maintenance phase is to treat for minimal residual disease with an immunotherapy-based regimen as part of a clinical trial. People who are ineligible to participate in a trial, or who participate but subsequently withdraw, are normally treated with isotretinoin alone.

The technology

Eflornithine (as eflornithine hydrochloride, brand name unknown, Norgine) does not currently have a marketing authorisation in the UK for neuroblastoma. It is administered orally. It has been studied in single arm clinical trials in children, young people and adults with high-risk neuroblastoma that is either in remission or newly diagnosed.

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Intervention(s)	Eflornithine
Population(s)	People with high-risk neuroblastoma that is in remission after first-line therapy
Comparators	Established clinical management without eflornithine
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. 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	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 Omburtamab for treating relapsed neuroblastoma. NICE technology appraisal guidance [ID1664]. Publication date to be confirmed. Dinutuximab for treating high-risk neuroblastoma. NICE technology appraisal guidance [ID799]. Suspended Related Guidelines: 'Improving outcomes in children and young people with

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	cancer' NICE guideline (2005) Review proposal date: TBC 'Suspected cancer: recognition and referral'. NICE guideline (2015, updated 2021) Related Quality Standards: 'Cancer services for children and young people' (2014). NICE quality standard 55.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Specialist cancer services for adults, Chapter 105. 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

Which treatments are considered to be established clinical practice in the NHS for the induction and consolidation stages of treatment for high-risk neuroblastoma?

Which treatments are considered to be established clinical practice in the NHS for maintenance treatment of high-risk neuroblastoma?

Is isotretinoin considered established clinical practice in the NHS for maintenance treatment of high-risk neuroblastoma?

Are immunotherapy-based regimens considered established clinical practice in the NHS for maintenance treatment of high-risk neuroblastoma? If so, which specific immunotherapy regimens are used?

Is eflornithine used in combination with other therapies for maintenance treatment of high-risk neuroblastoma?

Have any relevant comparators for eflornithine not been included in the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom eflornithine 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:

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- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which eflornithine 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.

Where do you consider insert the technology will fit into the existing care pathway for the disease?

Would the technology be a candidate for managed access?

Do you consider eflornithine 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 eflornithine 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 committee to take account of these benefits.

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. Evageliou, NF et.al. (2016) Polyamine Antagonist Therapies Inhibit Neuroblastoma Initiation and Progression. *Clinical Cancer Research*. 22(17):4391

2. Bassiri H et.al. (2015) Translational development of difluoromethylornithine (DFMO) for the treatment of neuroblastoma. *Translational pediatrics*. 4(3):226-38

3. NHS Digital. Hospital Admitted Patient Care Activity 2020-21. [online accessed February 2022]

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4. Office for National Statistics. Cancer registration statistics, England. [online accessed February 2022]

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