NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Health Technology Appraisal

Erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of erythrocyte encapsulated asparaginase within its marketing authorisation for treating acute lymphoblastic leukaemia.

Background

Acute lymphoblastic leukaemia (ALL) is a cancer of lymphocyte-producing cells. Lymphocytes are white blood cells that are vital for the body's immune system. In ALL there is an excess production of immature lymphocyte-precursor cells, called lymphoblasts or blast cells, in the bone marrow. This affects the production of normal blood cells and there is a reduction in the numbers of red cells, white cells and platelets in the blood.

ALL is most common in children, adolescent and young adults, with 65% of cases diagnosed in people aged under 25 years. A second increase in incidence is observed in people aged over 60 years. In England, 536 people were diagnosed with ALL in 2011 and 202 people died from ALL in 2012.

The aim of treatment in ALL is to achieve a cure. Treatment can take up to 3 years to complete and is generally divided into 3 phases; induction phase, consolidation and maintenance. The choice of treatment can depend on the phase. There is currently no NICE guidance for treating ALL. During induction, newly diagnosed ALL is generally treated with chemotherapy combinations including prednisone, vincristine, anthracycline and asparaginase. During the consolidation phase, intensified chemotherapy is used, which may include high dose methotrexate with mercaptopurine, high dose asparaginase, or a repeat of the induction therapy. During the maintenance phase low dose chemotherapy is used, which typically consists of weekly methotrexate and daily mercaptopurine for an extended period of time to prevent relapse. Relapse has a very poor prognosis, therefore after relapse, ALL is typically treated in a clinical trial setting.

The technology

Erythrocyte encapsulated asparaginase (GRASPA, Orphan Europe) is an encapsulated L-asparaginase. Asparaginase is an enzyme that breaks down asparagine (an amino acid) leading to cell death. Erythrocyte encapsulated asparaginase is administered by intravenous injection.

Erythrocyte encapsulated asparaginase does not currently have a marketing authorisation in the UK for treating acute lymphoblastic leukaemia. It is being studied in clinical trials compared with L-asparaginase, both in combination with multi-agent chemotherapy regimens in people with relapsed acute lymphoblastic leukemia (ALL), with or without known hypersensitivity to L-asparaginase.

Intervention(s)	Erythrocyte encapsulated asparaginase plus established clinical management without asparaginase
Population(s)	People with previously treated acute lymphoblastic leukaemia
Comparators	Established clinical management without erythrocyte encapsulated asparaginase
Outcomes	The outcome measures to be considered include: • treatment response rates (including cytogenetic and haematologic responses) • time to and duration of response • progression-free survival • overall 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.
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	Related Guidelines: 'Improving outcomes in children and young people with

Pathways	cancer' (August 2005) Cancer Service Guideline, Review proposal date: June 2016 Referral for suspected cancer (June 2005) Cancer Service Guideline. Review proposal date: TBC 'Improving outcomes in haematological cancers' (October 2003) Cancer Service Guideline. Review proposal date: September 2019 Related Quality Standards: 'Children and young people with cancer' (February 2014) NICE quality standard 55 Review date TBC Related NICE Pathways: Blood and bone marrow cancers' (June 2015) NICE pathway http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	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 Blood and marrow transplantation services (all ages), Chapter 29, Manual for Prescribed Specialised Services 2013/14 http://www.england.nhs.uk/wp-content/uploads/2014/01/pss-manual.pdf Department of Health, NHS Outcomes Framework 2014-2015, Nov 2013. Domains 1 and 2 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/256456/NHS_outcomes.pdf

Questions for consultation

How many people with ALL would be expected to be treated with erythrocyte encapsulated asparaginase in England?

Have all relevant comparators for erythrocyte encapsulated asparaginase been included in the scope? How would established clinical management without erythrocyte encapsulated asparaginase be defined?

Would erythrocyte encapsulated asparaginase be expected to be used in combination with specific chemotherapy drugs or regimens? If so, which chemotherapy combinations should be included in this appraisal?

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

Where do you consider erythrocyte encapsulated asparaginase will fit into the existing NICE pathway, Blood and bone marrow cancers?

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 erythrocyte encapsulated asparaginase 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 erythrocyte encapsulated asparaginase 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 erythrocyte encapsulated asparaginase 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)