NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Health Technology Appraisal

Erythrocyte encapsulated asparaginase for treating acute lymphoblastic leukaemia

Final scope

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, 820 people were diagnosed with ALL in 2013 and 240 people died from ALL in 2014[1].

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. In England treatment for ALL is governed by the UKALL2011 and UKALL2014 protocols which state that pegylated asparaginase treatment will be given as part of 1st line ALL treatment, and in cases of hypersensitivity reactions, a switch to erwinia-derived asparaginase will be necessary. 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. Although, there is currently no standard of care for people with relapsed or refractory ALL, possible treatment options may include a combination chemotherapy based regimen of fludarabine, cytarabine and granulocyte colony-stimulating factor (FLAG), followed by stem cell transplantation where

a suitable donor can be found or best supportive care (including palliative care).

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 acute lymphoblastic leukaemia who are intolerant or allergic to asparaginase or have disease that has relapsed on asparaginase treatment.
Comparators	• E.coli asparaginase • Pegylated asparaginase • Erwina-derived asparaginase
Outcomes	The outcome measures to be considered include: • time to and duration of response • event-free survival • overall survival • rate of allergic reactions • therapeutic drug monitoring (asparaginase levels) • 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 Technology Appraisals in development: Leukaemia (acute lymphoblastic) – pegaspargase. NICE technology appraisals guidance. ID863. Publication expected September 2016. Related Guidelines: 'Improving outcomes in children and young people with cancer' (August 2005) Cancer Service Guideline, Review decision: Will be updated in July 2018 Cancer services for children and young people (June 2015) NICE 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	B05. Children and Young Adult Cancer Services. 2015 https://www.england.nhs.uk/wp-

	content/uploads/2013/09/b17.pdf https://www.england.nhs.uk/wp-content/uploads/2013/06/e04-paedi-oncol.pdf F01. Blood and Marrow Transplantation 2013. https://www.england.nhs.uk/wp-content/uploads/2013/06/b04-haema-adult.pdf NHS England: NHS Outcomes Framework – 5 domains resources https://www.england.nhs.uk/resources/resources-for-ccgs/out-frwrk/

References

1. Cancer Research UK (2014) Acute lymphoblastic leukaemia (ALL) statistics, Accessed August 2016