NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Pegaspargase for treating acute lymphoblastic leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of pegaspargase 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.[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, 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 L-asparaginase. During the consolidation phase, intensified chemotherapy is used, which may include high dose methotrexate with mercaptopurine, L-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.

The technology

Pegaspargase (Oncaspar, Baxalta) is a polyethylene glycol conjugate of *Escherichia coli* derived L-asparaginase. L- asparaginase is an enzyme that hydrolyses asparagine (an amino acid) leading to cell death. The polyethylene glycol conjugation of L-asparaginase is expected to extend its duration of activity, increase bioavailability and improve tolerability. It is given intramuscularly or intravenously.

Pegaspargase does not currently have a marketing authorisation in the UK for ALL. It has received a a positive opinion from the Committee for Medicinal Products for Human Use (CHMP) ‘as a component of antineoplastic combination therapy in acute lymphoblastic leukaemia (ALL) in paediatric patients from birth to 18 years, and adult patients'.

Intervention(s)	Pegaspargase plus standard chemotherapy
Population(s)	People with acute lymphoblastic leukaemia
Comparators	Non-pegylated forms of: • *Escherichia coli* derived L-asparaginase plus standard chemotherapy • *Erwinia chrysanthemi* derived L-asparaginase (crisantaspase) plus standard chemotherapy
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • treatment response rates • event-free survival • asparaginase activity • 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	Related Guidelines: ‘Improving outcomes in children and young people with

and NICE Pathways	cancer' (August 2005) Cancer Service Guideline, Review proposal date: June 2016 '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

References

Cancer Research UK (2014) Acute lymphoblastic leukaemia (ALL) statistics, Accessed December 2015