NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Blinatumomab with chemotherapy for consolidation treatment of Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with no measurable residual disease ID6405

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of blinatumomab with chemotherapy within its marketing authorisation for consolidation treatment of Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with no measurable residual disease.

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 number of red cells, white cells and platelets in the blood. ALL can be classified into 3 groups based on immunophenotyping: B-precursor ALL (also known as precursor-B-cell ALL); mature B-cell ALL and T-cell ALL. In adults, around 75-80% of ALL cases are classified as B-precursor ALL.[1] B-precursor ALL is characterised by the presence of cytoplasmic immunoglobulins and CD10, CD19, CD22 and CD79a expression. A specific chromosomal abnormality known as the 'Philadelphia chromosome' is present in 20 to 30% of adults with ALL.[2]

ALL is most common in children, adolescents and young adults, with around 62% of cases diagnosed in people aged under 25.[3] A second increase in incidence is observed in people aged over 60 (around 16% of cases).[3] It is also more common in males (around 6 out of 10 cases) than females.[3] In the UK, around 350 cases of ALL are diagnosed in adults each year.[4]

The aim of treatment in ALL is to achieve a cure. Treatment for newly diagnosed ALL can take up to 3 years to complete and is generally divided into 3 phases: induction, consolidation and maintenance.

During induction, newly diagnosed ALL is generally treated with chemotherapy combinations including prednisolone, vincristine, an anthracycline and asparaginase. Consolidation treatment typically includes intensified chemotherapy, followed by low-dose chemotherapy in the maintenance phase. A tyrosine kinase inhibitor (such as imatinib or dasatinib) would also be offered to people with Philadelphia-chromosome-positive ALL at all phases of treatment (i.e., in addition to induction, consolidation and maintenance therapy). Other treatment options may include stem cell transplantation if a suitable donor can be found, or best supportive care (including palliative care). NICE technology appraisal 589 recommends blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity.

Around 45% of ALL relapses after, or becomes refractory to initial treatment and requires further treatment.[5] There is no universally accepted treatment approach for relapsed or refractory ALL.[6]

The technology

Blinatumomab (Blincyto, Amgen Ltd) with chemotherapy does not currently have a marketing authorisation in the UK for consolidation treatment of Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with no measurable residual disease. It has been studied in a clinical trial compared with chemotherapy in people with breakpoint cluster region (BCR)-c-abl oncogene 1, non-receptor tyrosine kinase (ABL)-negative B cell precursor ALL who are minimal residual disease negative after induction and intensification chemotherapy.

Blinatumomab, as monotherapy, has a marketing authorisation in the UK for:

- "adults with Philadelphia chromosome negative CD19 positive B-precursor ALL in first or second complete remission with minimal residual disease (MRD) greater than or equal to 0.1%",

- "adults with CD19 positive relapsed or refractory B-precursor acute lymphoblastic leukaemia (ALL)".

Intervention(s)	Blinatumomab with chemotherapy
Population(s)	People with Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia with no measurable residual disease
Comparators	Established clinical management without blinatumomab with chemotherapy, including, • Blinatumomab • Chemotherapy (with or without corticosteroids) • Stem cell transplant
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival (including relapse-free and event-free survival) • treatment response rate (including minimal residual disease, haematologic responses and complete remission) • rate of stem cell transplant • 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. The use of blinatumomab with chemotherapy is conditional on minimal residual disease status based on multiparameter flow cytometric (MFC) assessment of residual blasts. The economic modelling should include the costs associated with testing for minimal residual disease status in people with Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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:** Blinatumomab for treating acute lymphoblastic leukaemia in remission with minimal residual disease activity (2019) NICE technology appraisal guidance 589 Blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia (2017) NICE technology appraisal guidance 450 Pegaspargase for treating acute lymphoblastic leukaemia (2016) NICE technology appraisal guidance 408 **Related NICE guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47 **Related quality standards:** Haematological cancers (2017) NICE quality standard 150

Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2023) Manual for prescribed specialist services (2023/2024) Chapters 105 and 106

Questions for consultation

Where do you consider blinatumomab with chemotherapy will fit into the existing care pathway for Philadelphia-chromosome-negative CD19-positive B-precursor acute lymphoblastic leukaemia?

Is it anticapted that blinatumomab with chemotherapy will be used for children?

Have all relevant comparators for blinatumomab with chemotherapy been included in the scope? In particular, is stem cell transplant an appropriate comparator?

Please select from the following, will blinatumomab with chemotherapy be:
A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

Are the outcomes listed in the draft scope for this appraisal appropriate, particularly the rate of stem cell transplant?

Would blinatumomab with chemotherapy be a candidate for managed access?

Do you consider that the use of blinatumomab with chemotherapy can result in any potential 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.

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 blinatumomab with chemotherapy 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Leukaemia Foundation. Acute lymphoblastic leukaemia. Accessed April 2024.

2. Cancer Research UK. Research into acute lymphoblastic leukaemia. Accessed April 2024.

3. Cancer Research UK. Acute lymphoblastic leukaemia (ALL) statistics. Accessed April 2024.

4. Leukaemia Care. Acute Lymphoblastic Leukaemia (ALL). Accessed April 2024

5. Fielding AK, Richards SM, Chopra R et al. (2007) Outcome of 609 adults after relapse of acute lymphoblastic leukemia (ALL); an MRC UKALL12/ECOG 2993 study. Blood 109(3):944-50.

6. BMJ Best Practice. Acute lymphocytic leukaemia. Accessed April 2024.