NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Gemtuzumab ozogamicin for untreated, de novo CD33 positive acute myeloid leukaemia [ID982]

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of gemtuzumab ozogamicin within its marketing authorisation for untreated acute myeloid leukaemia.

Background

Acute myeloid leukaemia is a cancer of the blood and bone marrow. It is characterised by the overproduction of early immature myeloid cells (blasts). Acute myeloid leukaemia is classified into several types. In most types of acute myeloid leukaemia, the cancer cells are immature white blood cells. In acute promyelocytic leukaemia (a subcategory of acute myeloid leukaemia) the abnormal white blood cells are of the neutrophil type and are known as promyelocytes. In other less common types, immature platelets or immature red blood cells form the leukaemia cells. The CD33 antigen is expressed on the blast cells of most types of acute myeloid leukaemia. Anaemia, bleeding problems, serious infections, fatigue, weakness, breathlessness, fever, night sweats, weight loss and bone, joint or muscle pain are common symptoms in acute myeloid leukaemia.

The incidence of acute myeloid leukaemia has increased by 8% in the UK over the last decade. There were 2,590 new diagnoses of acute myeloid leukaemia and 2,127 deaths registered in England in 2014.[1] In the UK in 2012-2014, more than half (55%) of new diagnoses were in people aged 70 and over.[1]

Acute myeloid leukaemia typically develops rapidly and can be fatal unless treated. For people who are fit enough, intensive treatment is available. It is conducted in 2 phases: induction chemotherapy is given to achieve a remission, followed by consolidation therapy which is given to reduce the risk of leukaemia recurring. Drugs that may be used for intensive treatment include amsacrine, cytarabine, daunorubicin, etoposide, fludarabine, idarubicin, mitoxantrone and thioguanine.[2] Fludarabine does not currently have a marketing authorisation in the UK for treating acute myeloid leukaemia. A combination of fludarabine, idarubicin, cytarabine and granulocyte colony stimulating factor (G-CSF) can also be used in 'poor risk' patients classified according to cytogenetic profile or in patients for whom a rapid response is needed. In some circumstances, people may be offered haematopoietic stem cell transplantation.

NICE technology appraisal guidance 218 recommends azacitidine for adults who are not eligible for haematopoietic stem cell transplantation and have acute myeloid leukaemia with 20–30% blasts and multilineage dysplasia, according to the World Health Organization classification. NICE technology appraisal guidance 399 does not recommend azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts in people of 65 years or older who are not eligible for haematopoietic stem cell transplant.

The technology

Gemtuzumab ozogamicin (Mylotarg, Pfizer) is a recombinant humanised monoclonal antibody linked to a cytotoxic agent, calicheamicin. It is administered intravenously.

Gemtuzumab ozogamicin has received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP, European Medicines Agency) for 'patients age 15 years and above with previously untreated, de novo CD33-positive acute myeloid leukaemia (AML), except acute promyelocytic leukaemia (APL)'.

Intervention(s)	Gemtuzumab ozogamicin in combination with daunorubicin and cytarabine
Population(s)	People aged 15 years and older with untreated, de novo CD33-positive acute myeloid leukaemia (excluding acute promyelocytic leukaemia)
Comparators	Established clinical management without gemtuzumab ozogamacin, including but not limited to amsacrine, cytarabine, daunorubicin, etoposide, fludarabine, idarubicin, mitoxantrone, thioguanine and midostaurin (subject to ongoing NICE appraisal)
Outcomes	The outcome measures to be considered include: • event-free survival • overall survival • disease-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.
Other considerations	If evidence allows, consideration will be given to subgroups based on cytogenetics profile risk. If the evidence allows, a scenario analysis will be considered whereby stem cell transplant is included as a subsequent treatment for people who are fit enough to undergo the procedure and whose disease remitted after standard high-dose chemotherapy with or without gemtuzumab ozogamicin. This should reflect the proportion of people who proceed to stem cell transplant after each treatment regimen, as well as the costs and quality-adjusted life year benefits of the procedure. 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	'Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts' (2016) NICE Technology Appraisal 399. Review date July 2019. 'Azacitidine for the treatment of myelodysplastic syndromes, chronic myelomonocytic leukaemia and acute myeloid leukaemia' (2011) NICE Technology Appraisal 218. Static list: April 2014. Terminated appraisals 'Decitabine for the treatment of acute myeloid leukaemia' (terminated appraisal) (2012) NICE Technology Appraisal 270. Appraisals in development (including suspended appraisals) 'Midostaurin for untreated acute myeloid leukaemia' NICE technology appraisals guidance [ID894]. Publication expected April 2018.

	'Vosaroxin for treating relapsed or refractory acute myeloid leukaemia' NICE technology appraisals guidance [ID746]. Publication date to be confirmed. Related guidelines 'Haematological cancers: improving outcomes' (2016). NICE Guideline 47. Review date to be confirmed. Related NICE Pathways: Blood and bone marrow cancers (2016) NICE pathway
Related National Policy	Department of Health Cancer research and treatment Department of Health (2016) NHS Outcomes Framework 2016 to 2017: Domains 3, 4 and 5. Department of Health (2014) The national cancer strategy: 4th annual report NHS England (2016) Manual for prescribed specialised services 2016/17. Chapters 29 and 105.

References

1. Cancer Research UK (2014) Acute myeloid leukaemia (AML) statistics. Accessed September 2017.

2. Cancer Research UK (2016) Chemotherapy for acute myeloid leukaemia (AML). Accessed September 2017.