NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Liposomal cytarabine and daunorubicin for untreated acute myeloid leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of liposomal cytarabine and daunorubicin within its marketing authorisation for untreated, high risk, acute myeloid leukaemia.

Background

Acute myeloid leukaemia (AML) is a bone marrow cancer characterised by the overproduction of early immature myeloid cells (blasts). Myeloid neoplasms with more than 20% blasts in the peripheral blood or bone marrow are considered AML. AML is classified into several different types. In most types of AML, the leukaemia cells are immature white blood cells. In other less common types, too many immature platelets or immature red blood cells form the leukaemia cells. Anaemia, bleeding problems and serious infections are common symptoms in AML.

The incidence of AML in the UK is about 3100 cases per year. Around three quarters of all cases occur in people over 60 years and 55% of all cases occur in people over 70 years[1]. AML is slightly more common in men than in women.

AML is classified according to the World Health Organisation (WHO) classification which takes into account morphology, cytochemistry, immunophenotype, cytogenetics and clinical information and categorises AML into several clinically distinct types. Cytogenetics is the most important prognostic factor and classifies patients into 'favourable, intermediate or adverse risk' groups based on the presence or absence of specific chromosomal patterns. Poor prognostic factors, including intermediate and adverse risk cytogenetics, are more common in older people and make treatment more challenging.

AML typically develops rapidly and can be fatal unless treated. People for whom intensive chemotherapy is suitable are treated with cytotoxic agents such as an anthracycline in combination with cytarabine to induce remission. People who cannot tolerate or do not wish to receive intensive chemotherapy may have non-intensive chemotherapy such as low dose cytarabine[2]. NICE technology appraisal 218 recommends azacitidine for adults with acute myeloid leukaemia with 20–30% blasts and multilineage dysplasia (AML that has developed from a myelodysplastic syndrome), according to the WHO

classification and who cannot have haematopoietic stem cell transplantation. Azacitidine is not recommended by NICE for people with more than 30% blasts (NICE technology appraisal 399). If a person's leukaemia is in remission they may receive consolidation therapy or a haematopoietic stem cell transplant if suitable[2]. Other aspects of care include blood product replacement for anaemia and thrombocytopenia, antibiotics and antifungals for infections and intermittent low dose chemotherapy with hydroxycarbamide to keep the peripheral blood blast count low.

The technology

Liposomal cytarabine and daunorubicin (Vyxeos, Jazz Pharmaceuticals) is a liposomal encapsulated combination of cytarabine and daunorubicin in a 5 to 1 molar ratio. It is delivered by intravenous infusion.

Liposomal cytarabine and daunorubicin does not have a marketing authorisation for the treatment of acute myeloid leukaemia. It has been studied in a clinical trial in people aged 60 to 75 diagnosed with high risk AML, with at least 20% blasts in the peripheral blood or bone marrow. In the trial, liposomal cytarabine and daunorubicin was compared with cytarabine and daunorubicin in a '7 + 3 regimen' for first induction and a '5 + 2 regimen' for second induction and consolidation therapy.

Intervention(s)	Liposomal cytarabine and daunorubicin
Population(s)	People with newly diagnosed, high risk AML who are considered to be eligible for intensive therapy
Comparators	• Standard intensive induction and consolidation therapy • Azacitidine (for people who are not eligible for haematopoietic stem cell transplantation and have AML with 20-30% blasts and multilineage dysplasia) • Midostaurin (for people with FLT3-mutation-positive AML) (subject to ongoing NICE appraisal) • Gemtuzumab ozogamicin (subject to ongoing NICE appraisal)

Outcomes	The outcome measures to be considered include: • overall survival • event-free survival • disease-free-survival • remission • 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 patient access schemes for the intervention or comparator technologies will be taken into account.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 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. On static list. 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. Decitabine for acute myeloid leukaemia. NICE technology appraisals guidance [ID1114]. Suspended. Gemtuzumab ozogamicin for treating acute myeloid leukaemia. NICE technology appraisal guidance [ID982]. Publication date to be confirmed. Related guidelines: Haematological cancers: improving outcomes (2016). NICE guideline 47. Review date to be confirmed. Related quality standards: Haematological cancers (2017) Quality standard 150. Related NICE Pathways: Blood and bone marrow cancers (2017) NICE Pathway
Related National Policy	NHS England (2013) 2013/14 NHS standard contract for cancer: chemotherapy (adult) – service specification NHS England (2016) Manual for Prescribed Specialist Services 2016/17. Chapters 29,105 https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf Department of Health, NHS Outcomes Framework 2016-2017 (published 2016): Domains 1, 4 and 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance Department of Health (2007) Cancer reform strategy