NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

SingleTechnology Appraisal

Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of azacitidine within its marketing authorisation for treating acute myeloid leukaemia with more than 30% bone marrow blasts.

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 England is about 2500 cases per year[1]. Around three quarters of all cases occur in people over 60 years. 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. People in intermediate and poor-risk groups with good performance status may also receive allogeneic stem cells transplantation. People who cannot tolerate or do not wish to receive intensive chemotherapy are given non-intensive chemotherapy such as low dose cytarabine. NICE technology appraisal guidance No. 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. 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

Azacitidine (Vidaza, Celgene) is an analogue of nucleotide cytidine that reduces DNA methylation by inhibition of DNA methyltransferase. Azacitidine is administered subcutaneously.

Azacitidine does not currently have a marketing authorisation in the UK for acute myeloid leukaemia with more than 30% bone marrow blasts and when haematopoietic stem cell transplantation is not suitable. It has been studied in clinical trials in patients of age 65 years or more with acute myeloid leukaemia with bone marrow blasts more than 30%, who are not eligible for haematopoietic stem cell transplant compared with intensive chemotherapy with an anthracycline in combination with cytarabine, low dose cytarabine, or best supportive care.

Azacitidine has a UK marketing authorisation for acute myeloid leukaemia with 20-30 % blasts and multi-lineage dysplasia, according to the World Health Organisation classification.

Intervention(s)	Azacitidine
Population(s)	Adults with acute myeloid leukaemia with bone marrow blasts more than 30%
Comparators	• Intensive chemotherapy with an anthracycline in combination with cytarabine • Non-intensive chemotherapy with low dose cytarabine • best supportive care which may include blood product replacement, antibiotics, antifungals and intermittent low dose chemotherapy with hydroxycarbamide

Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • time to disease progression • response rates, including haematologic response and improvement • blood-transfusion independence • infections • 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 should be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered. These include: • people with AML secondary to myelodysplastic syndrome • people with adverse-risk cytogenetics 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: Technology Appraisal No. 218, March 2011, 'Azacitidine for the treatment of myelodysplastic syndrome, chronic myelomonocytic leukaemia and acute myeloid leukaemia'. Transferred to the 'static guidance list' April

	2014 Technology Appraisal No. 270, December 2012, Decitabine for the treatment of acute myeloid leukaemia (terminated appraisal). Related Cancer Service Guidance: Guidance on Cancer Services, CSGHO, October 2003, 'Improving outcomes in haematological cancers' Related NICE Pathways: NICE Pathway: Blood and bone marrow cancers, Pathway last updated: June 2015, http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers
Related National Policy	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

Reference:

1. Cancer Research UK, 2014, Acute myeloid leukaemia (AML) incidence statistics (accessed on 14/09/2015)