NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

Vosaroxin for treating relapsed or refractory acute myeloid leukaemia

Final scope

Remit/appraisal objective

To appraise the clinical and cost effectiveness of vosaroxin within its marketing authorisation for treating relapsed or refractory acute myeloid leukaemia.

Background

Acute myeloid leukaemia (AML) is a bone marrow cancer characterised by the overproduction of early immature myeloid cells (blasts). 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 leukaemia cells. Anaemia, bleeding problems and serious infections are the 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 typically develops rapidly and is fatal unless treated. People for whom intensive chemotherapy is suitable are treated with cytotoxic agents such as an anthracycline in combination with cytarabine. Those who cannot tolerate or do not wish to receive intensive chemotherapy are given non-intensive chemotherapy such as low dose cytarabine. If the disease does not respond to the treatment, then it is called refractory AML and if it returns after response to the initial treatment, it is called relapsed AML. Relapsed and refractory AML are associated with a poor prognosis.

The treatment of relapsed or refractory AML depends upon several factors such as age, general health, and certain features of leukaemia cells as well as the duration of remission (in case of relapsed AML). For people with good general health, the treatment typically includes salvage chemotherapy and allogeneic stem cell transplant. The aim of the salvage chemotherapy is to reduce the leukemic burden before stem cell transplant. Allogeneic stem cell transplant means that stem cells were donated by someone else, usually a sibling whose tissue type closely matches that patient's.

People with relapsed and refractory AML are offered salvage chemotherapy regimens containing high-dose of cytarabine such as fludarabine, cytarabine, idarubicin, and filgrastim (FLAG-Ida). People who cannot tolerate or do not wish to receive high-dose cytarabine are offered intermediate dose cytarabine regimen (IDAC).

People with relapsed and refractory AML also receive supportive care, which includes, blood product replacement, antibiotics, and antifungals. People who cannot have chemotherapy and stem cells transplant, need intermittent hydroxycarbamide to keep peripheral leukaemia cell count under control.

The technology

Vosaroxin (Qinprezo, Sunesis) is a quinolone derivative that intercalates DNA and inhibits the enzyme topoisomerase II, leading to site-selective DNA damage and inhibition of cell replication, resulting in cell death.

Vosaroxin does not currently have a marketing authorisation in the UK for treating acute myeloid leukaemia (AML). In a clinical trial, vosaroxin in combination with cytarabine has been compared with cytarabine plus placebo, in adults with AML whose disease did not respond to the treatment or had come back after response to the initial treatment.

Intervention(s)	Vosaroxin in combination with cytarabine
Population(s)	Adults with relapsed or refractory acute myeloid leukaemia
Comparators	Cytarabine based salvage chemotherapy • Fludarabine, cytarabine, idarubicin, and filgrastim (FLAG-Ida) • Intermediate dose cytarabine (IDAC)
Outcomes	The outcome measures to be considered include: • overall survival • progression free survival • time to disease progression • response rates, including haematologic response • blood-transfusion independence • stem cell transplant • 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.
Other considerations	If the evidence allows the following subgroups will be considered. • Adults with AML that is refractory to the induction treatment • Adults with AML that has relapsed after the initial response 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: 'Azacitidine for the treatment of myelodysplastic syndrome, chronic myelomonocytic leukaemia and acute myeloid leukaemia' (2011) Technology Appraisal No. 218. Transferred to the 'static guidance list' April 2014 Decitabine for the treatment of acute myeloid leukaemia (terminated appraisal) (2012). Technology Appraisal No. 270. Appraisals in development 'Azacitidine for treating acute myeloid leukaemia with more than 30% bone marrow blasts' [ID 829] Publication date July 2016 Related Cancer Service Guidance: Guidance on Cancer Services, CSGHO, October 2003, 'Improving outcomes in haematological cancers' Currently being updated. May 2016 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	NHS England (2016) Manual for Prescribed Specialised Services 2016/17. Chapters 29, 105. https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf **National Service Frameworks** Cancer **Department of Health** Department of Health, NHS Outcomes Framework 2015-2016, Nov 2014. Domains 1 and 2 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf Department of Health (2014) The national cancer strategy: 4th annual report https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report Department of Health (2011) Improving outcomes: a strategy for cancer Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 http://www.cancerresearchuk.org/sites/default/files/achieving_world-class_cancer_outcomes_-_a_strategy_for_england_2015-2020.pdf

References

Cancer Research UK, 2014, Acute myeloid leukaemia (AML) incidence statistics (accessed on 14/10/2016)