NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Azacitidine for the treatment of myelodysplastic syndrome and acute myeloid leukaemia

Draft scope (Pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of azacitidine within its licensed indication for the treatment of high risk patients with myelodysplastic syndrome and acute myeloid leukaemia (<30% blasts)

Background

Myelodysplastic syndromes (MDS) are a diverse group of haematological disorders in which the bone marrow functions abnormally and insufficient numbers of mature blood cells are produced. Red blood cells, white blood cells platelets may all be affected by MDS, resulting in anaemia and increased risk of bleeding and infections. MDS are associated with an increased risk of transformation to acute myeloid leukaemia (AML). AML is a progressive form of MDS that is characterised by rapidly growing cancer of the blood and bone marrow. It is the commonest type of acute leukaemia in adults.

There were 1,993 people newly diagnosed with MDS in England in 2004, with over 90% of patients aged over 60 at the time of diagnosis. Men are more likely than women to have MDS. Median survival of MDS is around 20 months. High risk subgroups of MDS patients are defined on the basis of the proportion of blasts, cytogenetics and blood cytopenia under the International Prognostic Scoring System (IPPS) to predict disease progression. Median survival in such high risk subgroups is less than six months.

Such high risk MDS or AML subgroups with <30% blasts corresponds to refractory anaemia with excess blasts in transformation (RAEB-T), as defined under the French-American-Britain (FAB) classification system. The FAB classification of RAEB-T is equivalent to ‘acute myeloid leukemia with multilineage dysplasia following a myelodysplastic syndrome’ under the World Health Organisation 1997 classification system. Under the FAB system, RAEB-T is characterised by 20-29% blasts; 30% blasts is AML.

Treatment options for myelodysplastic syndromes range from chemotherapy, supportive care (transfusion therapy, antibiotics) and chemotherapy with stem cell transplant.

The technology

Azacitidine (Vidaza, Pharmion) is an anticancer drug that is thought to act by an epigenetic mechanism of action. Epigenetic therapies are thought to work by re-establishing cancer cells’ natural mechanisms to control abnormal

growth rather than by causing cell death. Azacitidine is administered subcutaneously.

Azacitidine does not currently hold a UK marketing authorisation for the treatment of MDS. It has been studied in clinical trials (as a monotherapy) for the treatment of patients with MDS of both high-risk and low-risk subtypes. .

Intervention(s)	Azacitidine
Population(s)	People with high-risk myelodysplastic syndromes and acute myeloid leukemia (<30% blasts)
Standard comparators	• best supportive care • chemotherapy (such as cytarabine and anthracyclines) • stem cell transplantation
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • time to transformation to AML • 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	Details of the components of best supportive care should be clearly described. Guidance will only be issued in accordance with the marketing authorisation.

Related NICE recommendations	Related Technology Appraisals: None Related Guidelines: Cancer Service Guidance, October 2003, Improving outcomes in haemato-oncology cancer. Related Interventional Procedures: None Related Public Health Guidance/Guidelines: None

Questions for consultation

- What are the implications of different classification systems of myelodysplastic syndromes for defining the population to be included? Is the population correctly defined in the draft scope?

- Have the most appropriate comparators for the treatment of MDS and AMD (<30% blasts) been included in the scope?

    - Which chemotherapy regimens are routinely used in clinical practice?

    - Is stem cell transplantation an appropriate comparator?

    - How should best supportive care be defined?

- Are there any subgroups of patients in whom the technology is expected to be more clinically effective and cost effective or other groups that should be examined separately?

- Are there any issues that require special attention in light of the duty to have due regard to the need to eliminate unlawful discrimination and promote equality?

- Which process would be the most suitable for appraising this technology, the single technology or multiple technology process?

  (Information on these processes is available at http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp)