# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

## Health Technology Appraisal

## Decitabine for the treatment of acute myeloid leukaemia

## Draft scope

### Remit/appraisal objective

To appraise the clinical and cost effectiveness of decitabine within its licensed indication for the treatment of acute myeloid leukaemia

### Background

Acute myeloid leukaemia (AML) is a bone marrow cancer characterised by the overproduction of early immature myeloid cells. 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 are made. Anaemia, bleeding problems and serious infections are the common symptoms in AML.

The incidence of AML in the UK is about 2000 cases per year. Two-thirds of all cases occur in those over 60 years. It is slightly more common in men than in women.

AML typically develops quite quickly and rapidly and worsens in a few weeks unless treated. People of older age tend to have poorer outcomes than younger people, partly because they are less likely to be able to tolerate intensive chemotherapy. Complete remission rates in older people receiving intensive chemotherapy is often less than 60% and the median relapse-free survival is often less than 12 months. The median survival of older people who are not treated with intensive chemotherapy is about 2 to 3 months. Other factors that adversely influence prognosis are co-morbidities, antecedent haematological disorders and cytogenetics. Cytogenetic classification considers changes in chromosomal make up of the person to predict if they are predisposed to poor prognosis and is classified as ‘good, intermediate or poor risk’. Poor prognostic factors, including intermediate and high risk cytogenetics, are more common in older people, making treatment particularly challenging. Older people with poor prognostic factors do not usually receive intensive chemotherapy.

People for whom intensive chemotherapy is suitable are given standard treatment with cytotoxic agents such as anthracyclines in combination with cytarabine. Those who cannot tolerate or do not wish to receive intensive chemotherapy are given best supportive care or non-intensive (palliative) chemotherapy with agents such as low dose cytarabine, clofarabine, hydroxycarbamide, 6-mercaptopurine or etoposide.

## The technology

Decitabine (Dacogen, Janssen-Cilag and Eisai) is a nucleoside analogue of 2-deoxycytidine. It inhibits DNA methylation, leading to re-expression of tumour suppressor genes. This results in re-differentiation and maturation of cancer cells to normal.

Decitabine does not have a marketing authorisation for AML in the UK. In July 2012, the Committee for Medicinal Products for Human Use adopted a positive opinion, recommending that decitabine should be granted a marketing authorisation for the treatment of adult patients aged 65 years and above with newly diagnosed de novo or secondary AML, according to the World Health Organization (WHO) classification, who are not candidates for standard induction chemotherapy.

| | |
|---|---|
| **Intervention(s)** | Decitabine |
| **Population(s)** | People with newly diagnosed acute myeloid leukaemia for whom standard induction chemotherapy is considered inappropriate |
| **Comparators** | • Non-intensive chemotherapy such as:<br>  ○ low dose cytarabine<br>  ○ clofarabine<br>  ○ azacitidine<br>• Best supportive care, which may include:<br>  ○ chemotherapy such as hydroxycarbamide, 6-mercaptopurine, etoposide)<br>  ○ antibiotics<br>  ○ antifungals<br>  ○ blood transfusions |
| **Outcomes** | The outcome measures to be considered include:<br>• overall survival<br>• progression-free survival<br>• response rates<br>• adverse effects of treatment<br>• 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.<br>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.<br>Costs will be considered from an NHS and Personal Social Services perspective. |
| **Other considerations** | Guidance will only be issued in accordance with the marketing authorisation.<br>If evidence allows, there should be two subgroups: those for whom low dose cytarabine would be considered appropriate and those for whom best supportive care only would be considered appropriate. |
| **Related NICE recommendations** | Related Technology Appraisals :<br>Technology Appraisal No. 218, March 2011, 'Azacitidine for the treatment of myelodysplastic syndrome, chronic myelomonocytic leukaemia and acute myeloid leukaemia'. Review date February 2014<br>Related Cancer Service Guidance:<br>Guidance on Cancer Services, CSGHO, October 2003, 'Improving outcomes in haematological cancers' |

**Questions for consultation**

Have the most appropriate comparators for the treatment of acute myeloid leukaemia been included in the scope? Is azacitidine an appropriate comparator? Are the comparators listed routinely used in clinical practice?

Are there any other 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 (for example, a subgroup where non-intensive chemotherapy would be appropriate versus a subgroup where best supportive care would be appropriate)?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits