

## National Institute for Health and Care Excellence

## Single Technology Appraisal (STA)

## Vosaroxin for treating relapsed or refractory acute myeloid leukaemia

## Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

**Please note:** Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

## Comment 1: the draft remit

Section	Consultee/ Commentator	Comments [sic]	Action
Appropriateness	National Cancer Research Institute (NCRI)/ Royal College of Physicians (RCP)/ Association of Cancer Physicians (ACP)	Yes	Comment noted. No action required.
	Leukaemia CARE	Leukaemia CARE feels it appropriate to refer this topic to NICE appraisal.	Comment noted. No action required.
Wording	NCRI/RCP/ACP	See comments below	Comment noted.

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Timing Issues	NCRI/RCP/ACP	Quite urgent. This an area of unmet medical need	Comment noted. No action required.
	Leukaemia CARE	<p>As identified in the scope document, acute myeloid leukaemia (AML) is a rapidly developing disease that is fatal if not treated and makes up about 33% of all leukaemia cases in the UK.</p> <p>AML has been described as a "heterogeneous disease that is unlikely to respond in a uniform pattern to non-targeted" therapy. The existing cytarabine based regimens used to treat AML demonstrate "limited efficacy".</p> <p>Incidentally, little progress has been achieved in the 40 years in terms of prolonging survival for AML patients.</p> <p>The prognosis of the disease is poor. The median survival for a patient diagnosed with AML is less than twelve months. Overall, around 20% of all patients will survive for five years or more following an AML diagnosis. For AML patients that are over 65, only 5% will be in remission five years after their diagnosis. The prognosis for refractory and relapsed AML is even worse. This is because there are currently few effective treatment options to treat relapsed or refractory AML.</p> <p>This could be due to the fact that for many younger, fit patients, a stem cell transplant is an appropriate treatment option but for older or more frail patients, this is not always possible.</p> <p>The above statistics demonstrate that there is an urgent need for the development of and an increase of patient access to effective, innovative treatment options for AML (especially for patients where stem cell transplant is not an appropriate treatment option)</p>	Comment noted. No action required.

## Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	NCRI/RCP/ACP	Some of the salvage chemotherapy regimens mentioned here are rarely used in the UK. FLAG-Ida is commonly used in younger relapsed AML. MEC is rarely used	Comment noted. Description of salvage chemotherapy has been updated in the background section.
	Leukaemia CARE	As AML is an aggressive disease that has a poor prognosis, reference should be made to the emotional impact the disease has on patients, their carers and family. Feelings of shock, fear, anger, denial and isolation are usual following a cancer diagnosis. As such, there could be a profound impact on their emotional as well as physical wellbeing.	Comment noted. The scope aims to briefly describe the disease condition with appropriate information on its prognosis, epidemiology and alternative treatments currently used in the NHS. Please see section 2.2.1 of <a href="#">Guide to the methods of technology appraisal</a> (2013). The emotional impact of the disease on patients and their carers and families could be covered in the submissions from patient and carer groups involved in the appraisal. Patient

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			experts are also invited to submit a brief written personal statement prior to the appraisal committee meeting as well as to provide oral commentary during the meeting.
The technology/ intervention	NCRI/RCP/ACP	Yes	Comment noted. No action required.
Population	NCRI/RCP/ACP	Yes. In the clinical trial the benefit was seen primarily in older patients with relapsed/ refractory AML	NICE guidance is issued within the marketing authorisation, however noting NICE's obligations towards people protected by the equality legislation; it was decided that age restriction should not be specified in the remit or the scope at this stage.
Comparators	NCRI/RCP/ACP	There are some issues here. The aim of the treatment of relapsed AML in patients who are young enough is to get the patient into complete remission (CR) and consider an allo BMT. However CR may only be achieved in 50% of patients. Fit patients up to the age of 70 are suitable for such an approach. In younger patients FLAG-Ida is commonly used. Cladribine appears inferior. Older patients tolerate FLAG-Ida less well and this is an area of unmet	Comment noted. The comparators in the have been updated to; Cytarabine based salvage chemotherapy <ul style="list-style-type: none"> <li>• Fludarabine,</li> </ul>

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		medical need. IDAC (intermediate dose Cytarabine) is frequently used.	cytarabine, idarubicin, and filgrastim (FLAG-Ida) <ul style="list-style-type: none"> <li>• Intermediate dose cytarabine (IDAC)</li> </ul>
	Leukaemia CARE	As per the NICE guidance for the treatment of AML, azacitidine is considered as a treatment option - although is only currently recommended for patients with 20 - 30 % blasts and multilineage dysplasia. Could this be considered a comparator?	Comment noted. Azacitidine is used for a different subpopulation. Azacitidine is indicated, for those 'not eligible for haematopoietic stem cell transplantation', while the main aim of vosaroxin plus cytarabine therapy is to reduce the leukemic burden before stem cell transplant.
Outcomes	NCRI/RCP/ACP	Yes. Overall survival and CR are crucial endpoints particularly as the aim for many is to get to transplant in CR	Comment noted. No action required.
Economic analysis	NCRI/RCP/ACP	No comments	Response noted. No action required.
Equality and	NCRI/RCP/ACP	No comments	Response noted. No

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Diversity			action required.
Innovation	NCRI/RCP/ACP	Yes this is a first in class drug with a novel mode of action which has shown improved CR rates and improved survival in relapse/refractory, particularly in older patients, in a large randomised trial. Many other drugs have failed to show an improvement in this setting so this is an important advance.	Comment noted. The innovative nature of vosaroxin will be considered by the Committee during the appraisal.
	Leukaemia CARE	Vosaroxin has a different mechanism of action than other commonly used AML treatments. In a disease area where there are few effective treatment options, especially in the subgroup of patients over the age of 65, the phase III trial of vosaroxin in combination with cytarabine demonstrated some positive results. The number of patients achieving complete remission nearly doubled using vosaroxin compared to the placebo group. Results for patients over the age of 60 in particular showed that the addition of vosaroxin to cytarabine improved overall survival. Vosaroxin could be seen as an important step change in terms of an additional, more effective treatment option for patients with an aggressive disease that proffers a poor prognosis	Comment noted. The innovative nature of vosaroxin will be considered by the Committee during the appraisal.
Other considerations	NCRI/RCP/ACP	As mentioned above, the major benefit of the Vosaroxin/ Cytarabine combination was seen in patients >60 years	NICE guidance is issued within the marketing authorisation, however noting NICE's obligations towards people protected by the equality legislation; it was decided that age restriction should not be specified in the remit or

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			the scope at this stage.
Questions for consultation	NCRI/RCP/ACP	Vosaroxin would only be used in patients fit for intensive therapy. The best comparator is Cytarabine alone in older patients and FLAG-Ida in younger patients.	<p>Comment noted. The comparators in the have been updated to;</p> <p>Cytarabine based salvage chemotherapy</p> <ul style="list-style-type: none"> <li>• Fludarabine, cytarabine, idarubicin, and filgrastim (FLAG-Ida)</li> <li>• Intermediate dose cytarabine (IDAC)</li> </ul>
	Leukaemia CARE	<p><b>Would vosaroxin be used in people who otherwise may not be considered fit to receive salvage chemotherapy?</b></p> <p>Phase III study concluded that "this combination could be a treatment option for salvage therapy in patients aged 60 years or older". (F. Ravandi, E. K. Ritchie, et al)</p>	<p>NICE guidance is issued within the marketing authorisation, however noting NICE's obligations towards people protected by the equality legislation; it was decided that age restriction should not be specified in the remit or the scope at this stage.</p>

**The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope**

Department of Health  
Royal College of Nursing  
Sunesis Pharmaceuticals