National Institute for Health and Care Excellence

Single Technology Appraisal (STA)
KTE-X19 for treating relapsed or refractory mantle cell lymphoma in people who have received at least two previous lines of therapy
Response to consultee and commentator comments on the draft remit and draft scope

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	No comments received		
Wording ***Does the wording of the remit reflect the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider? If not, please suggest alternative wording.***	Lymphoma Action	KTE-X19 does not yet have marketing authorisation.	No action – the timing of a technology appraisal is aligned to information provided by the company about the indication in the anticipated marketing authorisation
	Kite, a Gilead company	To appraise the clinical and cost effectiveness of KTE-X19 within its anticipated marketing authorisation for treating relapsed or refractory mantle cell lymphoma who have received at least two previous lines of therapy	Comment noted. The remit and title have been kept broad, but the PICO table has been edited to include the following text '[people] who have received at least two previous lines of therapy'

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Timing Issues ***What is the relative urgency of this appraisal to the NHS?***	Lymphoma Action	Results of the ZUMA-2 trial of KTE-X19 in mantle cell lymphoma have not yet been released. Once the data is available, depending on the results, a NICE appraisal could be a priority.	No action – the timing of a technology appraisal is aligned to information about the anticipated regulatory timeline with a view to providing guidance as soon as possible following regulatory approval
	Kite, a Gilead company	There is a high unmet need for MCL patients who did not respond to two previous lines of therapy including Ibrutinib. At this stage life expectancy is very short and the disease extremely aggressive.	No action – the timing of a technology appraisal is aligned to information about the anticipated regulatory timeline with a view to providing guidance as soon as possible following regulatory approval
Additional comments on the draft remit	Kite, a Gilead company	No further comments	No action

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Kite, a Gilead company	No comments	No action

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Consider the accuracy and completeness of this information.			
The technology/ intervention ***Is the description of the technology or technologies accurate?***	Kite, a Gilead company	No comments	No action
Population ***Is the population defined appropriately? Are there groups within this population that should be considered separately?***	Lymphoma Action	This depends on the trial data when it is available. Potentially patients with p53 mutations, who may do better than with conventional therapy, might be considered as a separate group. However, there are likely to be very few if any of these patients in the trial when the data is available.	No action – the population of the appraisal is aligned to the indication in the anticipated marketing authorisation. This is because guidance will only be issued in accordance with the marketing authorisation. The committee will consider the generalisability of the trial evidence to the scope population throughout the appraisal
	Kite, a Gilead company	No comments	No action
Comparators	Lymphoma Action	Current treatment for relapsed mantle cell lymphoma is generally: First relapse: ibrutinib	Ibrutinib remains excluded from the list of comparators because the population of interest is patients

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Is this (are these) the standard treatment(s) currently used in the NHS with which the technology should be compared? Can this (one of these) be described as 'best alternative care'?		• Second relapse: no standard treatment but options include:
		  ○ R-BAC
		  ○ R-bendamustine
		  ○ R-CHOP
		  ○ more palliative regimens such as R-CVP or single agent high dose ara-C
		• Allogeneic stem cell transplant could also be a relevant comparator– although that would fall into established clinical management.
		• Venetoclax would be a consideration, although there is little data at present
			who have had at least two previous lines of therapy.
			The scope has been edited to specify the relevant chemotherapy regimens in this setting and it has been clarified that allogeneic stem cell transplant is included as part of established clinical management.
			Venetoclax has not been listed as a comparator because it is unclear from the consultation comments how often this treatment is used in NHS practice as it is not licensed for this indication.

	Kite, a Gilead company	There is no standard of care in this setting so 'best alternative care' cannot be detailed to a single chemotherapy regimen. We do not anticipate for autologous SCT to represent a possible comparator in this population	No action – it is stated in the scope that there is no standard of care in this setting and the comparators are not limited to a single chemotherapy regimen. Autologous stem cell transplant remains excluded from the scope comparators
Outcomes ***Will these outcome measures capture the most important health related benefits (and***	Kite, a Gilead company	The outcome measures to be considered include: • overall survival • progression-free survival	No action – the comment does not require any edits to the scope outcomes

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harms) of the technology?		• response rate • adverse effects of treatment • health-related quality of life Please note that while response rate will be considered as an outcome of interest in the clinical sections of the submission we do not anticipate it will play a prominent role in the CE model. The CE model will primarily be informed by the key clinical efficacy measures of overall survival and progression-free survival	
Economic analysis ***Comments on aspects such as the appropriate time horizon.***	Kite, a Gilead company	No comments	No action
Equality and Diversity ***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***	Kite, a Gilead company	No comments	No action

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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;***			

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• ***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.***			
Other considerations ***Suggestions for additional issues to be covered by the appraisal are welcome.***	Kite, a Gilead company	No comments	No action
Innovation ***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***	Lymphoma Action	Yes, if the clinical trial data is positive.	The committee will consider the innovative nature of KTE-X19 throughout the course of the appraisal
	Kite, a Gilead company	KTE-X19 is a personalised medicine in which the patient's own T cells are collected and engineered ex vivo to express a chimeric antigen receptor (CAR) which programmes them to target and kill the cancer cells when they are returned to the patient in a single infusion.	The committee will consider the innovative nature of KTE-X19 throughout the course of the appraisal

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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.		This CD19-directed genetically modified autologous T cell immunotherapy is a breakthrough treatment offering a potentially curative treatment option for patients with an extremely poor life expectancy and for whom there is no standard of care. We believe KTE-X19 will be associated with significant-health related benefits and represent a step-change in treatment for this heavily pre-treated patient population. Our submission will be supported by upcoming data from: • The ZUMA-2 trial • RWE on current treatment patterns and outcomes – unfortunately this will only be available post-submission (but prior to appraisal) and we would like to ask for the opportunity to submit this additional evidence to be considered by the review group	
Questions for consultation ***Please answer any of the questions for consultation if not covered in the above sections. If appropriate, please include comments on the proposed process this appraisal will follow (please note any***	Lymphoma Action	• Would KTE-X19 only be offered to patients who have previously received chemotherapy and ibrutinib? *Probably, because the anticipated licence is post BTKi, and ibrutinib has to be given at first relapse as per NICE guidance. However, it depends on the trial data when it is available. There may also be a small number of patients included in trials of front-line BTKi who could receive CAR-T without having chemotherapy.* • Is autologous stem cell transplant likely to be considered an alternative option to KTE-X19 in clinical practice or are patients more likely to receive KTE-X19 following a	Ibrutinib and autologous stem cell transplant remain excluded from the list of comparators because the population of interest is patients who have had at least two previous lines of therapy

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changes made to the process are likely to result in changes to the planned time lines).		transplant? *KTE-X19 would be used after autologous stem cell transplant because an autograft is part of front-line management and is not used at relapse.* • Where do you consider KTE-X19 will fit into the existing NICE pathway for Non-Hodgkin's lymphoma? *This is likely to be relapse after ibrutinib therapy, but it depends on who was included in the trial and the effectiveness at different lines of treatment.*	
	Kite, a Gilead company	Equality: No barriers in the adoption of this technology have been identified	No action
Additional comments on the draft scope	Lymphoma Action	Results of the ZUMA-2 trial are not yet available. All responses are dependent on the results of the trial.	No action

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

None