

## Appendix B

### NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

#### Health Technology Appraisal

#### KTE-X19 for treating relapsed or refractory mantle cell lymphoma

#### Final scope

##### Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of KTE-X19 within its marketing authorisation for treating relapsed or refractory mantle cell lymphoma.

##### Background

Lymphomas are cancers of the lymphatic system, which is a part of the immune system. Lymphomas are divided into Hodgkin lymphoma and non-Hodgkin lymphoma. Non-Hodgkin lymphomas (NHL) are a diverse group of conditions which are categorised according to the cell type affected (B-cell or T-cell), as well as the clinical features and rate of progression of the disease. Mantle cell lymphoma is a rare and often aggressive type of NHL which affects B-cells.

There were around 12,000 new cases of NHL in England in 2017<sup>1</sup> but only a small proportion of patients with NHL have mantle cell lymphoma (around 75 people are diagnosed with mantle cell lymphoma in the UK each year which is less than 1% of people who have NHL<sup>2</sup>). Regional data from the north-east of England collected between 2004 and 2011 indicates that the 1-year survival rate for people with mantle cell lymphoma is 70.8% and the 5-year survival rate is 26.8%<sup>3</sup>. Mantle cell lymphoma is more common in men than women (3:1 ratio)<sup>4</sup>.

NICE [technology appraisal 502](#) recommends ibrutinib as an option for treating relapsed or refractory mantle cell lymphoma in adults, if they have had only 1 previous line of therapy. There is no accepted standard of care for treating relapsed or refractory mantle cell lymphoma in people who have received at least two previous lines of therapy. A range of chemotherapy regimens are used such as, R-BAC (rituximab, bendamustine and cytarabine), rituximab plus bendamustine, R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone), R-CVP (rituximab, cyclophosphamide, vincristine, and prednisolone) and single-agent cytarabine. Allogeneic haemopoietic stem-cell transplantation is a potentially curative treatment in patients for whom it is suitable.

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### The technology

KTE-X19 (brand name unknown, Kite, a Gilead company) is a type of immunotherapy that uses autologous T cells directed against the tumour antigen CD19. It is administered intravenously.

KTE-X19 does not currently have a marketing authorisation in the UK for relapsed or refractory mantle cell lymphoma. It currently is being studied in a single arm clinical trial (ZUMA-2) in adult patients with relapsed or refractory mantle cell lymphoma who have received up to 5 prior treatment regimens (prior therapy must have included anthracycline or bendamustine-containing chemotherapy, anti-CD20 monoclonal antibody therapy and ibrutinib or acalabrutinib).

<b>Intervention(s)</b>	KTE-X19
<b>Population(s)</b>	People with relapsed or refractory mantle cell lymphoma who have received at least two previous lines of therapy
<b>Comparators</b>	Established clinical management including but not limited to: <ul style="list-style-type: none"><li>• Chemotherapy with or without rituximab</li><li>• Allogeneic haemopoietic stem cell transplant</li></ul>
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"><li>• overall survival</li><li>• progression-free survival</li><li>• response rate</li><li>• adverse effects of treatment</li><li>• health-related quality of life.</li></ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.</p>

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<b>Other considerations</b>	<p>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.</p> <p>The availability and cost of biosimilar products should be taken into account.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p>Related Technology Appraisals:</p> <p><a href="#">‘Ibrutinib for treating relapsed or refractory mantle cell lymphoma’</a> (2018). NICE Technology Appraisal 502. Review date January 2021.</p> <p>Terminated appraisals</p> <p><a href="#">‘Temsirrolimus for the treatment of relapsed or refractory mantle cell lymphoma’</a> (terminated appraisal) (2010). NICE Technology Appraisal 207.</p> <p>Appraisals in development (including suspended appraisals)</p> <p><a href="#">‘Lymphoma (mantle cell, relapsed, refractory) - lenalidomide’</a> NICE technology appraisals guidance [ID739]. Suspended.</p> <p>Related Guidelines:</p> <p><a href="#">‘Haematological cancers: improving outcomes’</a> (2016). NICE guideline 47. Review date to be confirmed.</p> <p><a href="#">‘Non-Hodgkin’s lymphoma: diagnosis and management’</a> (2016). NICE guideline 52. Review date to be confirmed.</p> <p><a href="#">Non-Hodgkin’s lymphoma: rituximab subcutaneous injection</a> (2014) NICE evidence summary of new medicines 46.</p> <p>Related Quality Standards:</p> <p><a href="#">‘Haematological cancers’</a> (2017). NICE quality standard 150.</p> <p>Related NICE Pathways:</p> <p>Non-Hodgkin’s lymphoma (2016) NICE pathway  <a href="http://pathways.nice.org.uk/">http://pathways.nice.org.uk/</a></p>
<b>Related National Policy</b>	<p>National Service Frameworks <a href="#">Cancer</a></p> <p>Other policies</p> <p>Department of Health (2016) <a href="#">NHS outcomes framework</a></p>

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	<p><a href="#">2016 to 2017</a> Domains 1-5</p> <p>Independent Cancer Taskforce (2015) <a href="#">Achieving world-class cancer outcomes: a strategy for England 2015-2020</a></p> <p>Department of Health (2014) <a href="#">The national cancer strategy: 4th annual report</a></p> <p>Department of Health (2011) <a href="#">Improving outcomes: a strategy for cancer</a></p> <p>NHS England (2017) <a href="#">Manual for Prescribed Specialised Services 2018/19</a>. Chapter 105.</p> <p>NHS England (2013) <a href="#">NHS standard contract for cancer: Chemotherapy (Adult) Section B part 1 Service specifications</a>. Clinical Commissioning Policy. Reference B15/S/a.</p>
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### References

1. [Office for National Statistics. Cancer Registration Statistics, England, 2017](#). Office of National Statistics. Accessed September 2019
2. [Mantle cell lymphoma](#). Cancer Research UK (using data from the Office for National Statistics and the regional cancer registries in Wales, Scotland and Northern Ireland using the latest data for 2017). Accessed September 2019
3. [Non-Hodgkin lymphoma survival statistics](#). Cancer Research UK. Accessed November 2018
4. M. Dreyling, E. Campo, O. Hermine, M. Jerkeman, S. Le Gouill, S. Rule, O. Shpilberg, J. Walewski, M. Ladetto, on behalf of the ESMO Guidelines Committee; Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, *Annals of Oncology*, Volume 28, Issue suppl\_4, 1 July 2017, Pages iv62–iv71