NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

KTE-X19 for treating relapsed or refractory mantle cell lymphoma

Draft 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[1] 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[2]). 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%[3]. Mantle cell lymphoma is more common in men than women (3:1 ratio)[4].

There is no accepted standard of care for treating relapsed or refractory mantle cell lymphoma. A range of chemotherapy regimens are used, some including rituximab, even though many people will have had rituximab as part of first line and maintenance treatment. NICE have recommended treatment with ibrutinib for people that have only had 1 previous line of therapy.

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).

Intervention(s)	KTE-X19
Population(s)	People with relapsed or refractory mantle cell lymphoma who have received at least two previous lines of therapy
Comparators	Established clinical management including but not limited to: • Chemotherapy with or without rituximab • Best supportive care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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. The availability of any patient access schemes for the intervention or comparator technologies will be taken into account.

Other considerations	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. The availability and cost of biosimilar products should be taken into account.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: 'Ibrutinib for treating relapsed or refractory mantle cell lymphoma' (2018). NICE Technology Appraisal 502. Review date January 2021. Terminated appraisals 'Temsirolimus for the treatment of relapsed or refractory mantle cell lymphoma' (terminated appraisal) (2010). NICE Technology Appraisal 207. Appraisals in development (including suspended appraisals) 'Lymphoma (mantle cell, relapsed, refractory) - lenalidomide' NICE technology appraisals guidance [ID739]. Suspended. Related Guidelines: 'Haematological cancers: improving outcomes' (2016). NICE guideline 47. Review date to be confirmed. 'Non-Hodgkin's lymphoma: diagnosis and management' (2016). NICE guideline 52. Review date to be confirmed. Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014) NICE evidence summary of new medicines 46. Related Quality Standards: 'Haematological cancers' (2017). NICE quality standard 150. Related NICE Pathways: Non-Hodgkin's lymphoma (2016) NICE pathway http://pathways.nice.org.uk/
Related National Policy	National Service Frameworks Cancer Other policies Department of Health (2016) NHS outcomes framework 2016 to 2017 Domains 1-5 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy

	for cancer NHS England (2017) Manual for Prescribed Specialised Services 2018/19. Chapter 105. NHS England (2013) NHS standard contract for cancer: Chemotherapy (Adult) Section B part 1 Service specifications. Clinical Commissioning Policy. Reference B15/S/a.

Questions for consultation

Is the population listed in the scope appropriate?

- Would KTE-X19 only be offered to patients who have previously received chemotherapy and ibrutinib?

Are the stated comparators appropriate?

- What chemotherapy regimens are considered to be established clinical practice in the NHS for treating relapsed or refractory mantle cell lymphoma?

- 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 transplant?

Are there any other relevant comparators that are not currently listed in the scope?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom KTE-X19 is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider KTE-X19 will fit into the existing NICE pathway for Non-Hodgkin's lymphoma?

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 KTE-X19 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 KTE-X19 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 KTE-X19 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.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

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