NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Pirtobrutinib for treating relapsed or refractory mantle cell lymphoma [ID3975]

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pirtobrutinib within its marketing authorisation for 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.

Symptoms of mantle cell lymphoma include loss of appetite and weight loss, nausea and/or vomiting, indigestion, abdominal pain or bloating, discomfort due to an enlarged liver or spleen, pressure or pain in the lower back, or fatigue due to anaemia.

There were around 500 new cases of mantle cell lymphoma diagnosed in England in 2020 (comprising 5-7% of all non-Hodgkin lymphoma cases).[1] Mantle cell lymphoma usually occurs in older adults with a median age at diagnosis of 72 years, and is more common in men than women with a ratio of 3:1.[2] Data from the UK between 2004 to 2016 indicates that the 1-year survival rate for people with mantle cell lymphoma is 72.7% and the 5-year survival rate is 41%.[3] Younger people tend to have better outcomes, with around 60% of those aged below 60 surviving for 5 years or more after diagnosis.[3]

Mantle cell lymphoma has been one of the most difficult types of non-Hodgkin's lymphoma to treat. Although it typically responds well to initial treatment, rates of relapse after initial treatment are high. Treatment is individualised based on the patient's comorbidities, age and performance status. First-line treatment may include rituximab chemotherapy, and stem cell transplant for fitter patients. 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. In adults who have previously had a BTK inhibitor, NICE technology appraisal 677 recommends autologous anti-CD19-transduced CD3+ cells for use within the Cancer Drugs Fund. Other treatment options include chemotherapy regimens 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.

The technology

Pirtobrutinib (brand name unknown, Lilly) is a highly-selective Bruton's tyrosine kinase (BTK) inhibitor. BTK inhibitors play a key role in the development, activation and survival of both normal and malignant B-cells. It is administered orally.

Pirtobrutinib does not currently have a marketing authorisation in the UK for mantle cell lymphoma. It has been studied in clinical trials compared with other BTKs in previously treated adults with lymphocytic leukaemia, small lymphocytic lymphoma and non-Hodgkin's lymphomas.

Intervention(s)	Pirtobrutinib
Population(s)	Adults with relapsed or refractory mantle cell lymphoma
Comparators	Established clinical management including but not limited to: • Chemotherapy with or without rituximab • Allogeneic haemopoietic stem-cell transplant • Ibrutinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • overall response rate • duration of response • 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 commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.
Other considerations	The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation for pirtobrutinib. 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.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** 'Ibrutinib for treating relapsed or refractory mantle cell lymphoma' (2018). NICE Technology Appraisal 502. A review in 2021 found nothing new to affect the guidance. No further review scheduled. 'Autologous anti-CD19-transduced CD3+ cells for treating relapsed or refractory mantle cell lymphoma' '(2021). NICE Technology Appraisal 677. Review date to be confirmed. **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):** 'Lenalidomide for treating relapsed or refractory mantle cell lymphoma' 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 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

Which treatments are considered to be established clinical practice in the NHS for treating relapsed or refractory mantle cell lymphoma, and in what order are they typically given?

Have all relevant comparators for pirtobrutinib been included in the scope?

Are the outcomes listed appropriate?

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

Where do you consider pirtobrutinib will fit into the existing NICE pathway, 'Non-Hodgkin's lymphoma overview - NICE Pathways'?

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 pirtobrutinib 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.

Would pirtobrutinib be a candidate for managed access?

Do you consider pirtobrutinib 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 pirtobrutinib 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).

NICE has published an addendum to its guide to the methods of technology appraisal (available at https://www.nice.org.uk/Media/Default/About/what-we-

do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum-cost-comparison.pdf), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technologies that has not been considered? Are there any important ongoing trials reporting in the next year?

References

1. Haematological Malignancy Research Network (HMRN) - Incidence statistics: Total incidence - All selected diagnoses. https://hmrn.org/statistics/incidence. Accessed July 2022.

2. M. Dreyling, et al, 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

3. Haematological Malignancy Research Network (HMRN) - Survival statistics: Mantle cell lymphoma - Relative survival. https://hmrn.org/statistics/survival Accessed July 2022.