NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Zanubrutinib for treating relapsed or refractory marginal zone lymphoma

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of zanubrutinib within its marketing authorisation for treating relapsed or refractory marginal zone lymphoma.

Background

Lymphomas are cancers of the lymphatic system, which is part of the body's immune system. They are divided into Hodgkin and non-Hodgkin lymphomas. Non-Hodgkin lymphomas are a heterogeneous group of conditions ranging from 'indolent' (low-grade) to 'aggressive' (high-grade) depending on the rate at which the abnormal lymphocytes divide. Indolent lymphomas are slow growing, with long median survival times but are less likely to be cured by treatment.

Marginal zone lymphoma is a type of indolent non-Hodgkin lymphoma that develops from B lymphocytes that are normally found at the edge of areas of lymph node tissue. Mucosa associated lymphoid tissue (MALT) lymphoma is the most common type of marginal zone lymphoma and it most commonly affects the stomach. Nodal marginal zone lymphoma starts in the lymph nodes and splenic marginal zone lymphoma starts in the spleen but can also be found in the bloodstream. Released disease is when a cancer returns and refractory disease is when the cancer stops responding to treatment.[1]

There were around 14,200 new non-Hodgkin lymphoma cases in the UK each year between 2016 and 2018.[2] Each year, more than a third of all new non-Hodgkin lymphomas in the UK are diagnosed in people aged 75 and over, and the incidence rates are highest in people aged 80 to 84.[2] Marginal zone lymphomas represent approximately 5 to 15% of all non-Hodgkin lymphoma cases.[3]

There are no NICE recommended treatment options for marginal zone lymphoma. The European Society for Medical Oncology recommends that all people with gastric MALT be treated with an anti *H. pylori* regimen to eradicate infection. Radiotherapy may also be considered in some cases of MALT lymphoma. Symptomatic treatment for marginal zone lymphoma typically involves rituximab (an anti-CD20 antibody) alone or in combination with chemotherapy (for example, chlorambucil, bendamustine, lenalidomide, CHOP [cyclophosphamide, doxorubicin, vincristine, prednisolone] or CVP [cyclophosphamide, vincristine, prednisolone]). People whose disease does not respond to treatment, or relapses after treatment is completed, will usually receive a different combination chemotherapy regimen, with or without rituximab. Stem cell transplantation may also be considered and splenectomy can be considered for splenic marginal zone lymphoma.[3]

The technology

Zanubrutinib (Brukinsa, BioGene Ltd) has marketing authorisation in the UK for the treatment of adult patients with marginal zone lymphoma who have received at least

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one prior anti-CD20-based therapy. It has been studied in clinical trials in adults with marginal zone lymphoma who have previously received one or more lines of therapy including at least one CD20-directed regimen with documented failure to achieve at least partial response or documented progressive disease after, the most recent systemic treatment.

Intervention	Zanubrutinib
Population(s)	Adults with marginal zone lymphoma who have had at least 1 anti-CD20-based therapy
Subgroups	Type of marginal zone lymphoma: o MALT lymphoma o Nodal marginal zone lymphoma o Splenic marginal zone lymphoma Number of previous treatments
Comparators	• Chemotherapy with or without rituximab • Stem cell transplant • Best supportive care • Splenectomy (for splenic marginal zone lymphoma only)
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rates • duration of response • adverse effects of treatment • health-related quality of life.

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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. The availability and cost of biosimilar and generic products should 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.
Related NICE recommendations	**Related technology appraisals in development:** Ibrutinib for treating relapsed or refractory follicular lymphoma and marginal zone lymphoma. NICE technology appraisal guidance [ID1251] Publication date to be confirmed. **Related NICE guidelines:** Non-Hodgkin's lymphoma: diagnosis and management (2016). NICE guideline 52. Haematological cancers: improving outcomes (2016). NICE guideline 47. Non-Hodgkin's lymphoma: rituximab subcutaneous injection (2014). NICE evidence summary of new medicines 46. Suspected cancer: recognition and referral (2015). NICE guideline 12. **Related quality standards:** Haematological cancers (2017). NICE quality standard 150.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan. NHS England (2018) NHS manual for prescribed specialist services (2018/2019). Chapter 29: Blood and marrow transplantation services (adults and children); Chapter 105: Specialist cancer services (adults)

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Questions for consultation

Where do you consider zanubrutinib will fit into the existing care pathway for marginal zone lymphoma?

What is current standard of care for relapsed or refractory marginal zone lymphoma? Do treatment options differ based on the type of marginal zone lymphoma?

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

Are the outcomes listed appropriate?

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

Would zanubrutinib be a candidate for managed access?

Do you consider that the use of zanubrutinib can result in any potential 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 committee to take account of these benefits.

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 zanubrutinib is 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. Lymphoma Action. Non-Hodgkin lymphoma. [Accessed July 2023]
2. Cancer Research (2022) Non-Hodgkin lymphoma statistics [Accessed July 2023]

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3. Zucca E, Arcaini L, Buske C et al. Marginal zone lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up Annals of Oncology. 2020;31(1):17-29. [Accessed July 2023]

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