NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Acalabrutinib with bendamustine and rituximab for untreated mantle cell lymphoma ID6155

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of acalabrutinib with bendamustine and rituximab within its marketing authorisation for untreated 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 are around 590 new cases of mantle cell lymphoma diagnosed in the UK each year (comprising around 5% of all non-Hodgkin lymphoma cases).[1] Mantle cell lymphoma usually occurs in older adults and is more common in men than women at a ratio of 2.4:1.[2] Data from the UK between 2010 to 2019 indicates that the 5-year survival rate is 47%.[3]

NICE guideline 52 (NG52) recommends the following options for first-line treatment of mantle cell lymphoma:

- Chemotherapy in combination with rituximab for people with advanced stage mantle cell lymphoma who are symptomatic, taking into account the person's fitness when deciding on chemotherapy intensity.
    - Since NG52, bendamustine with rituximab is available for first-line use through an NHS England commissioning policy for treating mantle cell lymphoma. It is an option for less fit patients, as an alternative to other regimens such as rituximab with cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP), bortezomib with rituximab, cyclophosphamide, doxorubicin and, prednisone (VR-CAP) and rituximab, cyclophosphamide, vincristine and prednisolone (R-CVP).
- Cytarabine-based immunochemotherapy for people with advanced-stage mantle cell lymphoma who are fit enough to have it.
- Radiotherapy for people with localised stage 1 or 2 mantle cell lymphoma.
- 'Watch and wait' for people with clinically non-progressive disease who are asymptomatic and when radiotherapy is not suitable.

- NICE Technology appraisal guidance TA370 recommends bortezomib as an option for previously untreated mantle cell lymphoma in adults for whom haematopoietic stem cell transplantation is unsuitable.

NG52 recommends consolidation with autologous stem cell transplantation when mantle cell lymphoma has had at least a partial response to induction chemotherapy in people who are fit enough for transplantation. Maintenance treatment with rituximab is recommended for some people with newly diagnosed mantle cell lymphoma, including those who are not fit enough for high-dose chemotherapy and where there has been a response to R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone)-based immunochemotherapy, or where there is remission after cytarabine-based induction and high-dose chemotherapy.

The technology

Acalabrutinib (Calquence, AstraZeneca UK Ltd) with bendamustine and rituximab does not currently have a marketing authorisation in the UK for untreated mantle cell lymphoma. It has been studied in a clinical trial compared with bendamustine and rituximab with placebo in adults with previously untreated mantle cell lymphoma.

Acalabrutinib with or without obinutuzumab is indicated for the treatment of adults with previously untreated chronic lymphocytic leukaemia (CLL). Acalabrutinib monotherapy is indicated for the treatment of adults with CLL who have received at least one prior therapy.

Intervention(s)	Acalabrutinib with bendamustine and rituximab
Population(s)	Adults with previously untreated mantle cell lymphoma
Comparators	Established clinical management without acalabrutinib, including: • chemotherapy in combination with rituximab, including bendamustine with rituximab • cytarabine-based immunochemotherapy • radiotherapy • bortezomib
Outcomes	The outcome measures to be considered include: • progression-free survival • overall survival • response rates • 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.
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:** Bortezomib for previously untreated mantle cell lymphoma (2015) NICE technology appraisal guidance 370 **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 46. **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 (2023) Manual for prescribed specialist services (2023/2024) Chapter 29 - Haematopoietic stem cell transplantation services (adults and children). Chapter 105 - Specialist cancer services (adults) NHS England (2019) Clinical Commissioning Policy Statement Proton Beam Therapy for Adult Lymphoma. (URN: 1852) [190702P]. NHS England (2018) Commissioning Policy: Bendamustine with rituximab for first line treatment of mantle cell lymphoma (all ages). 17088P. NHS England (2016) Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) for lymphoplasmacytic lymphoma (adults). 16067/P.

	NHS England (2013, updated 2015) Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) (All Ages): Revised. NHSCB/B04/P/a. NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a. NHS England (2013) 2013/14 NHS Standard Contract for Haematopoietic Stem Cell Transplantation (Adult). B04/S/a.

Questions for consultation

Where do you consider acalabrutinib with bendamustine and rituximab will fit into the existing care pathway for untreated mantle cell lymphoma?

Would people treated with acalabrutinib with bendamustine and rituximab potentially be suitable for stem cell transplantation?

Have all relevant comparators for acalabrutinib with bendamustine and rituximab been included in the scope? Are the comparators listed appropriate?

Please select from the following, will acalabrutinib with bendamustine and rituximab be:

A. Prescribed in primary care with routine follow-up in primary care
B. Prescribed in secondary care with routine follow-up in primary care
C. Prescribed in secondary care with routine follow-up in secondary care
D. Other (please give details):

For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

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

Are the outcomes listed appropriate?

Would acalabrutinib with bendamustine and rituximab be a candidate for managed access?

Do you consider that the use of acalabrutinib with bendamustine and rituximab 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 acalabrutinib with bendamustine and rituximab 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.

NICE intends to evaluate this technology through its Single Technology Appraisal 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. Haematological Malignancy Research Network (HMRN). Statistics: UK incidence. https://hmrn.org/statistics/incidence/uk. Accessed May 2024.

2. Haematological Malignancy Research Network (HMRN). Statistics: QuickStats. https://hmrn.org/statistics/quickstats. Accessed May 2024.

2. Haematological Malignancy Research Network (HMRN). Statistics: Survival. https://hmrn.org/statistics/survival. Accessed May 2024.