

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Health Technology Evaluation

### Acalabrutinib with bendamustine and rituximab for untreated mantle cell lymphoma

#### Final scope

#### 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).<sup>1</sup> Mantle cell lymphoma usually occurs in older adults and is more common in men than women at a ratio of 2.4:1.<sup>2</sup> Data from the UK between 2010 to 2019 indicates that the 5-year survival rate is 47%.<sup>3</sup>

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) and rituximab, cyclophosphamide, vincristine and prednisolone (R-CVP).
  - NICE [Technology appraisal guidance TA370](#) recommends bortezomib with rituximab, cyclophosphamide, doxorubicin and, prednisone (VR-CAP) as an option for previously untreated mantle cell lymphoma in adults for whom haematopoietic stem cell transplantation is unsuitable.
- 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.
- 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.

<b>Intervention(s)</b>	Acalabrutinib with bendamustine and rituximab
<b>Population(s)</b>	Adults with previously untreated mantle cell lymphoma
<b>Comparators</b>	Established clinical management without acalabrutinib, including: <ul style="list-style-type: none"> <li>• chemotherapy in combination with rituximab, including bendamustine with rituximab</li> <li>• bortezomib with rituximab, cyclophosphamide, doxorubicin and, prednisone (VR-CAP)</li> <li>• cytarabine-based immunochemotherapy</li> <li>• radiotherapy</li> </ul>
<b>Outcomes</b>	The outcome measures to be considered include: <ul style="list-style-type: none"> <li>• progression-free survival</li> <li>• overall survival</li> <li>• response rates</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>

<p><b>Economic analysis</b></p>	<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><b>Other considerations</b></p>	<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><b>Related NICE recommendations</b></p>	<p><b>Related technology appraisals:</b></p> <p><a href="#">Bortezomib for previously untreated mantle cell lymphoma</a> (2015) NICE technology appraisal guidance 370</p> <p><b>Related NICE guidelines:</b></p> <p><a href="#">Non-Hodgkin's lymphoma: diagnosis and management</a> (2016) NICE guideline 52.</p> <p><a href="#">Haematological cancers: improving outcomes</a> (2016) NICE guideline 47.</p> <p><a href="#">Non-Hodgkin's lymphoma: rituximab subcutaneous injection</a> (2014) NICE Evidence summary 46.</p> <p><b>Related quality standards:</b></p> <p><a href="#">Haematological cancers</a> (2017) NICE quality standard 150.</p>
<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan (2019) <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2023) <a href="#">Manual for prescribed specialist services (2023/2024)</a> Chapter 29 - Haematopoietic stem cell transplantation services (adults and children). Chapter 105 - Specialist cancer services (adults)</p> <p>NHS England (2019) <a href="#">Clinical Commissioning Policy Statement Proton Beam Therapy for Adult Lymphoma</a>. (URN: 1852) [190702P].</p> <p>NHS England (2018) <a href="#">Commissioning Policy: Bendamustine with rituximab for first line treatment of mantle cell lymphoma (all ages)</a>. 17088P.</p> <p>NHS England (2016) <a href="#">Clinical Commissioning Policy: Haematopoietic Stem Cell Transplantation (HSCT) for lymphoplasmacytic lymphoma (adults)</a>. 16067/P.</p>

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