NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ibrutinib with R-CHOP for untreated mantle cell lymphoma when an autologous stem cell transplant is suitable ID6596

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of ibrutinib with R-CHOP (rituximab with cyclophosphamide, doxorubicin, vincristine and prednisolone) within its marketing authorisation for untreated mantle cell lymphoma when an autologous stem cell transplant (ASCT) is suitable.

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] Around 20-30% of people with untreated mantle cell lymphoma may be eligible for ASCT.[4]

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 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-based immunochemotherapy, or where there is remission after cytarabine-based induction and high-dose chemotherapy.

The British Society for Haematology Guideline for diagnosis and management of mantle cell lymphoma[5] states that when ASCT is suitable, people should be offered an induction regimen containing rituximab and high-dose cytarabine. If there is a response to induction, consolidation with ASCT should be offered, followed by rituximab maintenance therapy.

The technology

Ibrutinib (Imbruvica, Janssen-Cilag) with R-CHOP has a marketing authorisation in the UK for treating adults with previously untreated mantle cell lymphoma who would be eligible for an autologous stem cell transplant. The marketing authorisation states that treatment with ibrutinib plus R-CHOP should be alternated with R-DHAP (rituximab, dexamethasone, cytarabine, and cisplatin) (or R-DHAOx: rituximab, dexamethasone, cytarabine, and oxaliplatin) without ibrutinib, and followed by ibrutinib monotherapy (see the Summary of Product Characteristics for more detail).

Intervention(s)	Ibrutinib with R-CHOP, alternating with R-DHAP or R-DHAOx without ibrutinib, followed by ibrutinib monotherapy.
Population(s)	Adults with untreated mantle cell lymphoma
Comparators	**Induction phase:** • Established clinical management without ibrutinib, including but not limited to alternating R-CHOP and R-DHAP or R-DHAOx. • Acalabrutinib with bendamustine and rituximab (subject to NICE evaluation) **Consolidation phase:** • Established clinical management without ibrutinib, including but not limited to ACST. **Maintenance phase:** • Established clinical management without ibrutinib, including but not limited to rituximab.

Outcomes	The outcome measures to be considered include: • overall survival • failure-free survival • progression-free 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. 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:** Bortezomib for previously untreated mantle cell lymphoma (2015) NICE technology appraisal guidance 370 **Related technology appraisals in development:** Acalabrutinib with bendamustine and rituximab for untreated mantle cell lymphoma NICE technology appraisal guidance [ID6155] publication to be confirmed **Related NICE guidelines:** Non-Hodgkin's lymphoma: diagnosis and management (2016) NICE guidance NG52

Questions for consultation

Where do you consider ibrutinib with R-CHOP will fit into the existing care pathway for untreated mantle cell lymphoma?

Which induction regimens are used most commonly for untreated mantle cell lymphoma when an autologous stem cell transplant is suitable?

Please select from the following, will ibrutinib with R-CHOP 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.

Would ibrutinib with R-CHOP be a candidate for managed access?

Do you consider that the use of ibrutinib with R-CHOP 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 ibrutinib with R-CHOP 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. (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 August 2025.

2. Haematological Malignancy Research Network (HMRN). Statistics: QuickStats. https://hmrn.org/statistics/quickstats. Accessed August 2025.

3. Haematological Malignancy Research Network (HMRN). Statistics: Survival. https://hmrn.org/statistics/survival. Accessed August 2025.

4. Martin P, Cohen JB et al. Treatment Outcomes and Roles of Transplantation and Maintenance Rituximab in Patients With Previously Untreated Mantle Cell Lymphoma: Results From Large Real-World Cohorts. J Clin Oncol. 2023 Jan 20;41(3):541-554. doi: 10.1200/JCO.21.02698.

5.. Eyre TA, Bishton MJ et al. Diagnosis and management of mantle cell lymphoma: A British Society for Haematology Guideline. *Br J Haematol*. 2024; 204(1): 108–126.