Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

One Wales Medicines Assessment Group Recommendation
Bendamustine in combination with rituximab for the treatment of previously untreated and relapsed mantle cell lymphoma (OW09)

Date of advice: March 2017
Date of last review: April 2026
AWTTC reference number: OW09

Bendamustine in combination with rituximab can be made available within NHS Wales for the treatment of previously untreated and relapsed mantle cell lymphoma in patients currently deemed unsuitable for anthracycline-based therapy or other health technology appraisal-approved regimens.

The risks and benefits of the off-label use of bendamustine plus rituximab for this indication should be clearly stated and discussed with the patient to allow informed consent.

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This recommendation has been endorsed by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.

This advice has been reviewed 7 times by OWMAG since its issue in 2017 with no new evidence identified to affect the current recommendation. Therefore, this advice will no longer undergo review by OWMAG unless new evidence becomes available.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions.

One Wales advice assists consistency of access across NHS Wales.

AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Seventh Review of One Wales Decision – January 2026
OW09: Bendamustine in combination with rituximab for the treatment of previously untreated and relapsed mantle cell lymphoma

This report was prepared by the All Wales Therapeutics and Toxicology Centre in January 2026. It summarises any new evidence available and patient outcome data collected since the last review in October 2023.

Background: Bendamustine with rituximab (BR) is available in NHS England through clinical commissioning for the treatment of previously untreated and relapsed and refractory mantle cell lymphoma. Although rituximab is not licensed for treating mantle cell lymphoma, the National Institute for Health and Care Excellence (NICE) mantle cell lymphoma treatment pathway recommends it in combination with chemotherapy as first-line treatment of advanced-stage mantle cell lymphoma.
A cohort of patients, identified through data from individual patient funding request panels, and clinicians in Wales, have confirmed there to be an unmet need within the service. This cohort includes people with untreated and relapsed mantle cell lymphoma for whom anthracycline-based therapy is unsuitable. Based on this unmet need, this medicine combination was considered suitable for assessment via the One Wales process. Clinical experts consulted for this review supported the ongoing need for the option for use in NHS Wales for this cohort of patients.

Current One Wales Decision: Supported with restrictions

Licence status: Off-label use for this licensed medicine combination.

Guidelines: Since the last review one guideline has been updated and a new guideline published. The British Society for Haematology (BSH) guideline for diagnosis and management of mantle cell lymphoma was updated in 2023. The guideline recommends BR as one of the first line treatment options for patients with mantle cell lymphoma who are unsuitable for transplant or considered frail.

European Haematology Association (EHA) EU guidelines published in 2025 recommend bendamustine and rituximab followed by rituximab maintenance, as first-line treatment options for patients with mantle cell lymphoma aged ≥ 65–70 years who are unsuitable for intensive therapy.

Licensed alternative medicines or Health Technology Assessment advice for alternative medicines:

NICE TA1081: Zanubrutinib is recommended for treating relapsed or refractory mantle cell lymphoma in adults who have had 1 line of treatment only. Published: 10 July 2025

NICE ID6155: Acalabrutinib with bendamustine and rituximab for untreated mantle cell lymphoma, (in progress) expected publication date 4 June 2026.

NICE ID6569: Ibrutinib with R-CHOP (rituximab with cyclophosphamide, doxorubicin, vincristine and prednisolone) for untreated mantle cell lymphoma when an autologous stem cell transplant (ASCT) is suitable, (in progress) expected publication date to be confirmed.

Effectiveness: A literature search conducted by AWTTC identified one network meta-analysis relevant to the indicated recommendation. Clinical experts highlighted a study that provided an unplanned, indirect comparison relevant to the review.

Lewis et al (2025) report on a randomised, open-label superiority trial (ENRICH) conducted in patients 60 years and older with untreated MCL. Patients received either ibrutinib plus rituximab or rituximab plus immunochemotherapy (1:1). Ibrutinib plus rituximab is off-label for this indication and is not a relevant comparator therefore results of this arm are not reported for this review. Patients were stratified by investigator choice of immunochemotherapy prior to randomisation. In all, 53 patients received R-CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) and 145 received BR. Although the trial was not designed to compare R-CHOP with BR, survival outcomes for patients treated with BR were numerically superior when indirectly compared to those treated with R-CHOP. Probability of 5-year progression free survival (PFS) for the R-CHOP group was 19% (95% confidence interval [CI], 11 to 35) and for the BR group was 47% (95% CI, 39 to 57). Probability of 5-year overall survival was 46% (95% CI, 34 to 64) and 58% (95% CI, 50 to 68) for R-CHOP and BR respectively.

Jing et al (2023) conducted a meta-analysis of randomised controlled trials to assess the efficacy of front-line immunochemotherapy for mantle cell lymphoma (MCL) patients who are ineligible for transplants. Nine studies were included in the analysis of which five compared BR. In the analysis of progression-free survival (PFS), compared with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), BR plus ibrutinib followed by rituximab maintenance ranked highest (hazard ratio [HR] 0.14, 95% credible interval [CI] 0.02 to 0.99). BR followed by rituximab maintenance ranked second (HR 0.19, 95% CI 0.034 to 0.99); bendamustine, bortezomib and rituximab ranked third (HR 0.26, 95% CI

0.05 to 1.3) and BR alone ranked fourth (HR 0.3, 95% CI 0.08 to 1.0). For overall survival (OS) compared with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), BR ranked second (HR 0.86, 95% CI 0.35 to 2.1) to VR-CAP (bortezomib, rituximab, cyclophosphamide, doxorubicin, and prednisone [HR 0.66, 95% CI 0.37 to 1.2]).Results of this meta-analysis suggest that the BR regimen may provide better survival for MCL patients compared to the R-CHOP regimen. The authors concluded that BR plus ibrutinib with rituximab maintenance should be used as a first choice for improving PFS in MCL patients who are unsuitable for transplantation. BR plus ibrutinib is not licensed for this indication.

Safety: No relevant safety analyses were identified in this repeat literature search.

Cost-effectiveness: No relevant cost-effectiveness analyses identified in the repeat literature search.

Budget impact: Six patients in South East Wales have received treatment with BR in the 2 years since the last review. Extrapolating these figures to the population for all of Wales provides an estimate of 6 patients treated annually. This is lower than the original estimate of 12 patients, however, there are more health technology-assessed treatment options available for mantle cell lymphoma since the original assessment in 2017. No further information on patient numbers has been provided on which to assess the budget impact.

Impact on health and social care services: Minimal.

Patient outcome data: Six patients have received treatment with BR in Southeast Wales, [confidential information removed]. Clinicians note the limited usage of this treatment in Wales but would value its continued availability through One Wales when treatment is required.

Next review date: This advice has been reviewed annually by OWMAG since its issue in 2017 with no new evidence identified to affect the current recommendation. Therefore, this advice will no longer undergo review by OWMAG unless new evidence becomes available.

References: a full reference list is available on request.

This document includes evidence published since the last review or full assessment of this medicine for the indication under consideration. It does not replace the original full evidence status report. Any previous reviews and the original full evidence status report are available on request by email to AWTTC@wales.nhs.uk.

Care has been taken to ensure the information is accurate and complete at the time of publication. However, the All Wales Therapeutics and Toxicology Centre (AWTTC) do not make any guarantees to that effect. The information in this document is subject to review and may be updated or withdrawn at any time. AWTTC accept no liability in association with the use of its content. An Equality and Health Impact Assessment (EHIA) has been completed in relation to the One Wales policy and this found there to be a positive impact. Key actions have been identified and these can be found in the One Wales Policy EHIA document.

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