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

# Bendamustine in combination with rituximab for the treatment of previously untreated and relapsed mantle cell lymphoma (OW09)

**February 2024**

## ONE WALES INTERIM DECISION

**Bendamustine in combination with rituximab for the treatment of previously untreated and relapsed mantle cell lymphoma**

**Date of original advice: March 2017**
**Date of review: December 2023**

**The following One Wales Medicines Assessment Group (OWMAG) recommendation has been noted by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.**

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.

Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after two years or earlier if new evidence becomes available.

**Clinician responsibility**
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment Group decision.

**Health board responsibility**
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes.

**One Wales advice promotes consistency of access across NHS Wales.**

**This is a summary of new evidence available and patient outcome data collected, to inform the review.**

**This report was prepared by the All Wales Therapeutics and Toxicology Centre in October 2023. It summarises any new evidence available and patient outcome data collected since the last review in October 2022.**

**Background:** Bendamustine with rituximab 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, confirmed there to be an unmet need within the service. This cohort included 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:** No updates to guidelines since last review.

**Licensed alternative medicines or Health Technology Assessment advice for alternative medicines:**
NICE ID3975: pirtobrutinib for treating relapsed or refractory mantle cell lymphoma. Currently in scoping, publication TBC.

NICE ID6155: acalabrutinib with bendamustine and rituximab for untreated mantle cell lymphoma. Currently in scoping, publication TBC.

NICE ID3879: venetoclax with ibrutinib for treating relapsed mantle cell lymphoma. Currently in scoping, publication TBC.

**Effectiveness:**
A repeat literature search conducted by AWTTC identified one study relevant to the indicated recommendation.

The Swedish mantle cell lymphoma (MCL) project (Jerkeman et al. 2023) is a nationwide assessment of treatment strategies and outcomes in MCL. Patients diagnosed with MCL between 2006–2018 (n = 1367) were followed up to August 2021. Bendamustine/rituximab (BR) was the most common first (n = 368) and second-line (n = 185) treatment regimen used. Median progression free survival (PFS) from treatment initiation for BR, Nordic MCL2 regimen (n = 342), and rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP; n = 165) was 2.7 (95% CI: 2.1–3.2), 5.1 (95% CI: 4.2–6.1) and 1.5 (95% CI: 1.1–2.0) years respectively. Median overall survival (OS) for the same treatments was 4.1 (95% CI: 3.5–5.0), 11.7 (95%

CI: 7.8–not reached) and 2.9 (95% CI: 2.2–4.1) years respectively. When considering disease progression (by first relapse within 24 months or after 24 months), treatment with first line BR resulted in similar rates of OS and PFS, whereas such an effect following treatment with Nordic MCL2 and R-CHOP was less apparent (with first relapse within 24 months trending towards poorer OS and PFS rates). Median PFS from initiation of second-line BR was 1.2 years (95% CI, 0.9–1.4), and median OS was 2.2 years (95% CI: 1.6–3.0); this effect was seen across all regimens.

**Safety:** No relevant safety analyses identified in the repeat literature search.

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

**Budget impact**: No information on patient numbers has been provided.

**Impact on health and social care services:** Minimal.

**Patient outcome data:** No patient outcome data have been received.

**Evaluation of evidence**

The clinical evidence presented supports the current use of bendamustine with rituximab as a treatment option in line with the current One Wales decision. Bendamustine in combination with rituximab for the treatment of mantle cell lymphoma should only be used in circumstances where other licensed and health technology appraisal-approved regimens are unsuitable.

**Next review date:** 24 months

**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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