



# 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**

**July 2019**

### **ONE WALES INTERIM COMMISSIONING DECISION**

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

**Date of original advice: April 2017**

**Date of review: July 2019**

**The following Interim Pathways Commissioning Group (IPCG) recommendation has been endorsed by health board Chief Executives.**

Bendamustine in combination with rituximab can continue to 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.

Bendamustine in combination with rituximab is not a licensed regimen to treat this indication and is therefore 'off-label'. Each provider organisation must ensure all internal governance arrangements are completed before these medicines are prescribed in combination.

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

Providers should consult the [General Medical Council Guidelines](#) on prescribing unlicensed medicines before any off-label medicines are prescribed.

This advice will be reviewed after 12 months 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 Interim Commissioning decision.

#### **Health board responsibility**

Health boards will take responsibility for implementing One Wales Interim Commissioning decisions and ensuring that a process is in place for monitoring clinical outcomes.

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

**One Wales Interim Commissioning Process  
Interim Pathways Commissioning Group (IPCG) summary of decision  
rationale**

Medicine: **bendamustine in combination with rituximab**

Indication: **treatment of previously untreated and relapsed mantle cell lymphoma**

Meeting date: **29 May 2019**

<b>Criteria</b>	<b>IPCG opinion</b>
Final recommendation	IPCG recommends that the current One Wales decision should remain unchanged.
Summary of rationale	IPCG are content that there is no new significant information or evidence to warrant a full reassessment of bendamustine in combination with rituximab.

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

### **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<sup>1,2</sup>. 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<sup>3</sup>.

A cohort of patients had been identified through data from individual patient funding request panels and clinicians in Wales considered 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.

### **Current One Wales Interim Commissioning Decision**

Bendamustine in combination with rituximab can continue to 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. May 2018.

### **Licence status**

Bendamustine in combination with rituximab for the treatment of mantle cell lymphoma is off-label.

### **Guidelines**

British Journal of Haematology: Guideline for the management of mantle cell lymphoma (2018)<sup>4</sup>. The guideline recommends that the first-line treatment of patients who are unsuitable for autologous stem cell transplantation should be rituximab in combination with cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) as this gives the best outcome data. However, rituximab in combination with bendamustine is noted to be efficacious and to have a more favourable side effect profile. The guideline states that there is no standard approach for relapse<sup>4</sup>.

European Society for Medical Oncology consensus-based recommendations for the clinical management of elderly patients with malignant lymphoma (2018)<sup>5</sup>. The panel recommendations for the first-line treatment of mantle cell lymphoma in elderly patients include bendamustine with rituximab as an option for fit patients; and a reduced dose of bendamustine with rituximab as an option for vulnerable patients with or without severe comorbidities. Bendamustine with rituximab is not included as a treatment option for relapsed or refractory disease<sup>5</sup>.

### **Licensed alternative medicines/Health Technology Appraisal advice for alternative medicines**

A technology appraisal is in progress with NICE: ibrutinib for untreated mantle cell lymphoma<sup>6</sup>. Ibrutinib is not yet licensed for this indication and the expected publication of NICE advice is to be confirmed.

### **Efficacy/Effectiveness**

Five-year follow-up data of the BRIGHT study has been published as a report<sup>7</sup>. The associated conference abstract was described in the 2018 One Wales review report. Bendamustine plus rituximab demonstrated better long-term disease control than R-CHOP or rituximab plus cyclophosphamide, vincristine and prednisone (R-CVP) in patients with treatment-naïve non-Hodgkin's lymphoma or mantle cell lymphoma, as previously reported<sup>7</sup>.

### **Safety**

Safety results were published for the BRIGHT five-year follow-up study<sup>7</sup>. A statistically significantly ( $p = 0.022$ ) higher incidence of secondary malignancy was observed in the bendamustine plus rituximab group compared with the R-CHOP/R-CVP group, most notably in the incidence of squamous and basal cell carcinomas of the skin. Other safety signals were in line with those previously reported<sup>7</sup>.

**Cost effectiveness**

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

**Budget impact**

[Confidential data removed.]

**Impact on health and social care services**

The impact on the service remains minimal.

**Patient outcome data**

[Confidential data removed.]

**References**

1. NHS England Specialised Commissioning Team. Clinical Commissioning Policy: Bendamustine with rituximab for first line treatment of mantle cell lymphoma (all ages). July 2018. Available at: <https://www.england.nhs.uk/publication/clinical-commissioning-policy-bendamustine-with-rituximab-for-first-line-treatment-of-mantle-cell-lymphoma-all-ages/>. Accessed April 2019.
2. NHS England Specialised Commissioning Team. Clinical Commissioning Policy: Bendamustine with rituximab for relapsed and refractory mantle cell lymphoma (all ages). June 2018. Available at: <https://www.england.nhs.uk/publication/clinical-commissioning-policy-bendamustine-with-rituximab-for-relapsed-and-refractory-mantle-cell-lymphoma-all-ages/>. Accessed April 2019.
3. National Institute for Health and Care Excellence. Non-Hodgkin's lymphoma overview. 2019. Available at: <https://pathways.nice.org.uk/pathways/non-hodgkins-lymphoma>. Accessed April 2019.
4. McKay P, Leach M, Jackson B et al. Guideline for the management of mantle cell lymphoma. *British Journal of Haematology*. 2018;182(1):46-62.
5. Buske C, Hutchings M, Ladetto M et al. ESMO Consensus Conference on malignant lymphoma: general perspectives and recommendations for the clinical management of the elderly patient with malignant lymphoma. *Annals of Oncology*. 2018;29:544-562.
6. National Institute for Health and Care Excellence. Technology Appraisal in development ID1221. Ibrutinib for untreated mantle cell lymphoma. Expected publication date TBC. Available at: <https://www.nice.org.uk/guidance/indevelopment/gid-ta10185>. Accessed April 2019.
7. Flinn I, van der Jagt R, Kahl B et al. First-line treatment of patients with indolent non-hodgkin lymphoma or mantle-cell lymphoma with bendamustine plus rituximab versus R-CHOP or R-CVP: results of the BRIGHT 5-year follow-up study. *Journal of Clinical Oncology*. 2019.