www.scottishmedicines.org.uk

Advice document
SMC2819

zanubrutinib hard-capsules (Brukinsa®)

BeiGene

04 July 2025

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and, following review by the SMC executive, advises NHS Boards and Area Drug and Therapeutics Committees (ADTCs) on its use in NHSScotland. The advice is summarised as follows:

ADVICE: following an abbreviated submission

zanubrutinib (Brukinsa®) is accepted for use within NHSScotland.

Indication under review: as monotherapy for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

Zanubrutinib offers an additional treatment choice in the therapeutic class of Bruton's tyrosine kinase inhibitors (BTKi).

Another BTKi was accepted for use under the end of life and ultra-orphan process.

This advice applies only in the context of approved NHSScotland Patient Access Scheme (PAS) arrangements delivering the cost-effectiveness results upon which the decision was based, or PAS/ list prices that are equivalent or lower.

Co-Vice Chair
Scottish Medicines Consortium

Published 11 August 2025

1. Clinical Context

1.1. Medicine background

Zanubrutinib (Brukinsa®) is a highly selective, irreversible inhibitor of Bruton's tyrosine kinase (BTK), which blocks B-cell receptor-induced BTK activation thereby inhibiting proliferation and survival of malignant B-cells. The recommended total daily dose of zanubrutinib is 320 mg. The daily dose may be taken either once daily (four 80 mg capsules) or divided into two doses of 160 mg twice daily (two 80 mg capsules). Treatment should be continued until disease progression or unacceptable toxicity. [1, 2]

1.2. Relevant comparator

Ibrutinib (Imbruvica®) is another oral BTK inhibitor within the same therapeutic class as zanubrutinib. Ibrutinib as a single agent is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) (SMC 1150/16). [3]

2. Summary of Clinical Evidence

2.1. Evidence to support comparable efficacy with relevant comparators

Two studies supported the marketing authorisation of zanubrutinib for the licensed indication above. The studies were multicentre, open-label and single arm. BGB-3111-AU-003 was an international phase I/II study that included patients with relapsed or refractory MCL. Part 1 of the study was a dose escalation phase and was followed by part 2, an expansion phase which included 32 patients with relapsed or refractory MCL treated with the licensed dose of zanubrutinib. BGB-3111-206 was a phase II study based in China, which enrolled 86 patients with relapsed or refractory MCL, patients were treated with 1 to 5 lines of prior therapy. The efficacy of zanubrutinib was demonstrated in both studies and safety outcomes were reported.[4, 5] The BGB-3111-AU-003 study observed an objective response rate (ORR) of 84% (95% CI 67.2 to 94.7) at a median follow up of 18.8 months. In the BGB-3111-206 study the ORR was 84% (95% CI, 74 to 91) at a median follow up of 18.4 months.

There is no direct evidence comparing zanubrutinib (320 mg daily) and ibrutinib (560 mg daily), and so an unanchored matching adjusted indirect comparison (MAIC) was conducted to compare their efficacy and safety for the treatment of relapsed or refractory MCL. Outcomes assessed included progression-free survival, overall survival, and four safety outcomes related to grade ≥3 treatment emergent adverse events. BGB-3111-AU-003 and BGB-3111-206 were pooled to provide data for zanubrutinib[4,5], and data for ibrutinib came from a pooled analysis of one RCT and two single-arm studies.[6]

Notwithstanding the limitations inherent in an unanchored MAIC, the results provide reasonable assurance that the clinical effectiveness of zanubrutinib is similar to that of ibrutinib in adult patients with MCL who have received at least one prior therapy.

3. Company Estimate of Eligible Population, Uptake and Budget Impact

3.1. Company's number of patients assumed to be eligible for treatment

SMC is unable to publish the estimated patient numbers as the company considered that these were commercial in confidence.

3.2. Budget Impact assumption

Medicines reviewed under the abbreviated submissions process are estimated to have a limited net budget impact and resource allocation across NHSScotland.

*Other data were also assessed but remain confidential.**

References

1. BeiGene. Zanubrutinib hard capsules (Brukinsa®) Summary of product characteristics. Electronic Medicines Compendium www.medicines.org.uk/emc/ Last updated [05 December 2025].
2. Medicines & Healthcare products Regulatory Agency. Public Assessment Report zanubrutinib 80 mg hard capsules (brukinsa), PLGB53789/0002. Available at www.products.mhra.gov.uk last updated June 2023.
3. Janssen-Cilag International NV. Ibrutinib film-coated tablets (Imbruvica®) Summary of product characteristics. European Medicines Agency www.ema.europa.eu. Last accessed [19 May 2025].
4. Tam CS. Zanubrutinib for the treatment of relapsed or refractory mantle cell lymphoma. Blood Advances. 2021.
5. Song Y, Zhou K, Zou D, Zhou J, Hu J, Yang H. Zanubrutinib in relapsed/refractory mantle cell lymphoma: long-term efficacy and safety results from a phase 2 study. Blood. 2022.
6. Rule S. Outcomes in 370 patients with mantle cell lymphoma treated with ibrutinib: a pooled analysis from three open-label studies. Br J Haematol. 2017;179:430-8.

This assessment is based on data submitted by the applicant company up to and including 23 June 2025.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

Medicine prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice is based on the estimation of at least similar comparative efficacy and limited net budget impact compared with other medicinal products, within the same therapeutic class, that are in routine use within NHSScotland.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after evaluation of the evidence submitted by the company. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.