

5.26 ZANUBRUTINIB, Tablet 160 mg, Brukinsa[®], BeiGene AUS Pty Ltd

1 Purpose of Submission

- 1.1 The Category 4 submission requested to list zanubrutinib (Brukinsa[®]) 160 mg tablet under the same circumstances as the PBS-listed 80 mg capsule on a cost-minimisation basis.
- 1.2 The submission advised that the sponsor would apply to delist the 80 mg capsule should the 160 mg tablet be recommended and listed, and anticipated PBS delisting and discontinuation by 1 December 2026.

2 Background

- 2.1 At the time of consideration, the 80 mg capsule was listed for the treatment of relapsed or refractory (R/R) mantle cell lymphoma (MCL), Waldenström macroglobulinaemia (WM), R/R and treatment naïve chronic lymphocytic leukaemia (CLL) and small lymphocytic lymphoma (SLL).
- 2.2 The recommended daily dose for these indications is 320 mg taken as either 320 mg (four 80 mg capsules) once daily, or as 160 mg (two 80 mg capsules) twice daily.

Registration status

- 2.3 Zanubrutinib 160 mg tablet was registered on the Australian Register of Therapeutic Goods (ARTG) on 9 October 2025 for the treatment of MCL, WM, CLL and SLL. Zanubrutinib 80 mg capsule is ARTG registered for the same indications.

Previous PBAC consideration

- 2.4 The 160 mg tablet had not been considered by the PBAC previously.

3 Requested listing

- 3.1 The submission requested listing the 160 mg tablet under the same circumstances as the PBS-listed 80 mg capsule.
- 3.2 An abridged listing is presented in this section. Refer to Section 7 for the full recommended restriction.

Public Summary Document – November 2025 PBAC Meeting

Category / Program: GENERAL – General Schedule (Code GE)					
MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
medicinal product pack					
ZANUBRUTINIB					
zanubrutinib 160 mg tablet, 60	NEW x 4 MP	1	60	5	Brukinsa
Indications (on separate PBS item codes):					
Authority Required					
<ul style="list-style-type: none"> • MCL (Restriction Summary 124951 / Treatment of Concept 12495 and Restriction Summary 12500 / ToC 12500) • WM (Restriction Summary 13028/ Treatment of Concept: 13008 and Restriction Summary 13026 / Treatment of Concept: 12999) • Naïve CLL/SLL (Restriction Summary 14337/ Treatment of Concept: 14337) • R/R CLL/SLL (Restriction Summary 14789/ Treatment of Concept: 14788) 					

3.3 The proposed maximum quantities and number of repeats of the 160 mg tablet would provide sufficient supply for the loading dose and 6 months of treatment, consistent with the 80 mg capsule listings.

3.4 At the July 2025 PBAC meeting, the PBAC recommended that zanubrutinib be made available for prescribing by nurse practitioners where prescribing continues existing treatment with the medicine and patient care is being shared with a medical practitioner.

4 Comparator

4.1 The submission nominated the 80 mg strength of zanubrutinib as the comparator for the same indications (MCL, WM, Naïve chronic CLL and SLL).

4.2 At its July 2021 PBAC meeting, the PBAC considered that ibrutinib is an appropriate comparator and acalabrutinib a relevant near-market comparator for zanubrutinib for the treatment of patients with MCL. The listing was recommended on a cost-minimisation basis against ibrutinib (Public Summary Document [PSD] July 2021 PBAC meeting). The PBAC considered that the equi-effective doses were:

- zanubrutinib 320 mg (four 80 mg capsules) taken orally once daily or 160 mg (two 80 mg capsules) twice daily being equivalent to ibrutinib 560 mg once daily, and advised that after adjustment for equi-effective doses, zanubrutinib should be listed on the PBS at a cost per day that is no higher than the cost per day of other BTK inhibitors recommended for listing by the PBAC for the treatment of MCL

4.3 At its July 2021 and March 2022 PBAC meetings, the PBAC considered that rituximab monotherapy is an appropriate comparator for zanubrutinib for the treatment of treatment-naïve patients WM and bendamustine+rituximab an appropriate comparator for the relapsed/refractory WM population. The PBAC recommended Zanubrutinib for WM on cost-utility analysis (PSD March 2021 and PSD March 2022).

4.4 At its March 2023 meeting, the PBAC considered that venetoclax plus obinutuzumab is an appropriate comparator for zanubrutinib for treatment of naïve CLL or SLL. The PBAC also considered that ibrutinib and acalabrutinib were appropriate comparators

Public Summary Document – November 2025 PBAC Meeting

for zanubrutinib for the treatment of relapsed/refractory CLL or SLL. The PBAC recommended that the listing of zanubrutinib would be cost-effective if it were cost-minimised to venetoclax plus obinutuzumab for the treatment of naïve CLL or SLL and to ibrutinib for the treatment of relapsed/refractory CLL or SLL (PSD March 2023 PBAC meeting). The equi-effective doses were:

- Naïve CLL or SLL: one initial and 8.67 continuing venetoclax scripts plus 7.355 obinutuzumab scripts are equivalent to 70.73 months of zanubrutinib treatment at a dose of 304 mg daily (68.09 zanubrutinib scripts).
- relapsed/refractory CLL or SLL: zanubrutinib 320 mg once daily (or 160 mg twice daily) = ibrutinib 420 mg once daily.

- 4.5 At its March 2022 meeting, the PBAC advised that zanubrutinib 80 mg capsule was more cost-effective than rituximab monotherapy and bendamustine+rituximab for the treatment of MW (zanubrutinib PSD March 2022 PBAC meeting). At its March 2023 meeting, the PBAC advised ibrutinib as an appropriate pricing comparator for zanubrutinib 80 mg capsule for the treatment of MLC, and relapsed/refractory CLL or SLL (zanubrutinib PSD July 2021 & March 2023 PBAC meeting). The PBAC advised that this pricing advice should apply to zanubrutinib 160 mg tablets.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer inputs

- 5.2 The PBAC noted and welcomed input from Rare Cancers Australia and Lymphoma Australia, as well as several individual patients and carers, via the Consumer Input facility on the PBS website. These organisations and individuals supported the PBS listing of the new form of zanubrutinib, highlighting that the 160 mg tablet offers a simplified dosing regimen, which may improve patient adherence, reduce pill burden, and enhance quality of life for people living with rare blood cancers. Carer perspectives described reduced treatment burden and improved wellbeing for both patients and families. The PBAC noted that some input referenced experiences with other therapies or broader issues of access, rather than zanubrutinib specifically. All consumer input was considered as part of the Committee's deliberations.

Justification of the requested listing

- 5.3 The submission referenced a phase I bioequivalence study, BGB-3111-114, to demonstrate that a 160 mg tablet is bioequivalent to 2 × 80 mg capsules. It likewise referenced a phase I bioavailability study, BGB-3111-115, to demonstrate that the 160 mg tablet is well tolerated and has no difference in safety profile compared to the 80 mg capsule. These trials were considered by the TGA as part of its assessment to register the 160 mg tablet.

Public Summary Document – November 2025 PBAC Meeting

Table 1: Clinical study report presented in the submission

Study ID	Protocol title	Purpose of the study
BGB-3111-114	Single-dose, Open-label, Randomized, Replicate Crossover Study in Healthy Adult Subjects	To demonstrate the bioequivalence of the 160 mg tablet to the 2x80 mg capsule.
BGB-3111-115	A Single-dose, Open-label, Randomized, Crossover Study in Healthy	To assess the bioavailability of the 160 mg tablet compared with 2x80 mg capsule.

Source: TGA clinical evaluation report of zanubrutinib 160 mg tablet.

- 5.4 The submission claimed the non-inferior comparative effectiveness and safety of 2 x 80 mg capsules to the 160 mg tablet for each of the respective indications.
- 5.5 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable.

Pricing considerations

- 5.6 The submission presented a cost-minimisation analysis of the 160 mg tablet versus the 80 mg capsule based on a claim of non-inferior effectiveness and safety.
- 5.7 The submission proposed an equi-effective daily dose of 320 mg as 2 x 160 mg tablets being equal to 4 x 80 mg capsules, consistent with the medicine doses and treatment regimens in the included studies and the draft TGA Product Information of zanubrutinib.

Table 2: Proposed AEMPs and equi-effective doses in the submission

Item	Zanubrutinib, 80 mg capsule	Zanubrutinib, 160 mg tablet
Equi-effective dose	320 mg daily	320 mg daily
Tablets or capsules/patient/day	4	2
Pack quantity	120	60
Packs/patient/30 days	1	1
Published AEMP/pack	\$7,769.96	\$7,769.96
Total drug cost/patient/30 days (\$)	\$7,769.96	\$7,769.96

Source: Table 32 of the submission, AEMP = approved ex-manufacturer price

- 5.8 The submission requested the existing effective pricing and Special Pricing Arrangement (SPA) for each PBS listed indication of the 80 mg capsule to apply to the 160 mg tablet. The PBAC considered this request was appropriate.
- 5.9 While not a matter for PBAC consideration, the PBAC noted that listing of the proposed form would not trigger a first new brand statutory price reduction under 99ACB(3A) of the Act as the form is not considered a new presentation of the existing listed form.

Public Summary Document – November 2025 PBAC Meeting

Table 3: Proposed effective price and Special Pricing Arrangement rebate per PBS listed indication

Item	Mantle cell lymphoma	Waldenström macroglobulinaemia	Chronic lymphocytic leukaemia or small lymphocytic lymphoma (first-line)	Chronic lymphocytic leukaemia or small lymphocytic lymphoma (relapsed/refractory)
Proposed effective AEMP: zanubrutinib 160 mg, 60 (\$)	████	████	████	████
Special Pricing Arrangement rebate ^a : current and proposed (%)	████	████	████	████

Source: Table 33 of the submission, AEMP = approved ex-manufacturer price

Estimated PBS usage and financial implications

5.10 The submission adopted a market share approach to estimate the utilisation and financial impact of listing the 160 mg tablet.

5.11 **Error! Reference source not found.** presents the estimated usage and financial implications of listing the 160 mg tablet. The submission estimated a nil net financial impact to the PBS/RPBS over a period of six years. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

Table 4: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts	████ ¹	████ ²	████ ³	████ ³	████ ³	████ ³
Estimated financial implications						
New PBS listing (\$)	████ ⁴	████ ⁵	████ ⁵	████ ⁵	████ ⁵	████ ⁵
Changed PBS listing (\$)	-████ ⁴	-████ ⁵	-████ ⁵	-████ ⁵	-████ ⁵	-████ ⁵
Net cost to PBS	\$0	\$0	\$0	\$0	\$0	\$0
New RPBS listing (\$)	████ ⁶	████ ⁶	████ ⁶	████ ⁶	████ ⁶	████ ⁶
Changed RPBS listing (\$)	-████ ⁶	-████ ⁶	-████ ⁶	-████ ⁶	-████ ⁶	-████ ⁶
Net cost to RPBS	\$0	\$0	\$0	\$0	\$0	\$0
Net financial implications						
Net cost to PBS/RPBS	\$0	\$0	\$0	\$0	\$0	\$0

Source: Submission’s financial model spreadsheet. Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme

The redacted values correspond to the following ranges:

¹ 10,000 to < 20,000

² 20,000 to < 30,000

³ 30,000 to < 40,000

⁴ \$70 million to < \$80 million

⁵ \$200 million to < \$300 million

⁶ \$0 to < \$10 million

5.12 As a Category 4 submission, no evaluation of the clinical evidence was undertaken.

6 PBAC Outcome

6.1 The PBAC recommended the listing of zanubrutinib (Brukinsa®) 160 mg tablet on the PBS under the same circumstances as the PBS-listed 80 mg capsule on a cost-minimisation basis.

Public Summary Document – November 2025 PBAC Meeting

- 6.2 The PBAC advised the equi-effective daily dose of 320 mg to be 2 x 160 mg tablets is equal to 4 x 80 mg capsules.
- 6.3 The PBAC advised that its July 2021, March 2022, and March 2023 pricing advice for zanubrutinib 80 mg (see paragraph 5.4) should apply to zanubrutinib 160 mg.
- 6.4 The PBAC considered the utilisation and financial estimates, and the estimated net financial impact to the PBS/RPBS over the first six years of listing, to be reasonable, based on the assumption that zanubrutinib 160 mg tablet is expected to only substitute for zanubrutinib 80 mg capsule.
- 6.5 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because zanubrutinib 160 mg tablet is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over zanubrutinib 80 mg capsule, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 6.6 The PBAC noted that this submission is not eligible for an Independent Review because it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 Pending implementation timing of the PBAC's July 2025 recommendations regarding nurse practitioner prescribing of haematology medicines (item 9.01 of the July 2025 meeting), if this November 2025 recommendation to list the new zanubrutinib strength proceeds to implementation before the July 2025 recommendation concerning nurse practitioners, add the new 160 mg strength as follows:

Public Summary Document – November 2025 PBAC Meeting

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MEDICINAL PRODUCT	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
ZANUBRUTINIB					
zanubrutinib 160 mg tablet, 60	NEW 3 MP	1	60	5	Brukinsa
Restriction Summary 14337/ Treatment of Concept: 14337: Authority Required					
Indication: Chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL)					
Treatment Phase: First line drug treatment of this indication					
Clinical criteria:					
The condition must be untreated with drug treatment at the time of the first dose of this drug; or					
Patient must have developed an intolerance of a severity necessitating permanent treatment withdrawal following use of another drug PBS-indicated as first-line drug treatment of CLL/SLL					
AND					
Clinical criteria:					
The treatment must only be prescribed for patients with active disease in accordance with the International Workshop on CLL (iwCLL) guidance (latest version) in relation to when to prescribe drug treatment for this condition					
AND					
Clinical criteria:					
The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this PBS indication.					
Treatment criteria:					
Patient must be undergoing initial treatment with this drug – this is the first prescription for this drug; or					
Patient must be undergoing continuing treatment with this drug – the condition has not progressed whilst the patient has actively been on this drug					

This restriction may be subject to further review. Should there be any changes made to the restriction the sponsor will be informed.

7.2 Should this November 2025 recommendation be implemented at the same time or after the July 2025 recommendation concerning nurse practitioner prescribing is implemented, then implement in line with the July 2025 recommendation (item 9.01) which will add the prescriber type of ‘NP’ for nurse practitioners to the prescribing rule as well as insert the following concepts to specify the conditions applying to nurse practitioners:

Treatment phase: Initial treatment (where it appears):

Treatment criteria:
Must be treated by a medical practitioner

Treatment phase: Continuing treatment (where it appears):

Treatment criteria:
Must be treated by a medical practitioner; or
Must be treated by a nurse practitioner where both of the following are occurring: (i) patient care is being shared with a medical practitioner, (ii) the prescription continues existing therapy with this medicine.

Public Summary Document – November 2025 PBAC Meeting

Initial versus Continuing treatment agnostic listings (i.e. no mention of initial or continuing):

Treatment criteria:
Must be treated by a medical practitioner; or
Must be treated by a nurse practitioner where both of the following are occurring: (i) patient care is being shared with a medical practitioner, (ii) the prescription continues existing therapy with this medicine.

8 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

9 Sponsor's Comment

The sponsor had no comment.