

5.21 DENOSUMAB, Injection 120 mg in 1 mL single use pre-filled syringe, Xgeva[®], Amgen Australia Pty Limited

1 Purpose of Submission

- 1.1 The Category 4 submission requested a General Schedule Authority Required (STREAMLINED) listings of a new form of denosumab (120 mg/1.0 mL injection, 1 mL pre-filled syringe; hereafter referred to as denosumab PFS) for the treatment of giant cell tumour of bone and bone metastases under the same circumstances as the currently listed denosumab (120 mg/1.7 mL injection, 1.7 mL vial; hereafter referred to as denosumab vial).

2 Background

- 2.1 Denosumab vial is currently listed on the PBS as General Schedule Authority Required (STREAMLINED) listings for giant cell tumour of bone and bone metastases.

Registration status

- 2.2 Denosumab PFS was TGA registered on 6 December 2024 for the:
- Prevention of skeletal related events in patients with multiple myeloma and in patients with bone metastases from solid tumours.
 - Treatment of giant cell tumour of bone in adults or skeletally mature adolescents that is recurrent, or unresectable, or resectable but associated with severe morbidity.
 - Treatment of hypercalcaemia of malignancy that is refractory to intravenous bisphosphonate.

Previous PBAC consideration

- 2.3 Denosumab PFS has not been previously considered by the PBAC.
- 2.4 At its July 2011 meeting, the PBAC considered and recommended denosumab vial as an Authority Required benefit for the treatment of bone metastases from breast cancer and hormone-resistant prostate cancer (pg 4, denosumab Public Summary Document (PSD), July 2011 PBAC meeting).
- 2.5 At its November 2013 meeting, the PBAC considered and recommended extending the listing of denosumab vial to include the treatment of giant cell tumour of bone in adults and skeletally mature adolescent patients (pg 6, denosumab PSD, November 2013 PBAC meeting).

Public Summary Document – March 2025 PBAC Meeting

2.6 At its November 2024 meeting, the PBAC recommended the new listing of the biosimilar brand of denosumab vial, Wyost, under the same circumstances as the PBS-listed reference brand, Xgeva, on a cost-minimisation basis (pg 7, denosumab PSD, November 2024 PBAC Meeting). Wyost has not yet listed on the PBS.

3 Requested listing

3.1 The submission requested the following new listings under the same circumstances as the existing denosumab vial listings. A shortened version of the requested listing is presented below in italics.

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
DENOSUMAB					
denosumab 120 mg/1.7 mL injection, 1.7 mL vial	10061M <i>MP NP</i>	1	1	5	Xgeva
<i>denosumab 120 mg/mL injection, 1 mL syringe</i>	<i>NEW</i> <i>MP NP</i>	1	1	5	
Restriction Summary / Treatment of Concept:					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Restriction Type: Authority required (Streamlined)					
Indication: Giant cell tumour of bone					

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
DENOSUMAB					
denosumab 120 mg/1.7 mL injection, 1.7 mL vial	5110Y <i>MP NP</i>	1	1	5	Xgeva
<i>denosumab 120 mg/mL injection, 1 mL syringe</i>	<i>NEW</i> <i>MP NP</i>	1	1	5	
Restriction Summary / Treatment of Concept:					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Restriction Type: Authority required (Streamlined)					
Indication: Bone metastases					
Restriction Summary / Treatment of Concept:					
Category / Program: GENERAL – General Schedule (Code GE)					
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners					
Restriction Type: Authority required (Streamlined)					
Indication: Bone metastases					

3.2 The pre-PBAC response stated that denosumab PFS should not be considered equivalent to any brand of denosumab vial noting that the forms are different. This was consistent with the PBAC recommendation that only the same form and strength

of denosumab vial should be treated as equivalent for the purposes of substitution (pg 8, denosumab PSD, November 2024 PBAC Meeting).

4 Comparator

- 4.1 The submission nominated denosumab vial as the main comparator. The PBAC considered that this was appropriate.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from individuals (3) and consumer group/organisations (1) via the Consumer Comments facility on the PBS website. The comments from the individuals emphasised the impact of myeloma on quality of life, particularly in reducing patients' ability to participate in activities crucial for social and mental well-being. The comments further expressed optimism about denosumab's potential to extend remission, save lives and offer convenient administration.
- 5.3 The PBAC noted input received from Rare Cancers Australia that outlined several benefits of treatment with denosumab, including ease of administration through injection, reduced burden of daily medication, and improved overall quality of life. The input highlighted concerns from patients about the need for regular doctor visits for injection, which can be challenging especially for those in rural or remote areas with limited access to healthcare facilities.

Clinical trials

- 5.4 The submission provided an overview of the approach in the TGA dossier to support bioequivalence based on evidence from study 20180142, an open-label, randomised, single-dose, parallel-group study in healthy subjects which assessed the bioequivalence of 120 mg denosumab subcutaneous (SC) dose when administered as 120 mg/mL PFS or as 2 x 60 mg/mL PFS.
- 5.5 The TGA Delegate Overview (DO) stated that the data from study 20180142 established bioequivalence between the 120 mg/mL and 60 mg/mL strengths of denosumab (i.e. 1 x 120 mg/mL PFS and 2 x 60 mg/mL PFS) and that no new safety concerns were reported. The DO noted that denosumab is always given SC (either from the vial or PFS) and the recommended total dose is 120 mg (regardless of concentration/strength of the drug product).
- 5.6 The TGA DO further noted that previous bioequivalence studies had demonstrated that:

- 60 mg/mL PFS denosumab is bioequivalent to 60 mg/mL denosumab vial (study 20050146).
- 1 x 120 mg/1.7 mL denosumab vial is bioequivalent to 2 x 60 mg/mL denosumab vial (study 20060446).

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

Clinical claim

- 5.8 The submission did not make any specific clinical claim. However, based on the content of the submission it is understood the applicant intends a claim of non-inferior comparative effectiveness and non-inferior comparative safety of denosumab PFS compared with denosumab vial.
- 5.9 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable.

Economic analysis

- 5.10 The submission did not provide a cost-minimisation approach and requested the same approved ex-manufacturer price (AEMP) and dispensed price for maximum quantity (DPMQ) for denosumab PFS as that of denosumab vial, stating the PFS and vial are bioequivalent with an equi-effective dose of 1 x denosumab 120 mg PFS = 1 x denosumab 120 mg vial.
- 5.11 As a Category 4 submission, the economic analysis has not been independently evaluated.

Estimated PBS usage and financial implications

- 5.12 The submission adopted a market share approach to estimate the utilisation and financial impact of listing denosumab PFS. The submission assumed that denosumab PFS would directly substitute for existing use of denosumab vial on a 1:1 basis. As such, the submission estimated the requested listing of denosumab PFS to be cost neutral to the PBS/RPBS.
- 5.13 Table 1 presents the estimated extent of use and the net financial implications to the PBS/RPBS of listing denosumab PFS.
- 5.14 The submission estimated that 100,000 to < 200,000 scripts would be supplied over the first six years of listing (30,000 to < 40,000 each year).
- 5.15 The submission estimated a nil net financial impact to the PBS/RPBS for the listing of denosumab PFS 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.

Public Summary Document – March 2025 PBAC Meeting

Table 1: 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	1	1	1	1	1
Estimated financial implications						
New PBS listing	2	2	2	2	2	2
Changed PBS listing	3	3	3	3	3	3
Net cost to PBS	4	4	4	4	4	4
New RPBS listing	4	4	4	4	4	4
Changed RPBS listing	3	3	3	3	3	3
Net cost to RPBS	4	4	4	4	4	4
Net financial implications						
Net cost to PBS/RPBS	4	4	4	4	4	4

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 30,000 to < 40,000

² \$10 million to < \$20 million

³ net cost saving

⁴ \$0 to < \$10 million

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of the new PFS form of denosumab (120 mg/1.0 mL injection, 1 mL pre-filled syringe) for the treatment of giant cell tumour of bone and bone metastases under the same circumstances as the currently listed vial form (120 mg/1.7 mL injection, 1.7 mL vial).
- 6.2 The PBAC considered the equi-effective dose of denosumab 120 mg PFS = denosumab 120 mg vial was appropriate.
- 6.3 The PBAC noted that the TGA established bioequivalence between denosumab PFS and denosumab vial based on evidence from study 20180142.
- 6.4 The PBAC noted its November 2024 recommendation of the biosimilar brand of denosumab vial, Wyost. The PBAC noted that the listing of Wyost or Xgeva PFS may trigger a first new brand statutory price reduction under division 3A of Part VII of the *National Health Act 1953*.
- 6.5 The PBAC noted the pre-PBAC response regarding the substitution between denosumab 120 mg vial and PFS presentations. The PBAC recalled its November 2024 consideration of Wyost, that only the same form and strength of denosumab vial should be treated as equivalent for the purposes of substitution (pg 8, denosumab PSD, November 2024 PBAC Meeting).
- 6.6 The PBAC considered that there would be no net financial implications to the PBS/RPBS as denosumab PFS is expected to list at the same price as denosumab vial with direct 1:1 substitution, resulting in no increase in overall market utilisation.
- 6.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because denosumab PFS is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over denosumab

Public Summary Document – March 2025 PBAC Meeting

vial, 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.

- 6.8 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 Add new medicinal product pack as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
DENOSUMAB					
denosumab 120 mg/1.7 mL injection, 1.7 mL vial	10061M MP NP	1	1	5	Xgeva
denosumab 120 mg/mL injection, 1 mL syringe	NEW MP NP	1	1	5	
Restriction Summary / Treatment of Concept:					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners				
	Restriction Type: Authority required (Streamlined)				
	Indication: Giant cell tumour of bone				
	Clinical criteria				
	Patient must be one in whom surgical resection is not feasible; or				
	Patient must be one in whom surgical resection is possible but surgery would result in significant morbidity				
	Population criteria				
	Patient must be an adult; or				
	Patient must be a skeletally mature adolescent				
	Administrative Advice:				
	Denosumab is not PBS-subsidised for use in patients who have undergone curative surgical resection.				
	*Continuing Therapy Only:., For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.				

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
DENOSUMAB					
denosumab 120 mg/1.7 mL injection, 1.7 mL vial	5110Y MP NP	1	1	5	Xgeva
denosumab 120 mg/mL injection, 1 mL syringe	NEW MP NP	1	1	5	

Public Summary Document – March 2025 PBAC Meeting

Restriction Summary / Treatment of Concept:	
	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners
	Restriction Type: Authority required (Streamlined)
	Indication: Bone metastases
	Clinical criteria
	The condition must be due to breast cancer
	Administrative Advice
	*Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.
Restriction Summary / Treatment of Concept:	
	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse Practitioners
	Restriction Type: Authority required (Streamlined)
	Indication: Bone metastases
	Clinical criteria
	The condition must be due to castration-resistant prostate cancer
	Administrative Advice
	*Continuing Therapy Only: For prescribing by nurse practitioners as continuing therapy only, where the treatment of, and prescribing of medicine for, a patient has been initiated by a medical practitioner. Further information can be found in the Explanatory Notes for Nurse Practitioners.

*Pending changing the ‘Continuing Therapy Only’ administrative note as per the recommendation of the November 2024 PBAC meeting to the review of PBS items for prescribing by nurse practitioners and endorsed midwives; the subset of PBS listings for Nurse Practitioner prescribing – Continuing Therapy Only review.

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

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.