

**5.30 DENOSUMAB,
Injection 60 mg in 1 mL pre-filled syringe,
Injection 120 mg in 1.7 mL,
Jubbonti[®], Wyost[®],
Sandoz Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 3 submission sought to list a new biosimilar brand of denosumab in the forms of 60 mg in 1 mL pre-filled syringe (Jubbonti[®]) under the same circumstances as the PBS-listed reference biologic Prolia[®], and 120 mg in 1.7 mL injection vial (Wyost[®]) under the same circumstances as the PBS-listed reference biologic Xgeva[®].

2 Background

- 2.1 Prolia is currently listed on the PBS as an Authority Required (STREAMLINED) listing for the treatment of osteoporosis (BMD T-score of -2.5 or less) in patients over 70 years old, and established osteoporosis (patients who have fracture due to minimal trauma).
- 2.2 Xgeva is currently listed on the PBS as an Authority Required (STREAMLINED) listing for the treatment of giant cell tumour of the bone, and bone metastases due to breast cancer or castration-resistant prostate cancer.
- 2.3 If listed, Jubbonti and Wyost will be the first PBS-listed biosimilar brands of denosumab.

Registration status

- 2.4 Jubbonti and Wyost were registered by the Therapeutic Goods Administration (TGA) on 24 August 2024, and determined to be biosimilar to Prolia and Xgeva, respectively.

Previous PBAC consideration

- 2.5 Jubbonti 60 mg in 1 mL pre-filled syringe and Wyost 120 mg in 1.7 mL injection vial have not been considered by the PBAC previously.
- 2.6 Prolia and Xgeva were first recommended for PBS listing by the PBAC in July 2010 and July 2011, respectively. These were subsequently listed on the PBS in December 2010 and December 2011, respectively.

3 Requested listing

- 3.1 The submission requested listing Jubbonti and Wyost under the same circumstances as Prolia and Xgeva respectively.
- 3.2 Additions proposed by the Secretariat were added in italics. As the submission did not request a change in the restriction criteria, an abridged version of the requested listing is presented below.

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	No.of Rpts	Available brands
DENOSUMAB						
denosumab 60 mg/mL injection, 1 mL syringe		5457F MP NP	1	1	0	^a Prolia ^a Jubbonti
Restriction Summary: 6548/ Treatment of Concept: 6548						
Concept ID (for internal Dept. use)		Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
		Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
PR level	New AA1	Administrative Advice: Biosimilar prescribing policy <i>Prescribing of the biosimilar brand Jubbonti is encouraged for treatment naive patients.</i>				
	29791	Administrative Advice: <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Medicines webpage (www.health.gov.au/health-topics/medicines).</i>				
7992		Indication: Osteoporosis				
Restriction Summary: 6524/ Treatment of Concept: 6524						
Concept ID (for internal Dept. use)		Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
		Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
8000		Indication: Established osteoporosis				

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	^a Xgeva ^a Wyost
Restriction Summary: 4504 / Treatment of Concept: 4504						
Concept ID (for internal Dept. use)		Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
		Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
PR level	10333	Administrative Advice: Denosumab is not PBS-subsidised for use in patients who have undergone curative surgical resection.				

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	7703	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.
	New AA1	Administrative Advice: Biosimilar prescribing policy <i>Prescribing of the biosimilar brand Wyost is encouraged for treatment naive patients.</i>
	29791	Administrative Advice: <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Medicines webpage (www.health.gov.au/health-topics/medicines).</i>
9579		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 MP NP	1	1	5	^a Xgeva ^a Wyost
Restriction Summary: 4158 / Treatment of Concept: 4158					
Concept ID (for internal Dept. use)	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
PR level	7703	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.			
	New AA1	Administrative Advice: Biosimilar prescribing policy <i>Prescribing of the biosimilar brand Wyost is encouraged for treatment naive patients.</i>			
	29791	Administrative Advice: <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Medicines webpage (www.health.gov.au/health-topics/medicines).</i>			
7699	Indication: Bone metastases				
Restriction Summary: 4150 / Treatment of Concept: 4150					
Concept ID (for internal Dept. use)	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
	Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
7699	Indication: Bone metastases				

4 Comparator

- 4.1 The submission nominated the respective reference brands of denosumab, Prolia and Xgeva, as the main comparator. 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 the Medical Oncology Group of Australia (MOGA) and Rare Cancers Australia via the Consumer Comments facility on the PBS website. The MOGA expressed its support for the listing of Jubbonti and Wyost. Rare Cancers Australia described a range of benefits of treatment with Jubbonti and Wyost including an alternative option to high-risk surgery, reduction of daily medication management, increase likelihood of living pain free and prevention of skeleton-related injuries.

Clinical trials

- 5.3 The submission presented the following clinical trials to support the claim of the biosimilarity of Jubbonti and Wyost to their respective reference brands.
- 5.4 The clinical trials presented in the submission formed part of the TGA submission to register Jubbonti and Wyost as biosimilar to Prolia and Xgeva respectively. The TGA Delegate's Overview advised that Jubbonti and Wyost demonstrated similar pharmacokinetics, efficacy and therefore bioequivalence compared to Prolia and Xgeva. Details of the trials are summarised in Table 1.

Table 1: Trials and associated reports presented in the submission

Trial ID	Protocol/Publication title	Study Objectives (Related to Safety)	Study Drug and Dose	No. of Subjects/ Patients Assigned to Treatment I
CGP24112101 (Phase I)	Pharmacokinetics and pharmacodynamics of the proposed biosimilar denosumab GP2411 and reference denosumab in healthy males.	Study in healthy males comparing the PK, PD, safety and immunogenicity of denosumab (JUBBONTI/WYOST) with EU approved denosumab (XGEVA), and US approved denosumab (XGEVA).	Treatments were administered as a single dose of 35 mg subcutaneously. The treatments were presented as 120 mg in 1.7 mL solution in single use vials.	502 patients randomised to treatment: 166 to JUBBONTI/WYOST, 171 to XGEVA-EU and 165 to XGEVA-US
NCT03974100 (Phase I/III)	Study Investigating PK, PD, Efficacy, Safety, and Immunogenicity of Biosimilar Denosumab (GP2411) in Patients With Postmenopausal Osteoporosis. PROTOCOL NUMBER CGP24112301	To compare the PK, PD, efficacy, safety and immunogenicity of denosumab - JUBBONTI/WYOST (GP2411) with denosumab -PROLIA in postmenopausal women with osteoporosis.	JUBBONTI/WYOST and PROLIA treatments were administered as a dose of 60 mg in 1 mL, by subcutaneous injection. Each participant was scheduled to receive three doses at 26-week intervals.	Sample size of 492 subjects with 246 in each arm.

Source: Table 2.3.1, p.13 of the submission.

5.5 As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

5.6 The submission claimed the non-inferior comparative effectiveness and non-inferior comparative safety of Jubbonti and Wyost compared with Prolia and Xgeva, respectively. This was on the basis that the TGA found Jubbonti and Wyost to be biosimilar to Prolia and Xgeva respectively. The TGA Delegate considered Jubbonti and Wyost to be biosimilar to Prolia and Xgeva with comparable pharmacokinetics, efficacy and safety.

5.7 The PBAC considered the claim of non-inferior comparative effectiveness was reasonable.

5.8 The PBAC considered the claim of non-inferior safety was reasonable.

Economic analysis

5.9 As a Category 3 submission, the economic analysis has not been independently evaluated.

5.10 The submission presented a cost-minimisation approach for Jubbonti and Wyost compared with Prolia and Xgeva, respectively. The equi-effective doses were estimated as Jubbonti 1 mg for Prolia 1 mg and Wyost 1 mg for Xgeva 1 mg.

Estimated PBS usage and financial implications

5.11 The submission adopted a market share approach to estimate the utilisation and financial impact of listing Jubbonti and Wyost. The submission extrapolated prescription data of Prolia and Xgeva from the 2018-2023 period on to Year 1 to Year 6 of the proposed listings of denosumab. The submission estimated an uptake ranging from 5% to 6% in Year 1 increasing to an uptake ranging from 17% to 32% in Year 6 between the two brands. This is presented in Table 2.

Table 2: Estimated denosumab prescriptions and market share of proposed listing

		Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
5457F	Prescriptions	1,224,052	1,300,969	1,377,885	1,454,802	1,531,718	1,608,635
	Annual change %	6.7%	6.3%	5.9%	5.6%	5.3%	5.0%
	Market share	5.0%	14.0%	16.0%	15.0%	16.0%	17.0%
10061M	Prescriptions	4,814	5,087	5,360	5,633	5,906	6,179
	Annual change %	6.0%	5.7%	5.4%	5.1%	4.8%	4.6%
	Market share	6.0%	29.0%	25.0%	29.0%	32.0%	32.0%
5110Y	Prescriptions	59,528	59,563	59,598	59,633	59,669	59,704
	Annual change %	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
	Market share	6.0%	29.0%	25.0%	29.0%	32.0%	32.0%
Total		1,288,395	1,365,619	1,442,844	1,520,069	1,597,293	1,674,518

Source: Main Body; Table 4.2-2 and 4.2-3, p.19

5.12 The requested price was based on the AEMP of the currently PBS listed denosumab brands. The DPMQ should be the same as the respective reference brand listings in order to list as a biosimilar listing for Prolia and Xgeva. It was noted that while the AEMPs were accurate, there were slight discrepancies in the DPMQ within the financial workbook for Jubbonti and Wyost. The pre-PBAC response highlighted that this was due to 1 July 2024 changes to dispensing fees and provided revised DPMQs which were the same as the comparators and provided an updated financial workbook.

5.13 The submission estimated that the financial impact of listing Jubbonti and Wyost would be cost-neutral over the first six years of listing. This is summarised in Table 3.

5.14 Although not a matter for the PBAC, the submission noted that the listing of Jubbonti and Wyost will trigger a 'first new brand' price reduction of 25% which may result in savings to the Government.

Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed ^a	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹	1 ¹
Estimated financial implications of denosumab (Jubbonti and Wyost)						
Cost to PBS/RPBS less co-payment	\$ ²	\$ ²	\$ ²	\$ ²	\$ ²	\$ ²
Estimated financial implications of other PBS-listed denosumab (Prolia and Xgeva)						
Cost to PBS/RPBS less co-payment	-\$ ²	-\$ ²	-\$ ²	-\$ ²	-\$ ²	-\$ ²
Net financial implications						
Net cost to PBS/RPBS	\$0	\$0	\$0	\$0	\$0	\$0

Source: Financial table workbook; Section 4; provided as part of the submission.

^a Assuming number of scripts per patient per year as estimated by the submission.

MBS = Medical Benefits Scheme; PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

The redacted values correspond to the following ranges:

¹ 1,000,000 to < 2,000,000

² \$300 million to < \$400 million

Quality Use of Medicines

5.15 It was noted all four products (Jubbonti, Wyost, Prolia and Xgeva) share the same administration advice on technique in the product information (PI) which states, “Administration should be performed by an individual who has been adequately trained in injection techniques.” In addition, the PI for the biosimilars, Jubbonti and Wyost, share the same manner of administration, container packaging and storage requirements to its respective reference brands, Prolia and Xgeva.

6 PBAC Outcome

6.1 The PBAC recommended the new listings of denosumab in the forms of 60 mg in 1 mL pre-filled syringe (Jubbonti) under the same circumstances as the PBS-listed reference biologic Prolia, and 120 mg in 1.7 mL injection vial (Wyost) under the same circumstances as the PBS-listed reference biologic Xgeva.

6.2 The PBAC considered the nomination of Prolia and Xgeva as respective comparators was appropriate.

6.3 The PBAC accepted the claim of the non-inferior comparative effectiveness and safety of Jubbonti and Wyost compared to Prolia and Xgeva, respectively. This was based on the TGA determination that Jubbonti and Wyost are biosimilar to Prolia and Xgeva, respectively.

6.4 The PBAC considered it was appropriate for Jubbonti and Wyost to be cost-minimised to the existing PBS listed brand of denosumab. The PBAC considered the equi-effective doses were:

- 1 mg of Jubbonti and 1 mg of Prolia

- 1 mg of Wyost and 1 mg of Xgeva
- 6.5 The PBAC noted the listing of Jubbonti and Wyost on the PBS was not expected to increase the overall use of denosumab on the PBS as it is expected that Jubbonti and Wyost would substitute for PBS listed Prolia and Xgeva, respectively. The PBAC therefore considered the estimated net cost to the PBS/RPBS would be nil.
- 6.6 The PBAC acknowledged the pre-PBAC response provided an updated financial workbook and noted no concerns with the revised DPMQ.
- 6.7 At the same meeting, the PBAC considered and reviewed a subset of PBS listings for nurse practitioner prescribing that have a Continuing Therapy Only (CTO) administrative note. The PBAC provided advice on whether the CTO note remains appropriate for each of the listings to which it currently applies. The PBAC noted that this review included denosumab listings.
- 6.8 The PBAC advised that a biosimilar uptake driver should apply to Jubbonti and Wyost in the form of an administrative note to encourage the uptake of biosimilar prescribing for treatment-naïve patients.
- 6.9 The PBAC advised, under Section 101 (4AACD) of the *National Health Act*, that:
- denosumab 60 mg in 1 mL pre-filled syringe (Jubbonti), and 60 mg in 1 mL pre-filled syringe (Prolia), should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule); and
 - denosumab 120 mg in 1.7 mL injection vial (Wyost) and denosumab and 120 mg in 1.7 mL injection vial (Xgeva) should be treated as equivalent to each other for the purposes of substitution (i.e. 'a' flagged in the schedule).
- 6.10 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Jubbonti and Wyost is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over Prolia and Xgeva respectively, or not expected to address a high and urgent unmet clinical need given the presence of alternative therapies, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met.
- 6.11 The PBAC noted this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 The full restrictions have not been populated below as no changes were recommended to the current eligibility criteria.

7.2 Add brands to existing items and amend existing listings:

MEDICINAL PRODUCT medicinal product pack		PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Available brands
DENOSUMAB						
denosumab 60 mg/mL injection, 1 mL syringe		5457F MP NP	1	1	0	^a Prolia ^a Jubbonti
Concept ID (for internal Dept. use)		Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
		Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
PR level	Add: New	Administrative Advice: Biosimilar prescribing policy <i>Prescribing of a biosimilar brand where available is encouraged for treatment naive patients.</i>				
	Add:	Administrative Advice: <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Medicines webpage (www.health.gov.au/health-topics/medicines).</i>				
Restriction Summary: 6548/ Treatment of Concept: 6548						
7992		Indication: Osteoporosis				
Restriction Summary: 6524/ Treatment of Concept: 6524						
8000		Indication: Established osteoporosis				

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	^a Xgeva ^a Wyost
Concept ID (for internal Dept. use)		Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)				
		Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners				
		Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)				
PR level		Administrative Advice: Denosumab is not PBS-subsidised for use in patients who have undergone curative surgical resection.				
		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.				
		Administrative Advice: Biosimilar prescribing policy <i>Prescribing of a biosimilar brand where available is encouraged for treatment naive patients.</i>				
		Administrative Advice: <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Medicines webpage (www.health.gov.au/health-topics/medicines).</i>				

Restriction Summary: 4504 / Treatment of Concept: 4504	
	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 MP NP	1	1	5	^a Xgeva ^a Wyost

Concept ID (for internal Dept. use)	Category / Program: <input checked="" type="checkbox"/> GENERAL - General Schedule (Code GE)
	Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners <input checked="" type="checkbox"/> Nurse practitioners
	Restriction type: <input checked="" type="checkbox"/> Authority Required (STREAMLINED)
PR level	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.
	Administrative Advice: Biosimilar prescribing policy <i>Prescribing of a biosimilar brand where available is encouraged for treatment naive patients.</i>
	Administrative Advice: <i>Encouraging biosimilar prescribing for treatment naive patients is Government policy. A viable biosimilar market is expected to result in reduced costs for biological medicines, allowing the Government to reinvest in new treatments. Further information can be found on the Medicines webpage (www.health.gov.au/health-topics/medicines).</i>

Restriction Summary: 4158 / Treatment of Concept: 4158	
	Indication: Bone metastases
	Clinical criteria:
	The condition must be due to breast cancer

Restriction Summary: 4150 / Treatment of Concept: 4150	
	Indication: Bone metastases
	Clinical criteria:
	The condition must be due to castration-resistant prostate cancer

*Pending the PBAC outcome of its November 2024 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.