5.28 TERIPARATIDE, Injection 250 micrograms per mL, 2.4 mL in multi-dose pre-filled pen, Ritosa, Sun Pharma ANZ Pty Ltd

1 Purpose of Submission

1.1 The Category 4 submission requested a General Schedule, Authority Required (STREAMLINED) listing of teriparatide injection 250 micrograms per mL, 2.4 mL in multi-dose pre-filled pen (Ritosa; hereafter referred to as 'Ritosa') under the same circumstances as the current PBS-listed teriparatide injections 250 micrograms per mL, 2.4 mL in multi-dose pre-filled pen; Teriparatide Lupin® (hereafter referred to as 'Teriparatide Lupin') and Terrosa® (hereafter referred to as 'Terrosa'), with an 'a'-flag to the existing listings.

1.2 Listing was requested on the basis of a cost-minimisation analysis versus current PBS-listed brands of teriparatide; Teriparatide Lupin and Terrosa.

2 Background

2.1 Teriparatide is currently listed on the PBS as an Authority Required (STREAMLINED) listing for severe established osteoporosis.

Registration status

2.2 Ritosa was Therapeutic Goods Administration (TGA) registered on 2 May 2024 for the treatment of osteoporosis in postmenopausal women and the treatment of primary osteoporosis in men when other agents are considered unsuitable and when there is a high risk of fractures.

2.3 The TGA considered Ritosa to be equivalent to the reference brand, Forteo.

Previous PBAC consideration

2.4 Forteo, the reference brand and innovator, was the first brand of teriparatide listed on the PBS for this population but has since been delisted from the PBS since 1 January 2022 at the request of the sponsor.

2.5 Terrosa PFC was previously considered for the same indication and recommended by the PBAC at its March 2021 meeting (Terrosa PSD, March 2021).

2.6 Teriparatide Lupin PFP was previously considered for the same indication and recommended by the PBAC at its November 2023 meeting (Teriparatide Lupin PSD, November 2023).

2.7 Ritosa has not been considered by the Pharmaceutical Benefits Advisory Committee (PBAC) previously.

3 Requested listing

3.1 The submission requested the listing of Ritosa under the same conditions as the existing listings for Terrosa and Teriparatide Lupin.

3.2 A shortened version of the requested listing is presented below. Proposed changes are in italics and deletions are in strikethrough.

30-day listing:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
TERIPARATIDE					
teriparatide 250 microgram/mL injection, 2.4 mL pen device	14093R MP	1	1	5	Teriparatide Lupin Terrosa
teriparatide 250 microgram/mL injection, 2.4 mL pen device	NEW MP	1	1	5	Ritosa

Restriction Summary 12476/ Treatment of Concept 12492	
	Category / Program: ☒ GENERAL - General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required – Streamlined [12492]
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised
	Administrative Advice: No increase in the maximum number of repeats may be authorised.
	Severity: Severe
	Condition: Established osteoporosis
	Indication: Severe established osteoporosis
	Treatment Phase: Initial treatment
Restriction Summary 12270 / Treatment of Concept 12270	
	Category / Program: GENERAL – General Schedule (Code GE)
	Prescriber type: ☒Medical Practitioners
	Restriction Type: ☒Authority Required – Streamlined [12270]
	Indication: Severe established osteoporosis
	Treatment Phase: Continuing treatment

60-Day MDQ Listing:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
TERIPARATIDE					
teriparatide 250 microgram/mL injection, 2.4 mL pen device	14482F MP 60DD	2	2	2	Teriparatide Lupin Terrosa
teriparatide 250 microgram/mL injection, 2.4 mL pen device	NEW MP 60DD	2	2	2	Ritosa
Restriction Summary 15588 / Treatment of Concept 15536					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction Type: ☒Authority Required – Streamlined [15536]				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Severity: Severe				
	Condition: Established osteoporosis				
	Indication: Severe established osteoporosis				
	Treatment Phase: Continuing treatment				

3.3 The clinical and treatment criteria for Ritosa is the same as that of the current PBS listings for both Terrosa and Teriparatide Lupin.

3.4 The submission requested for Ritosa to be treated as equivalent to Terrosa and Teriparatide Lupin for the purposes of substitution (i.e. 'a'-flagged in the schedule to allow for brand substitution to be undertaken at the point of dispensing). This was on the basis that Terrosa was treated as equivalent to Forteo prior to its delisting in June 2022 and Teriparatide Lupin was also TGA registered on a bioequivalence basis to Forteo. This is consistent with the 'a'-flagging arrangements that allow for brand substitution between Terrosa and Teriparatide Lupin on the PBS.

4 Comparator

4.1 The submission nominated Terrosa and Teriparatide Lupin as the main comparators. The PBAC considered that this was appropriate.

4.2 The submission claims no differences in the prescribing and administration profiles of Ritosa, Terrosa and Teriparatide Lupin and no differences in the monitoring for adverse events requirements.

4.3 Terrosa was TGA registered and subsequently PBS listed as a biosimilar of Forteo on 1 October 2021 (Terrosa PSD March 2021).

4.4 Teriparatide Lupin was TGA registered on a bio-equivalence basis to Forteo on 6 April 2023.

4.5 At its November 2023 meeting, the PBAC considered the Teriparatide Lupin submission and advised '…while the TGA has not established a direct bioequivalence between Lupin PFP and Terrosa PFC, both brands have been considered bioequivalent to the reference brand Forteo PFP' and recommended listing on a cost-minimisation basis to Terrosa (para 6.2, Teriparatide Lupin Public Summary Document November 2023).

4.6 The TGA considered Ritosa to be bioequivalent to the reference product Forteo, based on the results Study TER15. Although Forteo is no longer PBS listed, the Terrosa and Teriparatide Lupin brands remain available.

4.7 Due to TGA and PBAC's previous considerations of teriparatide listings, the submission claimed that Ritosa is bio-equivalent to Forteo, Teriparatide Lupin and Terrosa.

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 (1), via the Consumer Comments facility on the PBS website. The comments outlined significant affordability challenges for individuals who require medicines for rare diseases that are not PBS-listed, highlighting that teriparatide is required, but unaffordable.

Clinical trials

5.3 The demonstration of bioequivalence of Ritosa and Forteo was informed by the clinical trial, Study TER15.

5.4 Study TER15 was a randomised, open-label, single-dose, two-way crossover bioequivalence study performed in healthy adult human subjects comparing Ritosa 20 20 µg/80 µL single dose and Forteo 20 µg/80 µL single dose.

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

Clinical claim

5.6 The submission claimed non-inferior comparative effectiveness and safety of Ritosa compared to Terrosa and Teriparatide Lupin.

5.7 The submission did not provide a switching study between Ritosa, Terrosa and Teriparatide Lupin as there was no specific study available to determine the safety of switching between brands.

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

5.9 The PBAC considered that the claim of non-inferior comparative safety was reasonable.

Economic analysis

5.10 The submission presented a cost-minimisation analysis of Ritosa compared with Terrosa and Teriparatide Lupin. The submission stated the equi-effective doses were Ritosa 20 µg once daily subcutaneous injection to Terrosa 20 µg once daily subcutaneous injection and Teriparatide Lupin 20 µg once daily subcutaneous injection.

5.11 The submission requested the same approved ex-manufacturer price and dispensed price for maximum quantity for Ritosa as that of Teriparatide Lupin and Terrosa.

5.12 The submission stated that the proposed listing would result in no additional prescribing or administration costs, monitoring requirements and that there was no cost associated with the management of adverse events anticipated.

5.13 As a Category 4 submission, the economic analysis has not been independently evaluated.

Estimated PBS usage and financial implications

5.14 The requested price was based on the AEMP of Terrosa listed on the PBS October 2021 and Teriparatide Lupin listed on the PBS May 2024.

5.15 The submission presented a market share approach for Ritosa as a proportion of all teriparatide prescriptions. The submission assumed that Ritosa would substitute the existing use of Terrosa and Teriparatide Lupin on a 1:1:1 basis. As such, the submission estimated the requested listing of Ritosa to be cost neutral to the PBS/RPBS.

5.16 Refer to Table 1 which presents the estimated extent of use, cost of Ritosa to the PBS/RPBS and the net financial implications to the PBS/RPBS. The financial impact to Services Australia will be determined by that agency as part of the post PBAC process.

5.17 The submission estimated that 10,000 to < 20,000 scripts would be supplied of Ritosa over the first six years of listing (500 to < 5,000 in Year 1 to 500 to < 5,000 in Year 6).

5.18 The submission stated that the estimated net financial impact to the PBS/RPBS over six years for the listing of Ritosa is nil.

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 dispensed	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Estimated financial implications of Ritosa						
Cost to PBS/RPBS less co-payment	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]
Estimated financial implications of Terrosa and Teriparatide Lupin						
Cost to PBS/RPBS less co-payment	-$[redacted][2]	-$[redacted][2]	-$[redacted][2]	-$[redacted][2]	-$[redacted][2]	-$[redacted][2]
Net financial implications						
Net cost to PBS/RPBS	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]	$[redacted][2]

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.
Source: worksheet 3b impact – proposed (pub), UCM workbook
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *$0 to < $10 million*

6 PBAC Outcome

6.1 The PBAC recommended the General Schedule Authority Required (STREAMLINED) listing of teriparatide injection 250 micrograms per mL, 2.4 mL in multi-dose pre-filled pen (Ritosa®) under the same circumstances as the current PBS-listed teriparatide injections 250 micrograms per mL, 2.4 mL in multi-dose pre-filled pens (Teriparatide Lupin® and Terrosa®).

6.2 The PBAC considered Teriparatide Lupin and Terrosa as the appropriate comparators.

6.3 The PBAC considered the equi-effective dose of Ritosa 20 µg once daily subcutaneous injection = Terrosa 20 µg once daily subcutaneous injection = Teriparatide Lupin 20 µg once daily subcutaneous injection was appropriate.

6.4 The PBAC noted that the TGA established bioequivalence between Ritosa and the reference brand Forteo based on evidence from study TER15.

6.5 The PBAC advised, under Section 101(4AACD) of the *National Health Act 1953*, that brands Ritosa and Terrosa and Teriparatide Lupin of teriparatide injection 250 micrograms per mL, 2.4 mL in multi-dose pre-filled pen should be considered equivalent for the purposes of substitution (i.e., 'a' flagged I the Schedule with a NOTE stating PBS of one form and PBS of another form are equivalent for the purposes of substitution).

6.6 The PBAC considered that there would be no net financial implications to the PBS/RPBS as Ritosa is expected to list at the same price as Terrosa and Teriparatide Lupin with direct 1:1:1 substitution, resulting in no increase in overall market utilisation.

6.7 The PBAC recommended both a 30-day listing for the initial and continuing treatment phase, as well as a 60-day listing for the continuing treatment phase, to

be applied where the patient's condition is stable and suitable for the increased Maximum Dispensed Quantity (MDQ) measure in order to align with the current MDQ listings for both Teriparatide Lupin and Terrosa.

6.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Ritosa is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over Terrosa and Teriparatide Lupin, or 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.

6.9 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 An abbreviated version of the restriction overview can be found below. New medicinal product pack to be added to current PBS item codes as follows:

30-day listing:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
TERIPARATIDE					
teriparatide 250 microgram/mL injection, 2.4 mL pen device	14093R MP	1	1	5	Teriparatide Lupin Terrosa *Ritosa*
Restriction Summary 12476/ Treatment of Concept 12492					
	Category / Program: ☒ GENERAL - General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction Type: ☒Authority Required – Streamlined [12492]				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Severity: Severe				
	Condition: Established osteoporosis				
	Indication: Severe established osteoporosis				
	Treatment Phase: Initial treatment				
Restriction Summary 12270 / Treatment of Concept 12270					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction Type: ☒Authority Required – Streamlined [12270]				
	Indication: Severe established osteoporosis				
	Treatment Phase: Continuing treatment				

60-day MDQ listing:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. qty packs	Max. qty units	№. of Rpts	Available brands
TERIPARATIDE					
teriparatide 250 microgram/mL injection, 2.4 mL pen device	14482F MP 60DD	2	2	2	Teriparatide Lupin Terrosa *Ritosa*
Restriction Summary 15588 / Treatment of Concept 15536					
	Category / Program: GENERAL – General Schedule (Code GE)				
	Prescriber type: ☒Medical Practitioners				
	Restriction Type: ☒Authority Required – Streamlined [15536]				
	Administrative Advice: No increase in the maximum quantity or number of units may be authorised				
	Administrative Advice: No increase in the maximum number of repeats may be authorised.				
	Severity: Severe				
	Condition: Established osteoporosis				
	Indication: Severe established osteoporosis				
	Treatment Phase: Continuing treatment				

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

9 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.

10 Sponsor's Comment

The sponsor had no comment.