

**5.22 TERIPARATIDE,
Injection 250 micrograms per mL, 2.4 mL in multi-
dose pre-filled cartridge,
Terrosa[®],
Gedeon Richter Australia Pty Ltd**

1 Purpose of Application

- 1.1 The minor submission requested an Authority Required (STREAMLINED) listing for a new biosimilar brand of teriparatide (Terrosa[®]) in the form of injection 250 microgram per mL, 2.4 mL in multi-dose pre-filled cartridge.

2 Background

Registration status

- 2.1 Terrosa was TGA approved on 12 December 2020 and was determined to be biosimilar to the reference brand Forteo[®] (hereafter referred to as Forteo) for the following indications:
- Treatment of osteoporosis in postmenopausal women and the treatment of primary osteoporosis in men when other agents are considered unsuitable and where there is a high risk of fractures
 - Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at high risk of fracture.

Previous PBAC consideration

- 2.2 Terrosa has not been considered by the PBAC previously.
- 2.3 Forteo is PBS listed for severe established osteoporosis and is the only brand of teriparatide listed on the PBS.

3 Requested listing

- 3.1 The submission requested for the following biosimilar uptake drivers to apply to the listing of Terrosa:
- an Authority Required (STREAMLINED) listing for both initial and continuing treatment while maintaining it as Authority Required for Forteo;
 - a 'Biosimilar prescriber policy' note to be added to the prescribing instructions for both Forteo and Terrosa to reference the biosimilar prescribing policy.

These requests are appropriate and consistent with the Australian Government's Biosimilar Awareness Initiative.

- 3.2 The submission requested that Terrosa not be 'a'-flagged to prevent brand substitution between Terrosa and Forteo to be undertaken by pharmacist at the point of dispensing. The submission and TGA Delegate's Overview noted that Terrosa is a different device to Forteo. Terrosa pen device and cartridges are supplied separately and need to be assembled before use. In contrast, Forteo is supplied as a prefilled pen and assembling the pen is not necessary apart from attaching the needle for administration. It is noted that the manner of administration for Terrosa and Forteo are the same based on the approved Product Information (PI). The PBAC considered that the information about the education plan provided in the pre-PBAC response supported safe uptake of the Terrosa device. The PBAC considered there was minimal risk in 'a'-flagging Terrosa and Forteo, given teriparatide would be used in a specialist setting and that the difference in administration techniques between the two devices would be appropriately managed.
- 3.3 The submission noted that treatment with teriparatide is TGA recommended for a lifetime duration of 24 months (Terrosa PI and Forteo PI). This is different to the current PBS listing for Forteo, which allows a lifetime maximum of 18 months of therapy. It was noted that the maximum lifetime duration of treatment in the Forteo PI has changed from 18 months to 24 months since its PBS listing.

For more detail on the PBAC's view, see section 6 PBAC outcome.

4 Comparator

- 4.1 The minor submission nominated Forteo as the main comparator.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

- 5.3 As this was a minor submission, no evaluation of the clinical evidence was undertaken.
- 5.4 Details of the trials presented in the submission are provided in the table below.

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Table 1: Trials and associated reports presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Direct randomised trial(s)		
Study 001 (RGB10-001)	A Randomised, Double-Blind, Single, 20 microgram Fixed Dose, Two-Way Crossover Comparative Pharmacokinetic Study of RGB-10 and Forsteo® in Two Stages, in Healthy Adult Female Subjects	Clinical Study Report
Study 1023 (RGB1023O31)	RGB-10 Phase III Clinical Study – A comparative study to evaluate the similarity of RGB-10 to Forsteo® in patients with osteoporosis at high risk of fracture	Clinical Study Report

Source: Table 1.4-1 of submission. Forsteo is marketed as Forsteo in EU (refer to submission)

5.5 The clinical trials presented in the submission formed part of the TGA submission to register Terrosa as a biosimilar of Forsteo. The TGA Delegate considered the results of the PK study (Study 001) and the pivotal study (Study 1023) supported biosimilarity between Terrosa and Forsteo for the proposed indications (TGA Delegate’s overview, p13).

Clinical claim

5.6 The submission claimed that Terrosa was biosimilar to Forsteo which was supported by the TGA Delegate.

Economic analysis

5.7 The minor submission presented a cost-minimisation analysis of Terrosa compared with the public price of Forsteo. The equi-effective doses were estimated to be identical based on product information for both the Terrosa and Forsteo. Therefore, the equi-effective doses of Terrosa and Forsteo are: 20 micrograms of Terrosa = 20 micrograms of Forsteo.

Table 2: Requested price for Terrosa based on public price of Forsteo

	Pack Qty	Max Qty.	AEMP	DPMQ
Current essential details				
Forsteo 250 microgram/mL injection, 2.4 mL pen device	1	1	\$329.18	\$378.65
Essential details after applying 25% SPR				
Forsteo 250 microgram/mL injection, 2.4 mL pen device	1	1	\$246.89	\$285.74
Terrosa 250 microgram/mL injection, 2.4 mL cartridge	1	1	\$246.89	\$285.74

Source: Minor Submission, Table 3.4-1 ; AEMP = Approved Ex-Manufacturer Price; DPMQ= Dispensed Price for Maximum Quantity; SPR = statutory price reduction

Estimated PBS usage & financial implications

5.8 The minor submission estimated Terrosa will substitute for 0.48% of Forsteo prescriptions in Year 1, increasing to 45.02% in Year 6. The submission considered there to be no changes in PBS usage as the submission expects the incremental cost of Terrosa to be offset by that of Forsteo.

5.9 The submission proposed that the listing of Terrosa would result in cost savings to the PBS, assuming that a 25% Statutory Price Reduction would be applied to the price of

teriparatide in line with a statutory 'First New Brand Price Reduction', also triggering a move of the drug to F2.

- 5.10 As a minor submission, the financial estimates have not been independently evaluated.

For more detail on the PBAC's view, see section 6 PBAC outcome.

6 PBAC Outcome

- 6.1 The PBAC recommended the listing of biosimilar brand of teriparatide (Terrosa) as an Authority Required (STREAMLINED) listing for the same indications as the reference brand Forteo. The PBAC recommended listing Terrosa on a cost-minimisation basis to Forteo.
- 6.2 The PBAC advised the equi-effective doses of Terrosa and Forteo are: 20 micrograms of Terrosa = 20 micrograms of Forteo.
- 6.3 The PBAC noted that the TGA determined Terrosa to be a biosimilar to the reference brand Forteo.
- 6.4 The PBAC recommended the following biosimilar uptake drivers should be applied to Terrosa to encourage the uptake of biosimilar prescribing for treatment naïve patients, in accordance with the Australian Government's Biosimilar Uptake Driver policy:
- an Authority Required (STREAMLINED) listing for both initial and continuing treatment while maintaining it as Authority Required for Forteo;
 - a 'Biosimilar prescriber policy' note to be added to the prescribing instructions for both Forteo and Terrosa to reference the biosimilar prescribing policy:

Note

Biosimilar prescribing policy

Prescribing of the biosimilar brand Terrosa is encouraged for treatment naïve patients.

Encouraging biosimilar prescribing for treatment naïve 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 Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

- 6.5 The PBAC advised that, under Section 101(4AACD) of the *National Health Act 1953*, in the Schedule of Pharmaceutical Benefits, Terrosa should be treated as equivalent ('a' flagged) to Forteo at the pharmacy level for the purpose of substitution, for all approved indications. The PBAC was satisfied that the differences in administration techniques of Terrosa and Forteo were of minimal risk and would be appropriately

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managed based on the TGA information available and education materials described in the pre-PBAC response.

- 6.6 The PBAC noted that treatment with teriparatide is TGA registered for a lifetime duration of 24 months while the PBS listing allows for 18 months. The PBAC considered the lifetime treatment of teriparatide on the PBS should remain as 18 months, given PBAC has only assessed the cost effectiveness of teriparatide for this treatment duration. Additionally, the PBAC considered this would not disadvantage any patients given 18 months is the current treatment duration used in practice in Australia.
- 6.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Terrosa is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over Forteo, 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 2009* for Pricing Pathway A were not met.
- 6.8 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

- 7.1 Add new medicinal product pack: teriparatide 250 microgram/mL injection, 2.4 mL cartridge, based on the current listing for Forteo (Initial: Restriction Summary 6305 / Treatment of Concept: 6305; Continuing: Restriction Summary 4113 / Treatment of Concept: 4113) with the following changes:
- Change authority level to Authority required (STREAMLINED)
 - Add administrative note encouraging biosimilar prescribing for treatment naïve patients.
 - Add schedule equivalence ('a' flag) to Forteo

MEDICINAL PRODUCT Medicinal Product Pack	PBS item code	Max. qty packs	Max. qty units	No. of Rpts	Proprietary name and manufacturer
TERIPARATIDE teriparatide 250 microgram/mL injection, 2.4 mL cartridge	NEW	1	1	5	Terrosa Gideon Richter Australia Pty Ltd

Restriction Summary NEW / Treatment of Concept: NEW

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required): <input checked="" type="checkbox"/> Authority Required – Streamlined [new/existing code] (specification of 4-digit code by prescriber to certify that they have read the PBS restriction; no prior assessment by Medicare; retrospective audit of patient records possible)

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Indication: Severe established osteoporosis
Treatment Phase: Initial treatment
Treatment criteria: Must be treated by a specialist; or Must be treated by a consultant physician
AND
Clinical criteria: Patient must be at very high risk of fracture
AND
Clinical criteria: Patient must have a bone mineral density (BMD) T-score of -3.0 or less
AND
Clinical criteria: Patient must have had 2 or more fractures due to minimal trauma
AND
Clinical criteria: Patient must have experienced at least 1 symptomatic new fracture after at least 12 months continuous therapy with an anti-resorptive agent at adequate doses
AND
Clinical criteria: The treatment must be the sole PBS-subsidised agent
AND
Clinical criteria: The treatment must not exceed a lifetime maximum of 18 months therapy
Prescribing Instructions: A vertebral fracture is defined as a 20% or greater reduction in height of the anterior or mid portion of a vertebral body relative to the posterior height of that body, or, a 20% or greater reduction in any of these heights compared to the vertebral body above or below the affected vertebral body.
Prescribing Instructions: If treatment with anti-resorptive therapy is contraindicated according to the relevant TGA-approved Product Information, details of the contraindication must be documented in the patient's medical record at the time treatment with teriparatide is initiated.
Prescribing Instructions: If an intolerance of a severity necessitating permanent treatment withdrawal develops during the relevant period of use of one anti-resorptive agent, alternate anti-resorptive agents must be trialled so that the patient achieves the minimum requirement of 12 months continuous therapy. Details must be documented in the patient's medical record at the time treatment with teriparatide is initiated.
Prescribing Instructions: Anti-resorptive therapies for osteoporosis and their adequate doses which will be accepted for the purposes of administering this restriction are alendronate sodium 10 mg per day or 70 mg once weekly, risedronate sodium 5 mg per day or 35 mg once weekly or 150 mg once monthly, raloxifene hydrochloride 60 mg per day (women only), denosumab 60 mg once every 6 months and zoledronic acid 5 mg per annum.
Prescribing Instructions: Details of prior anti-resorptive therapy, fracture history including the date(s), site(s), the symptoms associated with the fracture(s) which developed after at least 12 months continuous anti-resorptive therapy and the score of the qualifying BMD measurement must be provided at the time of application.

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Administrative Advice: Details of accepted toxicities including severity can be found on the Department of Human Services website at www.humanservices.gov.au .
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.
Administrative Advice: Special Pricing Arrangements apply.
Administrative Advice: Biosimilar prescribing policy Prescribing of the biosimilar brand, Terrosa®, is encouraged for treatment naive patients. 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 Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

Restriction Summary NEW / Treatment of Concept: NEW

Category / Program: GENERAL – General Schedule (Code GE)
Prescriber type: <input type="checkbox"/> Dental <input checked="" type="checkbox"/> Medical Practitioners <input type="checkbox"/> Nurse practitioners <input type="checkbox"/> Optometrists <input type="checkbox"/> Midwives
Restriction Type – assessment time by Medicare – Method of obtaining authority approval (if Authority Required): <input checked="" type="checkbox"/> Authority Required – Streamlined [new/existing code] (specification of 4-digit code by prescriber to certify that they have read the PBS restriction; no prior assessment by Medicare; retrospective audit of patient records possible)
Indication: Severe established osteoporosis
Treatment Phase: Continuing treatment
Clinical criteria: Patient must have previously been issued with an authority prescription for this drug
AND
Clinical criteria: The treatment must not exceed a lifetime maximum of 18 months therapy
Administrative Advice: Up to a maximum of 18 pens will be reimbursed through the PBS.
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.
Administrative Advice: Special Pricing Arrangements apply.
Administrative Advice: Biosimilar prescribing policy Prescribing of the biosimilar brand, Terrosa®, is encouraged for treatment naive patients. 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 Biosimilar Awareness Initiative webpage (www.health.gov.au/biosimilars).

This restriction 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

Gedeon Richter welcomes the positive recommendation for Terrosa and will now work with the PBAC on the next steps of the process.