

Teriparatide (Forteo) for severe osteoporosis

(ter-i-PAR-a-tide)

Summary

- Teriparatide is subsidised on the Pharmaceutical Benefits Scheme for severe established osteoporosis in people at very high risk of fracture who develop one or more new symptomatic fractures despite at least 12 months of continuous antiresorptive therapy.
- PBS-subsidised treatment must be initiated by a specialist but can be continued by a GP.
- Teriparatide is given as a daily subcutaneous injection using a prefilled multidose delivery device (pen).
- Treatment with teriparatide is limited to a lifetime maximum duration of 18 months because of the possible risk of osteosarcoma. Informed consent is required.
- Some patients may benefit from restarting antiresorptive osteoporosis therapy after stopping teriparatide.
- Common adverse effects include nausea, arthralgia, headaches, dizziness and injection-site reactions.
- Ensure calcium and vitamin D intake are adequate. Supplement if necessary.

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PBS listing

Authority required

Initial treatment

Treatment as the sole PBS-subsidised agent for severe established osteoporosis in patients with a very high risk of fracture who have:

- a bone mineral density (BMD) T-score of -3.0 or less, AND
- 2 or more fractures* due to minimal trauma, AND
- at least one new symptomatic fracture after at least 12 months of continuous treatment with antiresorptive therapy at adequate doses.†

Treatment must be initiated by a specialist or consulting physician and can be continued by a general practitioner.

Only 18 months of treatment (a maximum of 18 pens) will be subsidised on the PBS.

The authority application must include:

- details of previous osteoporosis therapy
- fracture history, including the date(s), site(s) and symptoms associated with the fracture that developed during antiresorptive therapy
- qualifying BMD score.

Details of any contraindication to antiresorptive therapy, as described in the relevant Therapeutic Goods Administration (TGA) approved product information, must be provided at the time of application.

Continuing treatment

For patients who previously received PBS-subsidised teriparatide for severe established osteoporosis.

Patients who were prescribed teriparatide before the PBS listing date are now subsidised to receive teriparatide if they have severe established osteoporosis and a very high fracture risk.

Teriparatide must only be used for a lifetime maximum of 18 months of therapy.

* A vertebral fracture is defined as a $\geq 20\%$ reduction in height of an anterior or mid-portion vertebral body relative to the posterior height of that body, or a $\geq 20\%$ reduction in any vertebral height compared with vertebral height above or below the affected vertebral body.

† Antiresorptives and doses accepted for the purposes of this restriction: alendronate 10 mg daily or 70 mg weekly, risedronate 5 mg daily or 35 mg weekly, raloxifene 60 mg daily (women only), etidronate 200 mg with calcium carbonate 1.25 g daily, strontium 2 g daily and zoledronic acid 5 mg once a year. If severe intolerance occurs that requires permanent withdrawal of one antiresorptive agent, an alternative antiresorptive agent must be trialled so that a minimum of 12 months of continuous therapy is achieved.

Reason for PBS listing


The Pharmaceutical Benefits Advisory Committee (PBAC) recommended teriparatide for listing on the basis of acceptable cost-effectiveness compared with alendronate in the context of a very high clinical need (for patients who continue to experience fracture despite the availability of antiresorptives).¹

The PBAC recommended restricting use to people who experience new symptomatic fractures, because loss of quality and quantity of life in osteoporosis is expected to be associated with fracture symptoms rather than asymptomatic fracture.

Place in therapy


Teriparatide is recombinant human parathyroid hormone, given as a daily subcutaneous injection. In contrast to antiresorptive agents, which inhibit bone loss, teriparatide is an anabolic agent that activates osteoblasts and stimulates bone formation.²

Teriparatide is TGA approved for treating postmenopausal osteoporosis in women and primary osteoporosis in men (hypogonadal or idiopathic osteoporosis) when other treatments are considered unsuitable and there is a high risk of fracture.² It is also approved for the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in people at high risk of fracture.² The PBS listing restricts use to people with severe established osteoporosis and a very high risk of fracture, in whom at least one new symptomatic fracture develops despite antiresorptive therapy (see PBS listing).

As with other therapies for osteoporosis, adequate calcium and vitamin D should be ensured.² [www](#) 

Antiresorptive therapies should be stopped before starting teriparatide, and can be resumed after treatment with teriparatide has finished.

The duration of treatment with teriparatide is limited to a lifetime maximum of 18 months (see Safety issues).

[www](#)  Refer to this review at www.npsradar.org for more information on vitamin D deficiency and supplementation.

Teriparatide reduces the risk of vertebral and non-vertebral fractures in women but data on men are limited

In a trial of postmenopausal women with severe established osteoporosis (i.e. at least one previous vertebral fracture), teriparatide 20 micrograms daily increased BMD and reduced the risk of new vertebral and non-vertebral fractures compared with placebo (see Table 1).³ The trial was not designed to investigate the effect of teriparatide on specific types of non-vertebral fracture (e.g. hip, wrist, humerus).

There are limited data on fracture outcomes in men. Compared with placebo, teriparatide increases BMD in men with primary osteoporosis.⁴ Men in trials were generally young (mean age < 60 years) and recruited on the basis of BMD scores rather than a history of fracture.⁴

Teriparatide's effect on fracture rates has not been compared as a primary outcome with that of other established osteoporosis treatments. Some trials have shown greater increases in BMD with teriparatide compared with bisphosphonates, but the clinical significance of this has not been determined.⁵⁻⁷

Data from follow-up observational studies in women suggest that, compared with placebo, the risk of radiographically detected vertebral and all non-vertebral fractures is reduced for up to 18 months after stopping teriparatide.^{8,9}


Table 1: Effect of teriparatide (20 micrograms daily) on vertebral and non-vertebral fracture rates in postmenopausal women with severe osteoporosis^{3,10}

Fracture type	Relative risk: teriparatide versus placebo (95% confidence interval)	Numbers needed to treat (NNT) [‡]
New radiographically detected vertebral fracture**	0.35 (0.22 to 0.55)	11
New non-vertebral fracture	0.65 (0.43 to 0.98)	25
Hip fracture	0.50 (0.09 to 2.73)	NA
Wrist fracture	0.54 (0.22 to 1.35)	NA

** Defined as a $\geq 20\%$ reduction in vertebral height in previously normal vertebrae.

‡ NNT: number of patients who would need to be treated for 21 months (median trial duration) with teriparatide instead of placebo to prevent one additional fracture.

Ensure adequate calcium and vitamin D intake

Patients in all teriparatide clinical trials received supplemental calcium 1000 mg and at least 400 units vitamin D daily.^{3–5,11} Use supplements for all patients who cannot obtain adequate amounts of calcium and vitamin D through diet and sunlight exposure alone (see Table 2).^{2,12} [www](#) 

Some patients taking calcium supplements with teriparatide may develop hypercalcaemia (see Safety issues) and require less calcium.

Table 2: Recommended daily intakes of calcium and vitamin D for adults^{12,13}

Calcium	At least 1000 mg daily (1300 mg for women > 50 years and men > 70 years)
Vitamin D	At least 400–800 units (10–20 micrograms); higher (800–2000 units daily [20–50 micrograms]) in people with limited sun exposure

Stop antiresorptive therapies before starting teriparatide

Combining teriparatide with a bisphosphonate does not improve BMD compared with teriparatide alone^{6,7}; both these drugs may even act antagonistically¹⁴ and their combination is not PBS subsidised.

The anti-fracture efficacy of teriparatide in patients previously treated with antiresorptive therapy has not been established. Participants from trials were excluded if they had received medications that alter bone metabolism (such as bisphosphonates) in the lead-up to trials (up to 24 months).^{3,4}

There is no requirement for a washout period between stopping antiresorptive therapy and starting teriparatide.² A recent small unblinded study suggested that teriparatide improves BMD and markers of bone formation regardless of previous long-term antiresorptive therapy (at least a year), or the lag-time between stopping previous therapy and starting teriparatide.¹⁵

Consider antiresorptive therapy after stopping teriparatide

After stopping teriparatide, additional antiresorptive therapy may help to maintain or enhance gains in BMD.^{9,14,16,17} Women who did not receive subsequent treatment with a bisphosphonate lost total hip and femoral neck BMD over 30 months after withdrawal of teriparatide.⁹ Similarly in men, total hip BMD levels had reverted to near baseline levels at 30 months after the withdrawal of teriparatide, without subsequent osteoporosis drug therapy.¹⁷


Safety issues

Common adverse effects in patients treated with teriparatide include nausea, arthralgia, headache, dizziness and injection-site reactions.² Consider measuring baseline serum levels of calcium, vitamin D, creatinine, uric acid and parathyroid hormone to ensure that they are within acceptable limits before starting teriparatide.¹⁴ See Forteo product information for a complete list of adverse effects, interactions and precautions.²

Report suspected adverse reactions to the TGA online (www.ebs.tga.gov.au [then click 'Adverse reaction to a medicine' at left]) or by using the 'Blue Card' distributed with *Australian Prescriber*. For information about reporting adverse reactions, see the TGA website (www.tga.gov.au).

Possible risk of osteosarcoma with long-term treatment

The TGA-approved product information for teriparatide contains a boxed warning concerning the increased incidence of osteosarcoma in rats that were exposed to between 3 and 60 times the normal human exposure over a significant portion of their lives. In Australia the lifetime maximum duration of therapy is 18 months, to mitigate the theoretical risk of osteosarcoma in humans.²

[www](#)  Refer to this review at www.npsradar.org for more information on vitamin D deficiency and supplementation.

Avoid use of teriparatide in patients at increased risk of bone cancers, including people with:^{2,18,19}

- Paget's disease
- hyperparathyroidism
- bone disorders other than osteoporosis (including primary or secondary bone cancers)
- open epiphyses
- a history of skeletal radiation therapy
- unexplained increases in serum alkaline phosphatase concentration.

Avoid use of teriparatide in patients with pre-existing hypercalcaemia or urolithiasis.

Transient post-dose hypercalcaemia (serum calcium concentration > 2.6 mmol/L) occurred in 3–11% of trial participants who received teriparatide 20 micrograms daily, which usually returned to normal within 24 hours.¹¹ For patients at risk of hypercalcaemia, consider monitoring serum calcium levels before dosing, or at least 16 hours after the most recent injection.² If persistent hypercalcaemia occurs, withhold teriparatide, calcium and vitamin D supplements until the cause of hypercalcaemia is established.^{2,11}

Avoid in people with severe renal impairment

The safety and efficacy of teriparatide has not been evaluated in people with severe renal impairment.² In trials, elevation in serum uric acid concentration was more common in participants who received teriparatide than for those who received placebo (2.8% versus 0.7%).²

Circulating antiparathyroid hormone antibodies have been detected in teriparatide-treated patients; however, the clinical significance of this remains unknown.^{2,3}

Dosing issues

The recommended dose of teriparatide is 20 micrograms daily, administered as a once-daily subcutaneous injection into the thigh or abdomen. Teriparatide can be administered at any time of the day, but subsequent doses should be administered at or around the same time each day.²⁰

Teriparatide is available in a multi-dose prefilled delivery device (pen). Each pen contains enough teriparatide to deliver 28 daily doses. Instruct patients on the proper injection technique and ensure that they understand how to use and store the device and dispose of needles safely. Calcium and vitamin D supplements can be taken at the same time as teriparatide.²

Before starting treatment, the TGA-approved product information states that patients are required to provide informed consent regarding the lifetime maximum duration of treatment with teriparatide (18 months).

Teriparatide should be refrigerated at between 2 and 8 degrees Celsius.

Information for patients and carers

Advise patients of the following.^{2,20}

- Stop taking bisphosphonates or other antiresorptive medications before starting teriparatide.
- Do not stop taking daily calcium and vitamin D if these have been prescribed.
- The lifetime maximum duration of therapy is 18 months because of the possible risk of osteosarcoma with long-term use.
- Teriparatide needs to be kept refrigerated (but not frozen).
- Report any side effects to their doctor; nausea, arthralgia, headache, dizziness and injection-site reactions are common.
- Dizziness when standing up can occur, especially in the first few hours after the initial doses; sit or lie down until it passes.

Discuss the Forteo consumer medicine information (CMI) leaflet with the patient.

References

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