NEW ZEALAND DATA SHEET

1. PRODUCT NAME

Teriparatide-Teva, 250 mcg/mL, solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Teriparatide* 250 mcg/mL (or 20 micrograms/80 microlitres) as teriparatide acetate.

* teriparatide (1-34) is identical to the 34 N-terminal amino acid sequence of endogenous human parathyroid hormone.

Excipient with known effect: metacresol (3 mg/mL as preservative)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for Injection.

Clear, colourless solution, free from visible particles, packaged in a glass cartridge (2.4 mL cartridge) closed with a plunger at one end and with a rubber disc and aluminium cap (combiseal) at the other end. The filled cartridge is assembled into a pen injector.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Teriparatide-Teva, in combination with calcium and vitamin D, is indicated for the treatment of osteoporosis in postmenopausal women and in men at high risk of fracture (see 5.1 Pharmacodynamic properties - Clinical Efficacy and Safety).

Teriparatide-Teva is indicated for the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at high risk for fracture (see 5.1 Pharmacodynamic properties - Clinical Efficacy and Safety).

4.2 Dose and method of administration

Dose

The recommended dose of teriparatide is 20 microgram administered once daily by subcutaneous injection in the thigh or abdomen (see section 4.2 Dose and method of administration – Method of administration).

The maximum total duration of treatment with teriparatide should be limited to 24 months (see section 4.4 Special warnings and precautions for use). The 24 month course of teriparatide should not be repeated over a patient's lifetime.

Following cessation of teriparatide therapy, patients may be continued on other osteoporosis therapies.

Teriparatide-Teva should be administered in conjunction with calcium and vitamin D.

Patients must be educated to use the proper injection techniques. Please refer to the Instructions for Use included in the pack.

Age

Dosage adjustment based on age is not required (see section 5.2 Pharmacokinetic properties).

Gender

Dosage adjustment based upon gender is not required (see section 5.2 Pharmacokinetic properties).

Children
Teriparatide has not been studied in paediatric populations. Teriparatide should not be used in children or young adults with open epiphyses.

Patients with Renal Impairment
Teriparatide should not be used in patients with severe renal impairment (see section 4.3 Contraindications). In patients with moderate renal impairment, teriparatide should be used with caution. Dosage adjustment based on mild to moderate renal impairment is not required (see section 5.2 Pharmacokinetic properties).

Patients with Stable Heart Failure
Dosage adjustment based on the presence of mild or moderate heart failure is not required (see section 5.2 Pharmacokinetic properties).

Patients with Hepatic Impairment
Safety and efficacy have not been evaluated in patients with hepatic impairment. It is unlikely that hepatic impairment will have a clinically significant effect on systemic exposure to teriparatide (see section 5.2 Pharmacokinetic properties).

Method of administration
Refer to the Instructions for Use for the prefilled delivery device (pen).

The solution in the cartridge should be clear and colourless. Do not use if solid particles appear or if the solution is cloudy or coloured.

4.3 Contraindications
Teriparatide should not be used in patients with:

- hypersensitivity to teriparatide or to any of the excipients;
- pre-existing hypercalcaemia;
- severe renal impairment;
- metabolic bone diseases (including hyperparathyroidism and Paget's disease of the bone) other than primary osteoporosis or glucocorticoid-induced osteoporosis;
- unexplained elevations of alkaline phosphatase;
- prior external beam or implant radiation therapy to the skeleton;
- patients with skeletal malignancies or bone metastases;
- pregnancy and breast-feeding (see section 4.6 Fertility, pregnancy and lactation).

4.4 Special warnings and precautions for use

Duration of treatment
Studies in rats indicate an increased incidence of osteosarcoma with long term administration of teriparatide (see section 5.3 Preclinical safety data). Until further clinical data become available, the recommended lifetime treatment time of 24 months should not be exceeded.

Paediatric population and young adults with open epiphyses
The safety and efficacy of teriparatide in children and adolescents less than 18 years has not been established. Teriparatide should not be used in paediatric patients (less than 18 years), or young adults with open epiphyses.

Younger Adult Population
Experience in the younger adult population, including premenopausal women, is limited (see section 5.1 Pharmacodynamic properties). Treatment should only be initiated if the benefit clearly outweighs the risks in population.

Hypercalcaemia
In normocalcaemic patients, slight and transient elevations of serum calcium concentrations have been observed following teriparatide injection. Serum calcium concentrations reach a maximum between 4 and 6 hours and return to baseline by 16 to 24 hours after each dose of teriparatide. Routine calcium monitoring during therapy is not required.

Teriparatide has not been studied in patients with pre-existing hypercalcaemia. Hypercalcaemia should be excluded before treatment with teriparatide because of the possibility of exacerbating hypercalcaemia (see section 4.3 Contraindications).

Teriparatide can induce small, transient increases in serum calcium. If any blood samples are taken from a patient, this should be done at least 16 hours after the most recent teriparatide injection. Teriparatide may cause small increases in urinary calcium excretions, but the incidence of hypercalciuria did not differ from that in the placebo-treated patients in clinical trials.

Urolithiasis
Teriparatide has not been studied in patients with active urolithiasis. Teriparatide should be used with caution in patients with active or recent urolithiasis because of the potential to exacerbate this condition.

Hypotension
In short-term clinical studies with teriparatide, isolated episodes of transient orthostatic hypotension were observed. Typically, an event began within 4 hours of dosing and spontaneously resolved within a few minutes to a few hours. When transient orthostatic hypotension occurred, it happened within the first several doses, was relieved by placing subjects in a reclining position, and did not preclude continued treatment.

4.5 Interaction with other medicinal products and other forms of interaction

Teriparatide has been evaluated in pharmacodynamic studies with hydrochlorothiazide, furosemide, atenolol, and extended release preparations of diltiazem, nifedipine, felodipine and nisoldipine. No clinically significant interactions were noted.

Co-administration of raloxifene or Hormone Replacement Therapy (HRT) with teriparatide did not alter the effects of teriparatide on serum or urine calcium or on clinical adverse effects.

In a study of 15 healthy subjects administered digoxin daily to steady state, a single teriparatide dose did not alter the cardiac effect of digoxin. However, sporadic case reports have suggested that hypercalcaemia may predispose patients to digitalis toxicity. Because teriparatide transiently increases serum calcium, teriparatide should be used with caution in patients taking digitalis.

4.6 Fertility, pregnancy and lactation

Pregnancy
Teriparatide is contraindicated for use during pregnancy (see section 4.3 Contraindications).

Teriparatide produced no teratogenic effects in rats, mice, or rabbits.

In pregnant rabbits, embryo/foetal mortality that was attributable to increases in blood ionised calcium occurred at doses >3 microgram/kg.

Women of childbearing potential / Contraception in females
Women of childbearing potential should use effective methods of contraception during use of teriparatide. If pregnancy occurs, teriparatide should be discontinued.

Breastfeeding
Teriparatide is contraindicated for use during breast-feeding. It is not known whether teriparatide is excreted in human milk.

Fertility
Teriparatide had no effects on fertility of male or female rats at doses up to 300 microgram/kg.

4.7 Effects on ability to drive and use machines
No studies on the effects of teriparatide on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Of patients in the teriparatide trials, 82.8% of the teriparatide treated patients and 84.5% of the placebo patients reported at least 1 adverse event.

The most commonly reported adverse events in patients treated with teriparatide are nausea, pain in limb, headache and dizziness. Table 1, Table 2 and Table 3 give an overview of all treatment emergent adverse events that were observed in the trial populations, irrespective of causal relationship. The following events were observed in clinical trials in 1382 patients.

Table 1. Very Common Adverse Events (≥1/10)

SYSTEM ORGAN CLASS	Adverse Event	Teriparatide N=691 (%)	Placebo N=691 (%)
Musculoskeletal, Connective Tissue and Bone Disorders	Pain in limb	10.0	9.0

Table 2. Common Adverse Events (≥1/100 to <1/10)

SYSTEM ORGAN CLASS	Adverse Event	Teriparatide N=691 (%)	Placebo N=691 (%)
Blood and Lymphatic System Disorders	Anaemia	1.7	1.3
Metabolism and Nutrition Disorders	Hypercholesterolaemia	2.6	2.3
Psychiatric Disorders	Depression	4.1	2.5
Nervous System Disorders	Dizziness Headache	8.0 7.7	5.2 7.4
	Sciatica	1.3	0.7
Ear and Labyrinth Disorders	Vertigo	3.6	2.5
Cardiac Disorders	Palpitations	1.4	1.2
Vascular Disorders	Hypotension	1.0	1.0
Respiratory, Thoracic and Mediastinal Disorders	Dyspnoea	3.3	2.3
Gastrointestinal Disorders	Nausea	8.5	6.2
	Vomiting	3.3	2.6
	Hiatus Hernia	1.0	0.9
	Gastroesophageal reflux disease	1.0	0.4
Skin and Subcutaneous Tissue Disorders	Sweating increased	1.9	1.3
Musculoskeletal, Connective Tissue and Bone Disorders	Muscle cramps	3.6	2.9

General Disorders and Administration Site Conditions	Fatigue	4.8	4.3
	Chest pain	3.8	3.5
	Asthenia	1.6	1.2

Table 3. Uncommon Adverse Events (≥1/1,000 to <1/100)

SYSTEM ORGAN CLASS	Adverse Event	Teriparatide N=691 (%)	Placebo N=691 (%)
Cardiac Disorders	Tachycardia	0.9	0.9
Respiratory, Thoracic and Mediastinal Disorders	Emphysema	0.3	0
Gastrointestinal Disorders	Haemorrhoids	0.9	0.4
Renal and Urinary Disorders	Urinary incontinence	0.6	0.3
	Polyuria	0.3	0.1
	Micturition urgency	0.3	0
General Disorders and Administration Site Conditions	Injection site erythema	0.7	0
	Injection site reaction	0.3	0.1
Investigations	Weight increased	0.7	0.3
	Cardiac murmur	0.4	0.1

Teriparatide increases serum uric acid concentrations. In clinical trials, 2.8% of teriparatide treated patients had serum uric acid concentrations above the upper limit of normal compared with 0.7% of placebo patients. However, the hyperuricaemia did not result in an increase in gout, arthralgia, or urolithiasis.

In a large clinical trial, antibodies that cross-reacted with teriparatide were detected in 2.8% of women receiving teriparatide. Generally, antibodies were first detected following 12 months of treatment and diminished after withdrawal of therapy. There was no evidence of hypersensitivity reactions, allergic reactions, effects on serum calcium, or effects on BMD response.

The following table of adverse reactions is based on post-marketing spontaneous reports.

The following convention has been used for the classification of the adverse reactions: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1,000, <1/100), rare (>1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Table 4. Tabulated list of spontaneously reported adverse reactions

System organ class	Adverse reactions
General disorders and administration site conditions	Rare: possible allergic events soon after injection: acute dyspnoea, oro/facial oedema, generalized urticaria, chest pain, anaphylaxis. Common: mild and transient injection site events, including pain, swelling, erythema, localised bruising, pruritus and minor bleeding at injection site.
Metabolism and nutrition disorders	Uncommon: hypercalcaemia greater than 2.76 mmol/L (11 mg/dL). Rare: hypercalcaemia greater than 3.25 mmol/L (13 mg/dL).

Musculoskeletal and connective tissue and bone disorders	Common: Muscle spasms, such as leg or back, sometimes shortly after the first dose. Uncommon: myalgia, arthralgia Very Rare: Serious back spasms
Blood and lymphatic system disorders	Common: Anaemia
Renal and urinary disorders	Rare: Renal failure/impairment

There has been a report of metastatic osteosarcoma with subsequent fatal outcome in a 72 year old woman with osteoporosis and low back pain who had received teriparatide for 14 months prior to presentation. Causality cannot be established on the basis of this single case and a surveillance program continues. Osteosarcoma occurs at a rate of approximately 4 in one million per year (1 in 250,000 per year) in the general population over 60 years old and at the same rate in women over the age of 70 years. At present it is not known if humans treated with teriparatide have an increased risk of osteosarcoma.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose
Symptoms and Signs
No cases of overdose were reported during clinical trials. Teriparatide has been safely administered in single doses of up to 100 microgram. In a clinical study, doses of 60 microgram/day for 6 weeks were safely tolerated. The effects of overdose that might be expected include delayed hypercalcaemia and risk of orthostatic hypotension. Nausea, vomiting, dizziness, and headache might also occur.

In postmarketing spontaneous reports, there have been cases of medication error where the entire contents (up to 800 microgram) of the teriparatide pen have been administered as a single dose. Transient events reported have included nausea, weakness/lethargy and hypotension. In some cases, no adverse events occurred as a result of the overdose. No fatalities associated with overdose have been reported.

Management of Overdose
There is no specific antidote for teriparatide. Treatment of suspected overdose should include discontinuation of teriparatide, monitoring of serum calcium, and implementation of appropriate supportive measures, such as hydration.

For risk assessment and advice on the management of overdose please contact the National Poisons Information Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Calcium homeostasis, parathyroid hormones and analogues, ATC code: H05AA02

Teriparatide is a bone formation agent to treat osteoporosis. The skeletal effects of teriparatide depend upon the pattern of systemic exposure. Once-daily administration of teriparatide increases apposition of new bone on trabecular and cortical (endosteal and periosteal) bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity. In contrast, continuous excess of endogenous PTH, may be detrimental to the skeleton because bone resorption may be stimulated more than bone formation.

Mechanism of Action

Endogenous 84-amino-acid parathyroid hormone (PTH) is the primary regulator of calcium and phosphate metabolism in bone and kidney. Physiological actions of PTH include stimulation of bone formation by direct effects on bone forming cells (osteoblasts), indirectly increasing the intestinal absorption of calcium and increasing the tubular re-absorption of calcium and excretion of phosphate by the kidney. The biological actions of PTH are mediated through binding to PTH-specific cell-surface receptors. Teriparatide (rhPTH(1-34)) is the active fragment (1-34) of endogenous human parathyroid hormone, manufactured using recombinant DNA technology. Teriparatide binds to these receptors with the same affinity as PTH, and has the same actions in bone and kidney as PTH. Like endogenous PTH, teriparatide is not expected to accumulate in bone or other tissues.

Clinical Efficacy and Safety

Risk Factors

Independent risk factors, for example, low BMD, age, the existence of previous fracture, family history of hip fractures, high bone turnover and low body mass index should be considered in order to identify women and men at increased risk of osteoporotic fractures who could benefit from treatment.

Premenopausal women with glucocorticoid-induced osteoporosis should be considered at high risk for fracture if they have a prevalent fracture or a combination of risk factors that place them at high risk for fracture (eg, low bone density [eg, T score ≤-2], sustained high dose glucocorticoid therapy [eg, ≥7.5 mg/day for at least 6 months], high underlying disease activity, low sex steroid levels).

Postmenopausal Osteoporosis

The pivotal study included 1637 postmenopausal women (mean age 69.5 years), 1326 of whom had baseline and postbaseline follow-up vertebral x-rays. At baseline ninety percent of the patients had one or more vertebral fractures and on average, vertebral BMD was 0.82 g/cm^2 (equivalent to a T-score = - 2.6). Patients with metabolic bone disorders other than osteoporosis were excluded from the study. All patients received 1000 milligrams of calcium per day and at least 400 IU of vitamin D per day. Results from a treatment period of up to 24 months (median 19 months) with teriparatide, demonstrate significant anti fracture efficacy.

Effect on Vertebral Fractures

Teriparatide given for a median of 19 months significantly reduced the risk and severity of new vertebral fractures in postmenopausal women with osteoporosis, relative to placebo. Teriparatide reduced the incidence of one or more new vertebral fractures by 65% and multiple fractures by 77% (Table 5). Eleven women would need to be treated with teriparatide for a median of 19 months to prevent one or more new vertebral fractures.

Effect on Non-vertebral Fractures

Teriparatide significantly reduced the overall incidence of fragility non-vertebral fractures including wrist, ribs, ankle, humerus, hip, foot, pelvis and others, by 53%.

Effect on BMD

Teriparatide rapidly increased lumbar spine BMD. Significant increases were seen as early as 3 months and continued throughout the treatment period. After a median treatment period of 19 months, BMD had increased 9% and 4% in the lumbar spine and total hip, respectively, compared with placebo ($p<0.001$). Teriparatide was effective regardless of age, baseline rate of bone turnover, and baseline BMD.

In an open-label study, 503 postmenopausal women with severe osteoporosis and a fragility fracture within the previous 3 years (83% had received previous osteoporosis therapy) were treated with teriparatide for up to 24 months. At 24 months, the mean increase from baseline in lumbar spine, total hip and femoral neck BMD was 10.5%, 2.6% and 3.9% respectively. The mean increase in BMD

from 18 to 24 months was 1.4%, 1.2%, and 1.6% at the lumbar spine, total hip and femoral neck, respectively.

Effect on Back Pain
Teriparatide significantly reduced the incidence and severity of back pain. In women with postmenopausal osteoporosis, there was a significant (p = 0.017) 26% reduction in the spontaneous reports of new or worsened back pain compared to placebo.

Effect on Height Loss
For the 86 postmenopausal women who experienced vertebral fractures, those treated with teriparatide had significantly less height loss when compared to placebo (p = 0.001).

Bone Histology
The effects of teriparatide on bone histology were evaluated in iliac crest biopsies of 61 postmenopausal women treated for up to 24 months with placebo or teriparatide 20 microgram or 40 microgram per day. The increases in BMD and resistance to fracture achieved with teriparatide occurred without evidence of cellular toxicity or adverse effects on bone architecture or mineralisation. The findings in human bone samples paralleled those seen in preclinical primate studies.

Table 5. Fracture Incidence in Postmenopausal Women

	Placebo (N=544) (%)	Teriparatide (N=541) (%)	Relative risk (95% CI) vs. placebo
New vertebral fracture (≥1)[a]	14.3	5.0 [b]	0.35 (0.22, 0.55)
Multiple vertebral fractures (≥2)[a]	4.9	1.1 [b]	0.23 (0.09, 0.60)
Moderate or severe vertebral fracture (≥1)	9.4	0.9 [a]	0.1 (0.04, 0.27)
Non-vertebral fragility fractures [c]	5.5	2.6 [c]	0.47 (0.25, 0.87)
Major non-vertebral fragility fractures[c] (hip, radius, humerus, ribs and pelvis)	3.9	1.5 [c]	0.38 (0.17, 0.86)

Abbreviations: N = number of patients randomly assigned to each treatment group; CI = Confidence Interval.

[a] The incidence of vertebral fractures was assessed in 448 placebo and 444 teriparatide patients who had baseline and follow-up spine radiographs.

[b] p≤0.001 compared with placebo.

[c] p≤0.025 compared with placebo.

Post-treatment Fracture Efficacy
Following treatment with teriparatide, 1262 postmenopausal women from the pivotal trial enrolled in a post-treatment follow-up study. After 18 months, approximately 50% of the women in each former treatment group had begun an approved osteoporosis therapy (not including teriparatide) at the discretion of their physician. All women were offered 1000 milligrams of calcium per day and at least 400 IU of vitamin D per day.

During a median of 18 months following discontinuation of teriparatide treatment, there was a significant 40% reduction in relative risk for new vertebral fractures in women previously treated with teriparatide, compared to placebo. The relative risk reduction was similar for women with and without osteoporosis treatment (41% and 37%, respectively). During the same observation period,

there was a 42% risk reduction for non-vertebral fragility fractures in women previously treated with teriparatide, compared with placebo.

Data from this study demonstrate that regardless of the follow-up treatment options, fracture risk was reduced for women previously treated with teriparatide.

Male Osteoporosis
The efficacy of teriparatide once daily was demonstrated in a double-blind, placebo-controlled clinical study in 437 men (mean age 58.7 years) with either hypogonadal (defined as low morning free testosterone or an elevated FSH or LH) or idiopathic osteoporosis.

Baseline spinal and femoral neck bone mineral density mean T-scores were -2.2 and -2.1, respectively. At baseline, 35% of patients had a vertebral fracture and 59% had a non-vertebral fracture. All patients received 1000 milligrams of calcium per day and at least 400 IU of vitamin D per day and were treated for up to 14 months.

In this study teriparatide rapidly increased lumbar spine BMD in men, with significant increases as early as 3 months that continued throughout the treatment period. After a median treatment period of 11 months, BMD in the spine had (on average) increased by 5% and in the hip by 1%, compared to placebo. Increases in BMD were similar in men with hypogonadal or idiopathic osteoporosis. Teriparatide was effective regardless of age, baseline rate of bone turnover, and baseline BMD.

Glucocorticoid-induced osteoporosis
The efficacy of teriparatide in men and women (N=428) receiving sustained systemic glucocorticoid therapy (equivalent to 5 mg or greater of prednisone for at least 3 months) was demonstrated in a 36 month (18-month primary phase plus 18-month continuation phase), randomised, double-blind, comparator-controlled study (alendronate 10 mg/day). Twenty-eight percent of patients had one or more radiographic vertebral fractures at baseline. All patients were offered 1000 mg calcium per day and 800 IU vitamin D per day.

This study included postmenopausal women (N=277), premenopausal women (N=67), and men (N=83). At baseline, the postmenopausal women had a mean age of 61 years, mean lumbar spine BMD T score (number of standard deviations above or below the mean in healthy young women) of -2.7, median prednisone equivalent dose of 7.5 mg/day, and 34% had one or more radiographic vertebral fractures; premenopausal women had a mean age of 37 years, mean lumbar spine BMD T score of -2.5, median prednisone equivalent dose of 10 mg/day, and 9% had one or more radiographic vertebral fractures; and men had a mean age of 57 years, mean lumbar spine BMD T score of -2.2, median prednisone equivalent dose of 10 mg/day, and 24% had one or more radiographic vertebral fractures.

Sixty-nine percent of patients completed the 18-month primary phase. At the 18-month endpoint, teriparatide significantly increased lumbar spine BMD (7.2%) compared with alendronate (3.4%) ($p<0.001$). Teriparatide increased BMD at the total hip (3.6%) compared with alendronate (2.2%) ($p<0.01$), as well as at the femoral neck (3.7%) compared with alendronate (2.1%) ($p<0.05$). In patients treated with teriparatide, lumbar spine, total hip and femoral neck BMD increased between 18 and 24 months by an additional 1.7%, 0.9%, and 0.4%, respectively.

Figure 1 shows the mean percent changes from baseline in lumbar spine BMD in patients treated with teriparatide or alendronate who had BMD measurements at each time point.

The relative treatment effects of teriparatide and alendronate were consistent in subgroups defined by gender, age, geographic region, body mass index, underlying disease, prevalent vertebral fracture, baseline glucocorticoid dose, prior bisphosphonate use, and glucocorticoid discontinuation during trial.

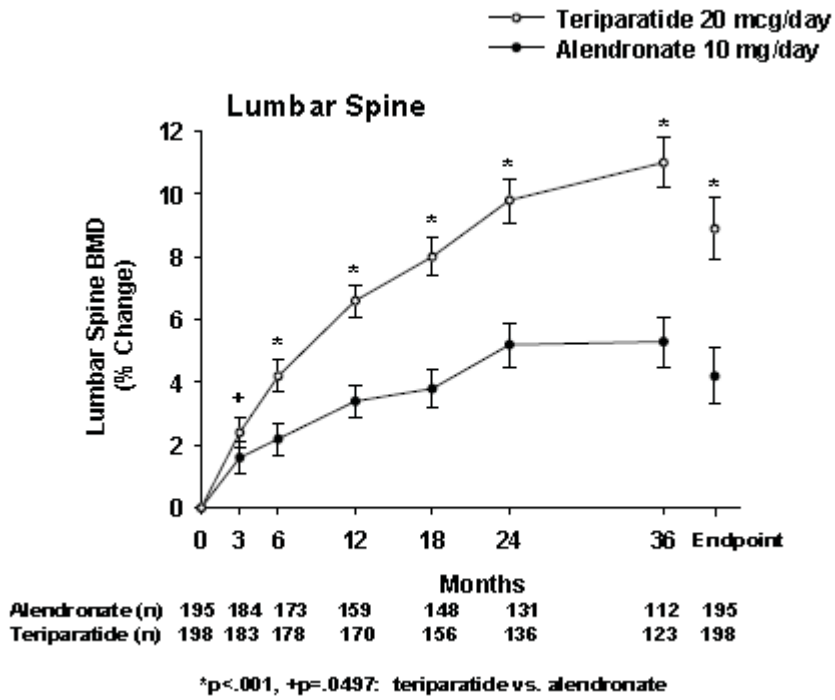

Figure 1. Percent Change in Lumbar Spine BMD (Mean ± SE) in Men and Women with Glucocorticoid-Induced Osteoporosis.

In premenopausal women, the increase in BMD from baseline to 36-month endpoint was significantly greater in the teriparatide group compared with the alendronate group at the lumbar spine (4.6% versus -0.9%; p=0.017) and total hip (4.8% versus 1.5%; p=0.026). However, no significant effect on fracture rates was demonstrated.

At 36 months, analysis of spinal X-rays from 169 alendronate patients and 173 teriparatide patients showed that 13 patients in the alendronate group (7.7%) had experienced a new vertebral fracture compared with 3 patients in the teriparatide group (1.7%) (p=0.01). In addition, 15 of 214 patients in the alendronate group (7.0%) had experienced a nonvertebral fracture compared with 16 of 214 patients in the teriparatide group (7.5%) (p=0.84).

Effects on Markers of Bone Turnover

In patients with glucocorticoid-induced osteoporosis who received either teriparatide 20 µcg/day or alendronate 10 mg/day, daily administration of teriparatide stimulated new bone formation as shown by increases from baseline in the serum concentration of biochemical markers of bone formation including bone-specific alkaline phosphatase (BSAP), procollagen I carboxy-terminal propeptide (PICP), and amino-terminal propeptide of type I collagen (PINP) (see **Table 6**). Teriparatide also stimulated bone resorption as shown by increases from baseline in serum concentrations of C-terminal telopeptide of type I collagen (CTX). Alendronate 10 mg/day induced decreases from baseline in the serum concentration of BSAP, PICP, PINP and CTX (see **Table 6**). The effects of teriparatide on bone turnover markers in patients with glucocorticoid-induced osteoporosis were qualitatively similar to the effects in postmenopausal women with osteoporosis not taking glucocorticoids.

Table 6. Median Percent Changes[a, b] from Baseline in Bone Biomarkers in Patients with Glucocorticoid-Induced Osteoporosis

	PINP µcg/L		BSAP µcg/L		PICP µcg/L		CTX pmol/L	
Treatment Duration	Teriparatide	ALN	Teriparatide	ALN	Teriparatide	ALN	Teriparatide	ALN
1 month	65	-17	19	-5	36	-12	11	-46
6 month	67	-50	31	-20	0	-27	45	-56
18 month	36	-48	16	-21	-11	-28	9	-64
36 month	38	-40	22	-18	-11	-26	5	-55

[a] The median percent changes in teriparatide-treated patients were significantly different ($p<0.01$) compared with alendronate-treated (ALN) patients for each biomarker at all time points.

[b] Values represent median percent changes with n=54 to 99 among the 4 biomarkers at the different time points.

5.2 Pharmacokinetic properties

After subcutaneous injection, teriparatide has an absolute bioavailability of 95%.

Absorption and elimination are rapid. Following a subcutaneous injection of a 20-microgram dose, peak molar concentrations of teriparatide briefly exceed the upper limit of normal for endogenous PTH (65 picogram/mL [7.0 picomolar]) by 4 to 5- fold for about 30 minutes and decline to non-quantifiable concentrations within 3 hours. The mean systemic exposure (endogenous PTH and teriparatide) over 24 hours does not exceed the upper limit of normal and is below the levels found in patients with mild hyperparathyroidism.

Teriparatide is eliminated through hepatic and extra-hepatic clearance (approximately 62 L/hr in women and 94 L/hr in men). The volume of distribution is approximately 1.7 L/kg. Between-subject variability in systemic clearance and volume of distribution is 25% to 50%. The half-life of teriparatide is approximately 1 hour when administered subcutaneously. No metabolism or excretion studies have been performed with teriparatide. However, the mechanisms of metabolism and elimination of PTH(1-34) and intact PTH have been extensively described. Peripheral metabolism of parathyroid hormone is believed to occur predominantly in liver and kidney.

Special Populations

Age

No differences in teriparatide pharmacokinetics were detected with regard to age (range 31 to 85 years). Dosage adjustment based on age is not required.

Gender

Systemic exposure to teriparatide is approximately 20% to 30% lower in men than in women. There were, however, no gender differences with respect to safety, tolerability, or pharmacodynamic responses. Dosage adjustment based upon gender is not required.

Renal Impairment

No clinically relevant pharmacokinetic or safety differences were identified in patients with mild, moderate, or severe chronic renal impairment administered a single dose of teriparatide, therefore dosage adjustment based on mild to moderate renal impairment is not required. However, patients with renal impairment had reduced calcaemic and calciuric responses to teriparatide. Long-term safety and efficacy have not been evaluated in patients with creatinine clearance <30 mL/min and thus teriparatide should not be administered to patients with severe renal impairment (see section 4.3 Contraindications).

Heart Failure
No clinically relevant pharmacokinetic, blood pressure, pulse rate or other safety differences were identified in patients with stable heart failure (New York Heart Association Class I to III and additional evidence of cardiac dysfunction) administered two 20-microgram doses of teriparatide. Dosage adjustment based on the presence of mild or moderate heart failure is not required. There is no data from patients with severe heart failure.

Hepatic Impairment
Safety and efficacy have not been evaluated in patients with hepatic impairment. Animal studies have shown that severely reduced hepatic blood flow decreases exposure of PTH to the principal cleavage system and consequently clearance of PTH(1-84). In vitro studies have demonstrated that high capacity liver-specific phagocytic cells in the hepatic sinusoidal capillaries, the hepatic Kupffer cells, rather than hepatocytes, are the principal site for the cleavage of PTH(1-34) and PTH(1-84) into fragments that are consequently cleared from the circulation by the kidney. Thus, it is unlikely that hepatic impairment will have a clinically significant effect on systemic exposure to teriparatide.

5.3 Preclinical safety data

Carcinogenicity
Two carcinogenicity bioassays were conducted in Fischer 344 rats. In the first study, male and female rats were given daily subcutaneous teriparatide injections of 5, 30, or 75 microgram/kg/day for 24 months from 2 months of age. These doses resulted in systemic exposures that were, respectively, 3, 20, and 60 times higher than the systemic exposure observed in humans following a subcutaneous dose of 20 microgram (based on AUC comparison). Teriparatide treatment resulted in a marked dose related increase in the incidence of osteosarcoma, a rare malignant bone tumour, in both male and female rats.

Osteosarcomas were observed at all doses and the incidence reached 40% to 50% in the high dose groups. Teriparatide also caused a dose related increase in osteoblastoma and osteoma in both sexes. No osteosarcomas, osteoblastomas or osteomas were observed in untreated control rats. The bone tumours in rats occurred in association with a large increase in bone mass and focal osteoblast hyperplasia.

The second 2 year study was carried out in order to determine the effect of treatment duration and animal age on the development of bone tumours. Female rats were treated for different periods between 2 and 26 months of age with subcutaneous doses of 5 and 30 microgram/kg (equivalent to 3 and 20 times the human exposure at the 20 microgram dose, based on AUC comparison). The study showed that the occurrence of osteosarcoma, osteoblastoma and osteoma was dependent upon dose and duration of exposure. Bone tumours were observed when immature 2 month old rats were treated with 30 microgram/kg/day for 24 months or with 5 or 30 microgram/kg/day for 6 months. Bone tumours were also observed when mature 6 month old rats were treated with 30 microgram/kg/day for 6 or 20 months. Tumours were not detected when mature 6 month old rats were treated with 5 microgram/kg/day for 6 or 20 months. The results did not demonstrate a difference in susceptibility to bone tumour formation, associated with teriparatide treatment, between mature and immature rats. The relevance of these rat findings to humans is uncertain.

Mutagenicity
Teriparatide was not genotoxic in any of the following test systems: the Ames test for bacterial mutagenesis with and without metabolic activation, the mouse lymphoma assay for mammalian cell mutation, the chromosomal aberration assay in Chinese hamster ovary cells, and the in vivo micronucleus test in mice.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glacial acetic acid
Sodium acetate trihydrate
Mannitol
Metacresol (3 mg/mL as preservative)
Hydrochloric acid
Sodium hydroxide
Water for injection

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Store in a refrigerator (2°C-8°C) at all times. The pen should be returned to the refrigerator immediately after use. Do not freeze.

Do not store the injection device with the needle attached.

6.5 Nature and contents of container

Pack size: One prefilled pen.

2.4 mL solution in cartridge (siliconized Type I glass) with a plunger (halobutyl rubber), disc seal (polyisoprene/bromobutyl rubber laminate)/aluminium assembled into a disposable pen.

6.6 Special precautions for disposal and other handling

Teriparatide Teva is supplied in a pre-filled pen. Each pen should be used by only one patient. A new, sterile needle must be used for every injection. Each Teriparatide Teva pack is provided with a package insert that fully describes the use of the pen. No needles are supplied with the product. The device can be used with insulin pen injection needles. After each injection, the Teriparatide Teva pen should be returned to the refrigerator.

The unopened Teriparatide-Teva pen may be removed from the refrigerator and stored at temperature up to 25°C for one single period of up to 5 days, after which it should be returned to the refrigerator (2 °C - 8°C). Discard the unopened Teriparatide-Teva pen if stored above 8 °C for more than 5 days.

Teriparatide Teva should not be used if the solution is cloudy, coloured or contains particles.

Please also refer to the Instructions for Use enclosed in the pack for instructions on how to use the pen.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

Teva Pharma (New Zealand) Limited
PO Box 128 244

Auckland, New Zealand
Telephone: 0800 800 097

9. DATE OF FIRST APPROVAL

15 December 2022

10. DATE OF REVISION OF THE TEXT

03 October 2025

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
1	To include the pharmaceutical form
4.2	Update - the maximum total duration of treatment
4.3	Update - Contraindication for metabolic bone disease and osteoporosis and addition of pregnancy and lactation.
4.4	Update – duration of treatment, use in paediatric population and young adults with open epiphyses, younger adult population Relocation of serum calcium paragraph from section 4.5
4.6	Update to use in pregnancy and addition of information for use in women of childbearing potential/contraception in females, update breastfeeding
4.8	Addition of anaemia and renal failure/impairment in Table 4 – Tabulated list of spontaneously reported adverse reactions