SUMMARY OF PRODUCT CHARACTERISTICS

BONSITY
(Teriparatide (Synthetic) Solution for Injection 250 mcg/ml,
2.4ml Pre-Filled Syringes)

1. NAME OF THE MEDICINAL PRODUCT

BONSITY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One pre-filled pen of 2.4 mL contains 600 micrograms of teriparatide (corresponding to 250 micrograms per mL)

For the full list of excipients, see **section 6.1.**

3. PHARMACEUTICAL FORM

Solution for injection

Clear, colourless solution free from visible particles

The pH is between 3.8 and 4.5. The osmolality is between 250 to 350 mOsmol.

4 CLINICAL PARTICULARS[1]

4.1 Therapeutic indications

BONSITY is indicated in adults.

Treatment of osteoporosis in postmenopausal women and in men at increased risk of fracture. In postmenopausal women, a significant reduction in the incidence of vertebral and non-vertebral fractures but not hip fractures has been demonstrated.

Treatment of osteoporosis associated with sustained systemic glucocorticoid therapy in women and men at increased risk for fracture.

4.2 Posology and method of administration

The recommended dose of **BONSITY** is 20 micrograms administered once daily.

The maximum total duration of treatment with **BONSITY** should be 24 months (see **section 4.4**). The 24-month course of **BONSITY** should not be repeated over a patient's lifetime.

Patients should receive supplemental calcium and vitamin D supplements if dietary intake is inadequate.

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

Special populations

Patients with renal impairment

Teriparatide must not be used in patients with severe renal impairment (see **section 4.3**). In patients with moderate renal impairment, teriparatide should be used with caution. No special caution is required for patients with mild renal impairment.

Patients with hepatic impairment

No data are available in patients with impaired hepatic function (see **section 5.3**). Therefore, teriparatide should be used with caution.

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.

Elderly patients

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

Method of administration

BONSITY should be administered once daily by subcutaneous injection in the thigh or abdomen.

Patients must be trained to use the proper injection techniques (see **section 6.6**). A user manual is also available to instruct patients on the correct use of the pen.

4.3 Contraindications

- Hypersensitivity to teriparatide or to any of the excipients listed in **section 6.1.**

- Pregnancy and breast-feeding (see **sections 4.4** and **4.6**)
- 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 should be excluded from treatment with teriparatide.

4.4 Special warnings and precautions for use

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Serum and urine calcium

In normocalcaemic patients, slight and transient elevations of serum calcium concentrations have been reported 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. Therefore, if blood samples for serum calcium measurements are taken, this should be done at least 16 hours after the most recent teriparatide injection. Routine calcium monitoring during therapy is not required.

Teriparatide may cause small increases in urinary calcium excretion, but the incidence of hypercalciuria did not differ from that in the placebo-treated patients in reported clinical studies.

Urolithiasis

The use of teriparatide has not been reported 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.

Orthostatic hypotension

Isolated episodes of transient orthostatic hypotension have been reported with teriparatide. Typically, an event reportedly began within 4 hours of dosing and spontaneously resolved within a few minutes to a few hours. When transient orthostatic hypotension reportedly occurred, it happened within the first several doses, was relieved by placing subjects in a reclining position, and did not preclude continued treatment.

Renal impairment

Caution should be exercised in patients with moderate renal impairment.

Younger adult population

Experience in the younger adult population, including premenopausal women, is limited. Treatment should only be initiated if the benefit clearly outweighs risks in this population.

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

Duration of treatment

Increased incidence of osteosarcoma has been reported with long-term administration of teriparatide in rats (see **section 5.3**). Until further clinical data become available, the recommended treatment time of 24 months should not be exceeded.

Sodium content

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

In a reported study of 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, it should be used with caution in patients taking digitalis.

No clinically significant interactions have been reported with teriparatide and hydrochlorothiazide.

Co-administration of raloxifene or hormone replacement therapy with teriparatide did not alter the effects of teriparatide on serum or urine calcium or on clinical adverse events.

4.6 Fertility, Pregnancy and lactation

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.

Pregnancy

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

Breast-feeding

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

Fertility

Reproductive toxicity has been reported in rabbits (see **section 5.3**). The effect of teriparatide on human foetal development has not been reported. The potential risk for humans is unknown.

4.7 Effects on ability to drive and use machines

Teriparatide has no or negligible influence on the ability to drive and use machines. Transient, orthostatic hypotension or dizziness has been reported in some patients. These patients should refrain from driving or the use of machines until symptoms have subsided.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions in patients treated with teriparatide are nausea, pain in limb, headache and dizziness.

Tabulated list of adverse reactions

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

The adverse reactions associated with the use of teriparatide in reported osteoporosis clinical studies and post-marketing exposure are summarised in the table below. The following convention has been used for the classification of the adverse reactions: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), very rare (< 1/10,000).

Blood and lymphatic system disorders *Common*: Anaemia
Immune System Disorder *Rare*: Anaphylaxis
Metabolism and nutrition disorders *Common*: Hypercholesterolaemia *Uncommon*: Hypercalcaemia greater than 2.76 mmol/L, hyperuricaemia *Rare*: Hypercalcaemia greater than 3.25 mmol/L
Psychiatric disorders *Common*: Depression
Nervous system disorders *Common*: Dizziness, headache, sciatica, syncope
Ear and labyrinth disorders *Common*: Vertigo
Cardiac disorders *Common*: Palpitations *Uncommon*: Tachycardia
Vascular disorders *Common*: Hypotension
Respiratory, thoracic and mediastinal disorders *Common*: Dyspnoea *Uncommon:* Emphysema
Gastrointestinal disorders *Common*: Nausea, vomiting, hiatus hernia, gastro-oesophageal reflux disease *Uncommon*: Haemorrhoids
Skin and subcutaneous tissue disorders *Common*: Sweating increased
Musculoskeletal and connective tissue disorders *Very common*: Pain in limb *Common*: Muscle cramps *Uncommon*: Myalgia, arthralgia, back cramp/pain*
Renal and urinary disorders *Uncommon*: Urinary incontinence, polyuria, micturition urgency, nephrolithiasis *Rare:* Renal failure/impairment
General disorders and administration site conditions

Common: Fatigue, chest pain, asthenia, mild and transient injection site events, including pain, swelling, erythema, localised bruising, pruritus and minor bleeding at injection site *Uncommon*: Injection site erythema, injection site reaction *Rare*: Possible allergic events soon after injection: acute dyspnoea, oro/facial oedema, generalised urticaria, chest pain, oedema (mainly peripheral)
Investigations *Uncommon*: Weight increased, cardiac murmur, alkaline phosphatase increase

* Serious cases of back cramp or pain have been reported within minutes of the injection.

Description of selected adverse reactions

In clinical trials the following reactions were reported at a ≥ 1 % difference in frequency from placebo: vertigo, nausea, pain in limb, dizziness, depression, dyspnoea.

Teriparatide increases serum uric acid concentrations. In clinical studies, 2.8 % of teriparatide patients had serum uric acid concentrations above the upper limit of normal compared with 0.7 % of placebo patients. However, the hyperuricaemia did not reportedly 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 reportedly first detected following 12 months of treatment and diminished after withdrawal of therapy. No evidence of hypersensitivity reactions, allergic reactions, effects on serum calcium, or effects on Bone Mineral Density (BMD) response has been reported.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the health authority ADR reporting tool.

4.9 Overdose

Signs and symptoms

Teriparatide has been administered in single doses of up to 100 micrograms and in repeated doses of up to 60 micrograms/day for 6 weeks.

The effects of overdose that might be expected include delayed hypercalcaemia and risk of orthostatic hypotension. Nausea, vomiting, dizziness, and headache can also occur.

Overdose experience based on post-marketing spontaneous reports.

In post-marketing spontaneous reports, there have been cases of medication error where the entire contents (up to 800 mcg) 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.

Overdose management

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

5. PHARMACOLOGICAL PROPERTIES[1]

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Calcium homeostasis, parathyroid hormones and analogues, ATC code: H05AA02

Mechanism of action

Endogenous 84-amino-acid parathyroid hormone (PTH) is the primary regulator of calcium and phosphate metabolism in bone and kidney. Teriparatide (rhPTH[1-34]) is the active fragment (1-34) of endogenous human parathyroid hormone. 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.

Pharmacodynamic effects

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 bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity.

5.2 Pharmacokinetics properties

Distribution

The volume of distribution is reported to be approximately 1.7 L/kg. The half-life of teriparatide is approximately 1 hour when administered subcutaneously, which reflects the time required for absorption from the injection site.

Biotransformation

No metabolism or excretion studies have been reported with teriparatide, but the peripheral metabolism of parathyroid hormone is believed to occur predominantly in liver and kidney.

Elimination

Teriparatide is eliminated through hepatic and extra-hepatic clearance (approximately 62 L/hr in women and 94 L/hr in men).

Elderly

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

5.3 Preclinical safety data

Teriparatide has been reported to be non-genotoxic in a standard battery of tests. It produced no teratogenic effects in rats, mice or rabbits. No important effects have been reported in pregnant rats or mice administered teriparatide at daily doses of 30 to 1,000 μg/kg. However, foetal resorption and reduced litter size have been reported in pregnant rabbits administered daily doses of 3 to 100 μg/kg. The embryotoxicity reported in rabbits may be related to their much greater sensitivity to the effects of PTH on blood-ionised calcium compared with rodents.

Rats treated with near-lifetime daily injections reportedly had dose-dependent exaggerated bone formation and increased incidence of osteosarcoma most probably due to an epigenetic mechanism. Teriparatide did not reportedly increase the incidence of any other type of neoplasia in rats. Due to the differences in bone physiology in rats and humans, the clinical relevance of these findings is probably minor. No bone tumours have been reported in ovariectomised monkeys treated for 18 months or during a 3-year follow-up period after treatment cessation. In addition, no osteosarcomas have been reported in clinical studies or during the post-treatment follow-up study.

Severely reduced hepatic blood flow has been reported to decrease exposure of PTH to the principal cleavage system (Kupffer cells) and consequently clearance of PTH(1-84) in animals.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glacial acetic acid, sodium acetate (anhydrous) (Parental Grade), mannitol (Parental Grade), metacresol (Parental Grade), hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) & 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

Once opened, the product may be stored for a maximum of 28 days at 2°C to 8°C.

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

2.4 mL solution in cartridge (USP Type I glass) with a plunger stopper, disc seal assembled into a disposable pen.

BONSITY is available in pack sizes of 1 pen. Each pen contains 28 doses of 20 micrograms (per 80 microlitres).

6.6 Special precautions for disposal and other handling

BONSITY 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 BONSITY pack is provided with a User Manual that fully describes the use of the pen. The device can be used with insulin pen injection needles. After each injection, the BONSITY pen should be returned to the refrigerator.

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

Please also refer to the user manual for instructions on how to use the pen.

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

7. MARKETING AUTHORISATION HOLDER

Sun Pharmaceutical Industries Limited,
Sun House, 201 B/1, Western Express Highway,
Goregaon (East), Mumbai-400063, Maharashtra, INDIA

8. MARKETING AUTHORISATION NUMBER(S)

CTD12313

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

3rd April 2026

10. DATE OF REVISION OF THE TEXT

October 2024