**NAME OF THE MEDICINAL PRODUCT**

BONMAX®PTH

**BONMAX®PTH** (Recombinant Human Parathyroid Hormone or hPTH 1-34) 20 µg per 50 ml for injection in cartridge.

**QUALITATIVE AND QUANTITATIVE COMPOSITION**

BONMAX®PTH is supplied as a sterile solution for injection in cartridge.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Quantity per ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teriparatide (hPTH 1-34) or Recombinant Human Parathyroid Hormone (rHPT)</td>
<td>250 µg</td>
</tr>
<tr>
<td>Glacial acetic acid – USP</td>
<td>0.41 mg</td>
</tr>
<tr>
<td>Sodium acetate anhydrous – USP</td>
<td>0.10 mg</td>
</tr>
<tr>
<td>Mannitol – USP</td>
<td>45.4 mg</td>
</tr>
<tr>
<td>Metacresol – USP</td>
<td>3.0 mg</td>
</tr>
<tr>
<td>Water for Injection – USP</td>
<td>q.s.</td>
</tr>
</tbody>
</table>

**Cartridge:** Each cartridge filled with 3 ml solution for injection contains 750 µg of teriparatide (250 µg per ml) for up to 28 days after opening. Each single dose as delivered by a pen loaded with the cartridge contains 20 µg of teriparatide per 80 µl.

**CLINICAL PARTICULARS**

**Therapeutic indications**

BONMAX®PTH is indicated for the treatment of patients with severe osteoporosis. BONMAX®PTH is indicated for the treatment of men and women with osteoporosis associated with systemic glucocorticoid therapy at high risk for fracture.

**Posology and method of administration**

BONMAX®PTH sterile solution should be administered subcutaneously in the thigh or abdomen. The recommended daily dose of teriparatide is 20 µg (60 µl solution of 250 µg per ml concentration). When in cartridge form, administration of BONMAX®PTH is available for up to 28 days after opening. Each single dose as delivered by a pen loaded with the cartridge contains 20 µg of teriparatide per 80 µl.

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The effect of teriparatide on bone mineral density has been studied in patients with severe osteoporosis. BONMAX®PTH is indicated for the treatment of men and women with osteoporosis associated with systemic glucocorticoid therapy at high risk for fracture.

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**Undesirable effects**

The most commonly reported adverse event in patients treated with teriparatide was increased bone turnover. However, patients with transient, orthostatic hypotension or dizziness should refrain from driving or the use of machines until symptoms have subsided. In case of inadequate dietary intake, patients should receive supplemental calcium and vitamin D.

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Clinical efficacy
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 at increased risk of osteoporotic fractures who could benefit from treatment. Prenumepausal women with glucocorticoid-induced osteoporosis should be considered at high risk for fracture if they have a prevalent fracture and a portion of risk factors that place them at high risk for fracture (e.g., low bone density, e.g., T-score ≤−2.5), sustained high dose glucocorticoid therapy (e.g., ≥7.5 mg/day for at least 6 months), high underlying disease activity, low sex steroid levels.

Postmenopausal osteoporosis
In a pivotal clinical trial of teriparatide conducted on 1637 postmenopausal women (mean age 69.5 years) with established osteoporosis (T-score between −2.5 in the presence of one or more fragility fractures or nineteen percentile of the normal vertebral fractures at baseline. All patients were offered 1000 mg calcium per day and at least 400 IU vitamin D per day. Results from up to 19 months’ treatment with teriparatide demonstrate statistically significant fracture reduction. To prevent one or more new vertebral fractures, women had to be treated for a median of 19 months.

Fracture Incidence in Postmenopausal Women:

<table>
<thead>
<tr>
<th>Placebo (%)</th>
<th>Teriparatide (1.25 μg or 2.5 μg / day) (%)</th>
<th>Relative risk (95% CI) vs. placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>New vertebral fracture ( ≥ 1a)</td>
<td>14.3</td>
<td>5.0b</td>
</tr>
<tr>
<td>Multiple vertebral fractures ( ≥ 2a)</td>
<td>4.9</td>
<td>1.1b</td>
</tr>
<tr>
<td>Non-vertebral fragility fractures</td>
<td>5.5%</td>
<td>2.67%</td>
</tr>
<tr>
<td>Major non-vertebral fragility fractures (hip, radius, humerus, ribs and pelvis)</td>
<td>3.9%</td>
<td>1.55%</td>
</tr>
</tbody>
</table>

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

- The incidence of vertebral fractures was assessed in 448 placebo and 444 teriparatide patients who had baseline and follow-up spine radiographs.
- p ≤ 0.001 compared with placebo.
- A significant reduction in the incidence of hip fractures has not been demonstrated.
- p ≤ 0.025 compared with placebo.
- After 19 months (median) treatment, bone mineral density (BMD) had increased in the lumbar spine and total hip, respectively, by 9% and 4% compared with placebo (p ≤ 0.001).

A pilot-in-treatment follow-up study, 1282 postmenopausal women were treated with teriparatide. The primary objective of the study was to collect safety data of teriparatide. During this observational period, other osteoporosis treatments were allowed and additional adjustment of treatment was performed. During a median of 18 months following discontinuation of teriparatide, there was a 41% reduction (p=0.004) compared with placebo in the number of patients with a minimum of one new vertebral fractures.

A prospective, multicentric, investigator-initiated, randomized, double-blind, placebo-controlled, single-blinded observed patients in the study had been carried out with BONMAX®PTH to evaluate the safety and efficacy of the drug in women with postmenopausal osteoporosis. A total of 8856 randomized, 70 postmenopausal women were chosen by dose group, osteoporosis with T-score < −2.5 to −4 at any one of the two sites measured (lumbar spine and femoral neck) were subjected to a 3-month study. The active treatment group (49 subjects) received BONMAX®PTH 20 μg OD SC once a day in the morning with breakfast. The half-life of teriparatide is approximately 1.7 h and reflects the time required for absorption from the injection site. No pharmacokinetic properties were performed with teriparatide but the peripheral metabolic pathways of parathyroid hormone is believed to occur predominantly in liver and kidney.

- Teriparatide is eliminated through hepatic and extra-hepatic clearance.
- No other organ including site of injection revealed histopathological effects that could be attributed to BONMAX®PTH.
- No other organ including site of injection revealed histopathological effects of BONMAX®PTH and the innovator drug.
- Pharmacokinetic properties

Teriparatide is eliminated through hepatic and extra-hepatic clearance (approximately 62 h / lhr in women and 94 l / h / lhr in men). The volume of distribution is approximately 1.7 l / kg. The half-life of teriparatide is approximately 1 h when administered subcutaneously, which corresponds to the time required for absorption from the injection site. No pharmacokinetic properties were performed with teriparatide but the peripheral metabolic pathways of parathyroid hormone is believed to occur predominantly in liver and kidney.

- Teriparatide is administered as a subcutaneous injection of 28 days dosing in a single pack.
- Cartridge: Teriparatide solution is filled in siliconized boro-silicate Type I glass cartridge with plugger rubber stopper and disc seal.

The results are also comparable with the published teriparatide reports.