# הודעה על החמרה ( מידע בטיחות)

 **תאריך : 31-12-2012**

**שם תכשיר באנגלית : PROLIA™ 60 MG**

**מספר רישום : 146-25-33253**

**שם בעל הרישום GlaxoSmithKline (ISRAEL) Ltd :**

בעלון לרופא

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|  **פרטים על השינוי/ים המבוקש/ים** |
| **פרק בעלון** | **טקסט נוכחי** | **טקסט חדש** |
| **4.4 Special warnings and precautions for use** |  | *Hypocalcemia*In the post-marketing setting, severe symptomatic hypocalcaemia has been reported (see section 4.8). |
|  | ~~Patients receiving Prolia may develop skin infections (predominantly cellulitis) leading to hospitalisation (see section 4.8). Patients should be advised to seek prompt medical attention if they develop signs or symptoms of cellulitis.~~*Infections*In a clinical trial of over 7800 women with postmenopausal osteoporosis, serious infections leading to hospitalization were reported more frequently in the Prolia group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract, and ear, were more frequent in patients treated with Prolia. Endocarditis was also reported more frequently in Prolia-treated patients. The incidence of opportunistic infections was similar between placebo and Prolia groups, and the overall incidence of infections was similar between the treatment groups.  |
|  | Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis. |
|  | Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. Consider the benefit-risk profile in such patients before treating with Prolia. In patients who develop serious infections while on Prolia, prescribers should assess the need for continued Prolia therapy. |
|  | *Dermatologic Adverse Reactions*In a large clinical trial of over 7800 women with postmenopausal osteoporosis, epidermal and dermal adverse events such as dermatitis, eczema, and rashes occurred at a significantly higher rate in the Prolia group compared to the placebo group. Most of these events were not specific to the injection site. Consider discontinuing Prolia if severe symptoms develop.  |
|  | *Atypical Subtrochanteric and Diaphyseal Femoral Fractures*Atypical low-energy or low trauma fractures of the shaft have been reported in patients receiving Prolia. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with anti-resorptive agents.Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture. During Prolia treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patient presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of Prolia therapy should be considered, pending a risk/benefit assessment, on an individual basis. *Suppression of Bone Turnover* In clinical trials in women with postmenopausal osteoporosis, treatment with Prolia resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment with Prolia are unknown. The long-term consequences of the degree of suppression of bone remodeling observed with Prolia may contribute to adverse outcomes such as osteonecrosis of the jaw, atypical fractures, and delayed fracture healing. Monitor patients for these consequences.  |
| * 1. **Undesirable effects**
 |  | *Serious Infections*Receptor activator of nuclear factor kappa-B ligand (RANKL) is expressed on activated T and B lymphocytes and in lymph nodes. Therefore, a RANKL inhibitor such as Prolia may increase the risk of infection. In the clinical study of 7808 postmenopausal women with osteoporosis, the incidence of infections resulting in death was 0.2% in both placebo and Prolia treatment groups. However, the incidence of nonfatal serious infections was 3.3% in the placebo and 4.0% in the Prolia groups. Hospitalizations due to serious infections in the abdomen (0.7% placebo vs. 0.9% Prolia), urinary tract (0.5% placebo vs. 0.7% Prolia), and ear (0.0% placebo vs. 0.1% Prolia) were reported. Endocarditis was reported in no placebo patients and 3 patients receiving Prolia. Skin infections, including erysipelas and cellulitis, leading to hospitalization were reported more frequently in patients treated with Prolia (< 0.1% placebo vs. 0.4% Prolia). The incidence of opportunistic infections was similar to that reported with placebo. |
|  | *Dermatologic Reactions*A significantly higher number of patients treated with Prolia developed epidermal and dermal adverse events (such as dermatitis, eczema, and rashes), with these events reported in 8.2% of the placebo and 10.8% of the Prolia groups (p < 0.0001). Most of these events were not specific to the injection site. |
| **Instructions for injecting with the Prolia™ pre-filled syringe with an automatic needle duard** | **The appearance** of Prolia. It must be a clear, colourless to slightly yellow solution. The solution shouid not be injected if it contains particles or is cloudy or discoloured. | **The appearance** of Prolia. It must be a clear, colourless to slightly yellow liquid. if it contains particles or is cloudy or discoloured, you must not use it. |

מצ"ב העלון, שבו מסומנות ההחמרות המבוקשות בצבע אדום. שינויים שאינם בגדר החמרות סומנו (בעלון) בטקסט ירוק.