Annex III

Amendments to the relevant sections of the summary of product characteristics and package leaflet

(injectable formulations)

A. Summary of Product Characteristics

4.1 Therapeutic indication

[the currently approved indications should be deleted and replaced by the following]

Prevention of acute bone loss due to sudden immobilisation such as in patients with recent osteoporotic fractures.

For the treatment of Paget's disease, only in patients who do not respond to alternative treatments or for whom such treatments are not suitable, for example those with severe renal impairment.

Treatment of hypercalcaemia of malignancy.

4.2 Posology and method of administration

[the wording below should be inserted]

[...]

Due to evidence of an increased risk of malignancies and long term calcitonin use (see section 4.4), the treatment duration in all indications should be limited to the shortest period of time possible and using the minimum effective dose.

Prevention of acute bone loss due to sudden immobilisation such as in patients with recent osteoporotic fractures

The recommended dosage is 100 I.U. daily or 50 I.U. twice daily administered subcutaneously or intramuscularly. The dose may be reduced to 50 IU. daily at the start of remobilisation. The recommended treatment duration is 2 weeks and should not exceed 4 weeks in any case due to the association of the increased risk of malignancies and long term calcitonin use.

Paget's disease

The recommended dosage is 100 I.U. per day administered subcutaneously or intramuscularly, however a minimum dosage regimen of 50 I.U. three times a week has achieved clinical and biochemical improvement. Dosage is to be adjusted to the individual patient's needs. Treatment should be discontinued once the patient has responded and symptoms have resolved. Duration of treatment should not normally exceed 3 months due to evidence of an increased risk of malignancies with long term calcitonin use. Under exceptional circumstances, e.g. in patients with impending pathologic fracture, treatment duration may be extended up to a recommended maximum of 6 months.

Periodic re-treatment may be considered in these patients, and should take into account the potential benefits and evidence of an increased risk of malignancies and long term calcitonin use (see section 4.4).

The effect of calcitonin may be monitored by measurement of suitable markers of bone remodelling, such as serum alkaline phosphatase or urinary hydroxyproline or deoxypyridinoline.

4.4 Special warnings and precautions for use

[the wording below should be inserted]

[…]

Analyses of randomised controlled trials conducted in patients with osteoarthritis and osteoporosis have shown that calcitonin is associated with a statistically significant increase in the risk of cancer compared to patients treated with placebo. These trials demonstrated an increase in the absolute risk of cancer occurrence for patients treated with calcitonin compared to placebo which varied between 0.7% and 2. 4% with long-term therapy. Patients in these trials were treated with oral or intra-nasal formulations however it is likely that an increased risk also applies when calcitonin is administered subcutaneously, intramuscularly or intravenously especially for long-term use, as systemic exposure to calcitonin in such patients is expected to be higher than for other formulations.

[…]

4.8 Undesirable effects

[the wording below should be inserted]

[…]

Malignancy (with long term use), frequency: common

[…]

B. Patient Information Leaflet

1. What <invented name> is and what it is used for:

[the currently approved wording should be deleted and replaced by the following]

<invented name> can be given for the following conditions:

- Prevention of bone loss in patients who have suddenly become immobile. For example, patients who are bed-bound because of a fracture.

- Paget's disease of bone in patients who cannot take other treatments for this condition, for example patients with serious kidney problems. Paget's disease is a slowly progressing illness which can cause a change in the size and shape of certain bones.

- Treatment of high calcium levels in the blood (hypercalcaemia) due to cancer.

2. Before you take <invented name>

[the wording below should be inserted]

[…]

Take special care with <invented name>

Please tell your doctor if you have been diagnosed with cancer. In clinical trials, patients treated with calcitonin for osteoporosis and osteoarthritis have shown an increase in the risk of cancer following

long term treatment. Your doctor will decide if calcitonin is a suitable treatment for you and for how long you can be treated.

3. How to take <invented name>

[the wording below should be inserted]

Your doctor will decide the correct dose and how long you should receive calcitonin treatment depending on your condition.

The usual doses are:

- For prevention of bone loss: 100 IU per day or 50 IU twice daily for 2 to 4 weeks, given into the muscle or the tissue just under the skin.

- For Paget's disease: 100 IU daily injected into a muscle or into the tissue just under the skin, normally for up to 3 months. In some cases, you doctor might decide to extend your treatment up to 6 months.

- For the treatment of high calcium levels: 100 IU every 6 to 8 hours, given into a muscle or into the tissue just under the skin. In some cases, it may be given by injection into a vein.

4. Possible side effects

[the wording below should be inserted]

[…]

Common side effects:

Cancer (following long term treatment)

[…]