



**Question: “We have a patient with severe hypercalcaemia that is resistant to treatment with bisphosphonates. Could calcitonin be used?”**

**March 2017**

**Summary**

Calcitonin can be used to treat hypercalcaemia of malignancy. However, it is rarely effective where bisphosphonates have failed to reduce serum calcium adequately. Its effect can wear off after a few days despite continued use. It is usually given intramuscularly or subcutaneously. In emergency situations it can be given by continuous intravenous infusion.

**Information**

There are two types of calcitonin in clinical use, synthetic calcitonin (salmon) and synthetic calcitonin (human). Calcitonin (salmon) is most commonly used in practice; it is the most potent and has the longest duration of action.<sup>1</sup> Miacalcic® (salmon calcitonin) solution for injection and infusion 100 units/ml and 50 units/ml are licensed preparations in Ireland.<sup>2,3</sup> Calcitonin (human) may be very difficult to source in Ireland.

**Mechanism of Action**

Calcitonin is a calciotropic hormone, which inhibits bone resorption by a direct action on osteoclasts.<sup>2,3</sup> By inhibiting osteoclast activity via its specific receptors, salmon calcitonin decreases bone resorption.<sup>2,3</sup> The calcium-lowering effect of calcitonin is caused both by a decrease in the efflux of calcium from the bone to the extracellular fluid (ECF) and inhibition of renal tubular reabsorption of calcium.<sup>2,3</sup>

Palliative Meds Info: Terms and Conditions

The information outlined above is intended for healthcare professionals only. The information outlined above is believed to accurately reflect the medical literature at the time of writing. Healthcare professionals must use their own judgment to determine the accuracy and relevance of the information. See [www.olh.ie](http://www.olh.ie) for full terms and conditions.

## **Place in Therapy**

Calcitonin is rarely effective where bisphosphonates have failed to reduce serum calcium adequately.<sup>4</sup> Calcitonins can be used in addition to rehydration and diuresis in the management of moderate to severe symptomatic hypercalcaemia, including that of malignancy.<sup>1</sup> They may be particularly useful in life-threatening hypercalcaemia, because of their rapid effect.<sup>1</sup> However, although they have a rapid effect it is usually short-lived; calcitonins are therefore generally given as an adjunct with other therapy such as a bisphosphonate.<sup>1</sup> The efficacy of calcitonin is limited to the first 48 hours, even with repeated doses, indicating the development of tachyphylaxis, perhaps due to receptor downregulation.<sup>5</sup> Because of its limited duration of effect, calcitonin is most beneficial in symptomatic patients with calcium >3.5 mmol/L, when combined with hydration and bisphosphonates.<sup>5</sup> Calcitonin and saline hydration should substantially reduce calcium levels within 12-48 hours.<sup>5</sup> The bisphosphonate becomes effective by day 2-4 which then maintains control of calcium levels.<sup>5</sup>

## **Dose**

The dosage information outlined below relates to salmon calcitonin only.

For the treatment of hypercalcaemia of malignancy in adults over 18 years, the recommended starting dose by subcutaneous or intramuscular injection is 100 units every 6–8 hours adjusted according to response.<sup>1,2,3</sup> If the response is not satisfactory, the dose may be increased to a maximum dose of 400 units every 6–8 hours.<sup>1,2,3</sup> In severe or emergency cases up to 10 units/kg of calcitonin can be given by intravenous infusion, in 500 ml 0.9% w/v sodium chloride solution, over at least 6 hours.<sup>1,2,3</sup>

Alternatively, calcitonin may be given by subcutaneous or intramuscular injection in a dose of 4 units/kg every 12 hours, increased if necessary after one or two days to 8 units/kg every 12 hours, up to a maximum of 8 units/kg every 6 hours after a further two days.<sup>1,6</sup> Calcitonin salmon has also been administered in a dosage of 2–16 units/kg by IV infusion every 12 hours in the management of hypercalcemia.<sup>6</sup> When the volume to be administered exceeds 2mL the IM route is preferred.<sup>6</sup> Calcitonin may be administered at bedtime to reduce the incidence of nausea and vomiting which may pose an issue particularly at the beginning of treatment.<sup>2,3</sup>

### **Monitoring**

Frequent monitoring of the clinical and laboratory response including the measurement of serum calcium is recommended especially in the early phase of treatment.<sup>2,3</sup> The dosing of Miacalcic® should be individualized to the patient's specific requirements.<sup>2,3</sup>

### **Intravenous Infusion**

Calcitonins have been given by intravenous infusion, but this is rarely necessary and may cause more adverse effects.<sup>1</sup> If intravenous use is essential, it has been suggested that some protein must be present in the solution to prevent adsorption onto the plastic of the giving set.<sup>1</sup> However, in practice this does not seem to be the case, the manufacturer recommends dilution with normal saline.<sup>1,2,3</sup> It is acknowledged that such dilution results in a loss of potency, and dosage is adjusted accordingly.<sup>1</sup>

### **Continuous Subcutaneous Infusion (CSCI)**

Mystakidou et al conducted a non-randomised trial to evaluate the efficacy of salmon calcitonin in controlling pain related to bone metastasis in cancer patients and the relation of salmon calcitonin analgesic efficacy with beta-endorphin blood levels.<sup>7</sup> One of the aims of the study was to evaluate the efficacy of high dose salmon calcitonin via a continuous infusion pump.<sup>7</sup> The study found that the administration of salmon calcitonin via a CSCI can provide satisfactory analgesia when combined with morphine for the treatment of cancer pain due to bone metastasis.<sup>7</sup> The pH of Miacalcic solution is 3.9-4.5.<sup>8</sup>

### **References**

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