# Calcitonin Therapeutics

## Brands
- Miacalcin nasal spray
- Miacalcin (for subcutaneous or intramuscular injection)
- Fortical (nasal spray)
- Calcimar

## Generic?
Yes

## Class
- Polypeptide hormone

## Commonly Prescribed For
(FDA approved in bold)
- Postmenopausal osteoporosis (intranasal calcitonin)
- Paget’s disease of bone (injectable calcitonin)
- Hypercalcemia (injectable calcitonin)
- Osteogenesis Imperfecta Tarda
- Prevention of osteoporosis
- Complex regional pain syndrome (CRPS)
- Acute pain associated with osteoporosis-related vertebral fractures
- Phantom limb pain
- Pain from spinal stenosis
- Osteoarthritis
- Postoperative pain

## How the Drug Works
Calcitonin is a 32-amino acid linear polypeptide hormone that is produced in humans primarily by the parafollicular cells (also known as C-cells) of the thyroid, and in some animals in the ultimobranchial body. The calcitonin receptor is found on osteoclasts, in renal tissue, in the ovaries and testes, and in the central nervous system. It is a G protein-coupled receptor. The hormone participates in calcium (Ca\(^{2+}\)) and phosphorus metabolism. Calcitonin counters parathyroid hormone (PTH) activity and lowers blood Ca\(^{2+}\) levels by inhibiting (1) intestinal Ca\(^{2+}\) absorption, (2) osteoclasts activity, (3) http://en.wikipedia.org/wiki/Nephronrenal resorption of Ca\(^{2+}\).

Calcitonin also inhibits renal phosphate reabsorption. Calcitonin may have CNS action involving the regulation of feeding and appetite. The analgesic mechanism of action of calcitonin is poorly understood. The role of calcitonin in the CNS has received increased, attention, as animal studies have indicated that the antinociception is possibly mediated via descending systems. Calcitonin binds to a G protein-coupled receptor, with cyclic-AMP and calcium acting as secondary messengers. A recent study demonstrated that calcitonin interacts with the opioid receptors, namely the \(\delta\)- and \(\kappa\)- agonists. Moreover, in rodents, calcitonin amplified the analgesic effects of tricyclic antidepressants. The calcitonin analgesic effect seems to last long, possibly secondary to its accumulation in CNS.

## How Long until It Works
Within the first week of treatment

### If It Works
- Long-term use
- Treatment may be given in cycles

### If It doesn’t Work
- Alternative pharmacological and non-pharmacologic pain therapies

## Best Augmenting Combos for Partial Response or Treatment Resistance
- Physical therapy program for pain conditions, such as CRPS or painful osteoarthritis

## Tests
- Baseline general chemistry including blood levels of calcium, phosphorus, and alkaline phosphatase, 25-OH vitamin D, PTH, and CBC with differential

## Adverse Effects (AEs)

### How Drug Causes AEs
- Undetermined
- Tetany is due to hypocalcemia

### Notable AEs
- Nausea, gastrointestinal disturbances, vomiting
- Nose bleeds, nasal irritation (from nasal spray)
- Decreased appetite
- Warmth, redness, itching, at the site of injection
- Dizziness
- Headache
- Flushing of the face
- Hypersensitivity reactions
- Increased urination, especially at night
- Eye pain
- Pedal edema
Life-Threatening or Dangerous AEs
- Tetany
- Anaphylaxis

Weight Gain
- No

Sedation
- Unlikely

What to Do About AEs
- Reduce the dose or discontinue the drug

Best Augmenting Agents for AEs
- Calcium and vitamin D supplementation

**DOSING AND USE**

**Usual Dosage Range**
- Dosage one nasal spray (200 IU) per day
- 50 to 100 IU subcutaneously or intramuscularly once a day

**Forms**
- Nasal spray
- Injection

**How to Dose**
- Calcitonin nasal is usually given as one spray per day in alternating nostrils

**Dosing Tips**
- No serious adverse reactions have been associated with high doses of intranasal calcitonin. Chronic administration of doses up to 600 IU of intranasal calcitonin per day has been studied without serious adverse effects

**Overdose**
There have been no reports of hypocalcemic tetany. However, the pharmacologic actions of calcitonin suggest that this could occur in overdose. Therefore, provisions for parenteral administration of calcium should be available for the treatment of overdose. A dose of 1000 IU of calcitonin injectable solution given subcutaneously may produce nausea and vomiting.

**Habit Forming**
No

**How to Stop**
No need for tapering.

**Pharmacokinetics**
- Calcitonin can be extracted from the ultimobranchial glands of salmon. Salmon calcitonin resembles human calcitonin, but is more active. Calcitonin can also be produced by recombinant DNA technology or by chemical peptide synthesis. Calcitonin when given intranasally is absorbed rapidly by the mucosa. Peak plasma concentrations are achieved at about 30 minutes after nasal administration compared to 15–25 minutes following parenteral dosing. In normal volunteers, approximately up to 30% of an intranasal dose can become bioavailable. The half-life of elimination of calcitonin-salmon is about 45 minutes. There is no accumulation of the drug on repeated administration at 10-hour intervals for up to 15 days. Following parenteral administration of 100 IU calcitonin, peak plasma concentration lies between about 200 and 400 pg/ml. Plasma protein binding is 30% to 40%. Higher blood levels may be associated with increased incidence of nausea and vomiting. Salmon calcitonin is almost exclusively degraded in the kidneys, forming pharmacologically inactive fragments of the molecule. Therefore, the metabolic clearance is much lower in patients with end-stage renal failure than in healthy subjects. However, the clinical relevance of this finding is unknown

**Drug Interactions**
- Calcitonin may decrease serum lithium levels by up to 30%. The mechanism may be related to an increase in lithium elimination or to a decrease in lithium absorption caused by calcitonin

**Other Warnings/Precautions**
- None

**Do Not Use**
- Hypersensitivity to drug
SPECIAL POPULATIONS

Renal Impairment
- Salmon calcitonin is primarily and almost exclusively degraded in the kidneys, forming pharmacologically inactive fragments of the molecule. Therefore, the metabolic clearance is much lower in patients with end-stage renal failure than in healthy subjects. If medically necessary, the drug is to be administered with all the recommended precautions and under close medical monitoring.

Hepatic Impairment
- No clinically relevant concerns

Cardiac Impairment
- No clinically relevant concerns

Elderly
- The incidence of nasal adverse events from calcitonin was higher in patients over the age of 65, particularly those over the age of 75.

Children and Adolescents
- There are no data to support the use of calcitonin in children. Contraindicated, unless medically necessary and under close medical monitoring.

Pregnancy
- Category C
- There are no adequate and well-controlled studies in pregnant women with calcitonin, which is not indicated for use in pregnancy.

Breast Feeding
- It is not known whether this drug is excreted in human milk. As a general rule, breast-feeding should not be undertaken while a patient is on this drug, since many drugs are excreted in human milk. Calcitonin has been shown to inhibit lactation in animals.

THE ART OF PAIN PHARMACOLOGY

Potential Advantages
- Intranasal route can be used in patients with swallowing problems.

Potential Disadvantages
- Not available as oral agent

Primary Target Symptoms
- Chronic pain

Pearls
- Patients should undergo testing for 25OH vitamin D serum levels; vitamin D insufficiency and deficiency need to be corrected prior to calcitonin therapy
- Vitamin D3 supplementation at the dose of 1000–2000 IU per day should be provided in order to minimize the risk of hypocalcemia
- Human calcitonin is an orphan drug that may be used in patients who develop resistance or an allergic reaction to salmon calcitonin
- Some evidence from studies with injectable preparations suggests that calcitonin may have significant actions on the gastrointestinal tract. Administration of calcitonin can result in marked decreases in the volume of gastric and pancreatic secretion
- Calcitonin may have a chondroprotective role in osteoarthritis. A disease-modifying effect of calcitonin on subchondral bone osteoclasts has been hypothesized
- Studies conducted in the early 1980s showed that subcutaneous injections of salmon calcitonin in patients suffering from mania resulted in significant decreases in irritability and hyperactivity. Calcitonin may be added to a treatment regimen for bipolar disorder. However, further work on this potential application is needed
- As for analgesia, the calcitonin nasal spray and the parenteral formulations might not be interchangeable
- The limited data available do not support utilizing calcitonin for the treatment of painful osseous metastases


