For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

Gemitrol NS

1. Generic Name

Calcitonin Salmon Nasal solution USP

2. Qualitative and quantitative Composition:

Each Actuation Delivers

Calcitonin (Salmon)I.P. ……... 200 I.U.

(synthetic origin)

Each ml contains:

Calcitonin (Salmon) I.P. ……... 2200 I.U.

(synthetic origin)

Preservatives:

Benzalkonium Chloride I.P. …….0.01 % w/v

Phenyl Ethyl Alcohol I.P. ……... 0.2 % w/v

Aqueous Base……... q.s.

The excipients used are Benzalkonium Chloride, Phenyl Ethyl Alcohol, Polysorbate-80, Citric Acid Monohydrate, Sodium Chloride.

3. Dosage form and strength

Dosage form: Nasal solution

Strength: 200 I.U and 2200 I.U.

4. Clinical particulars

4.1. Therapeutic indication

Gemitrol NS Nasal Spray is indicated for:

- Treatment of postmenopausal osteoporosis
- Bone pain associated with osteolysis and/or osteopenia.
- Paget's disease of bone (osteitisde formans).
- Neurodystrophic disorders (synonymous with algo dystrophy or Sudeck's disease) due to various etiological and predisposing factors such as posttraumatic painful osteoporosis, reflex dystrophy, shoulder arm syndrome, causalgia, drug-induced neurotrophic disorders.

4.2. Posology and method of administration

Gemitrol NS Nasal Spray is for intranasal use only. Gemitrol NS Nasal Spray delivers 200 IU calcitonin (salmon) per actuation.

Osteoporosis: The recommended dosage of Gemitrol NS Nasal Spray for the treatment of established post-menopausal osteoporosis is 200 IU once a day administered intranasally, alternating nostrils daily. Use of calcitonin (salmon) Nasal Spray is recommended in conjunction with an adequate calcium (at least 1000 mg elemental calcium) and vitamin D

(400 IU per day) intake to prevent progressive loss of bone mass. Calcitonin (salmon) for the treatment of postmenopausal osteoporosis is to be administered on a long-term basis.

Bone pain associated with osteolysis and/or osteopenia: 200-400 IU daily. Up to 200 IU may be administered as a single dose; in cases where a higher dosage is required it should be given in divided doses. Dosage should be adjusted to the individual patient's needs. It may take several days of treatment until the analgesic effect is fully developed. For continuing therapy, the initial daily dosage can usually be reduced and/or the interval between administration prolonged.

Paget's disease: 200 IU daily as a single dose. In some cases, 400 IU in divided doses may be necessary at the beginning of therapy. Treatment should be continued for at least 3 months, or longer if required. Dosage should be adjusted to the individual patient's needs.

Note: In Paget's disease, treatment with calcitonin (salmon) should be given for periods ranging from at least several months to a few years. Treatment markedly reduces serum alkaline phosphatase and urinary hydroxyproline excretion, often to normal levels. However, in rare cases, alkaline phosphatase and hydoxyproline excretion levels may rise after an initial fall; the physician must then judge from the clinical picture whether treatment should be discontinued and when it may be resumed. Disorders of bone metabolism may reoccur one or several months after treatment has been discontinued, necessitating a new course of Gemitrol nasal spray therapy.

Neurodystrophic disorders: Early diagnosis is essential, and treatment should start as soon as the diagnosis is confirmed. 200 IU daily in a single dose over a period of 2-4 weeks. An additional 200 IU may be further administered every second day for up to 6 weeks depending on clinical progress.

4.3. Contraindications

Hypersensitivity to synthetic calcitonin (salmon) or to any of the excipients of the formulation.

Calcitonin is also contraindicated in patients with hypercalcemia.

4.4. Special warnings and precautions for use

Periodical nasal examinations with visualization of the nasal mucosa, turbinates, septum and mucosal blood vessel status are recommended. Nasal examinations should be performed before treatment begins and in the case of nasal complaints, medication should not be started. If severe ulceration of the nasal mucosa occurs (e.g. penetration below the mucosa or association with heavy bleeding), calcitonin (salmon) nasal spray should be discontinued. In case of mild ulceration, medication is to be interrupted temporarily until healing occurs.

Because calcitonin is a peptide, the possibility of systemic allergic reactions exists and allergic type reactions including isolated cases of anaphylactic shock have been reported in patients receiving calcitonin (salmon) nasal spray. In patients with suspected sensitivity to calcitonin, skin testing should be considered prior to treatment. Allergic reactions should be differentiated from generalized flushing and hypotension. The excipient benzalkonium chloride solution is an irritant and may cause irritation of the nasal mucosa.

Calcitonin (salmon) nasal spray may cause transient dizziness, which may impair the reaction of the patient. Patients must therefore be warned that transient dizziness may occur in which case they should not drive or use machines.

4.5. Drugs interactions

No drug interactions with intranasal calcitonin (salmon) have been reported. Concomitant use of calcitonin and lithium may lead to a reduction in plasma lithium concentrations. The dose of lithium may need to be adjusted.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnant women: There are no adequate and well controlled studies in pregnant women or nursing mothers with calcitonin (salmon). Animal studies have shown no embryotoxic and teratogenic potential. It appears that calcitonin (salmon) does not cross the placental barrier in animals. Calcitonin (salmon) nasal spray is not indicated for use in Pregnancy.

Lactating women: It is not known whether calcitonin (salmon) is excreted into human breast milk. In animals, calcitonin (salmon) has been shown to decrease lactation and to be excreted in milk. As a general rule, nursing should not be undertaken while a patient is on this drug since many drugs are excreted in human milk.

Pediatric use: As intranasal calcitonin is indicated for postmenopausal women, its use in children is not appropriate.

Use in elderly patients/Renal impairment/Hepatic impairment: Extensive experience with the use of calcitonin (salmon) nasal spray in the elderly has shown no evidence of reduced tolerability or altered dosage requirements. The same applies to patients with altered renal or hepatic function. Priming(activation) of pump: Before the first dose and administration, calcitonin (salmon) nasal spray should be at room temperature. To prime the pump, the bottle should be held upright and the two white side arms of the pump depressed toward the bottle until a full spray is produced. The pump is primed once the first full spray is emitted. To administer, the nozzle should be carefully placed into the nostril with the head in the upright position, and the pump firmly depressed toward the bottle. The pump should not be reprimed before each daily dose.

4.7. Effects on ability to drive and use machines.

Calcitonin (salmon) nasal spray may cause transient dizziness, which may impair the reaction of the patient. Patients must therefore be warned that transient dizziness may occur in which case they should not drive or use machines.

4.8. Undesirable effects

The most frequently observed undesirable effects are local reactions such as rhinitis and nasal discomfort. They are generally mild and rarely require discontinuation of the treatment

Investigations: Development of neutralizing antibodies to calcitonin

Nervous system disorders: Dizziness, headache, dysgeusia.

Eye disorders: Visual disturbance.

Respiratory, thoracic and mediastinal disorders: Rhinitis (including nasal dryness, nasal oedema, nasal congestion, sneezing, allergic rhinitis), nasal discomfort (e.g. nasal irritation, nasal odour, rash papular, parosmia, nasal mucosal erythema, mucosal excoriation). Rhinitis ulcerative, sinusitis, epistaxis, pharyngitis, Cough.

Gastrointestinal disorders: Nausea, diarrhoea, abdominal pain, Vomiting.

Skin and subcutaneous tissue disorders: Pruritus, Rash generalized.

Musculoskeletal and connective tissue disorders: Musculoskeletal pain including arthralgia.

Vascular disorders: Flushing, Hypertension. General disorders and administration site conditions: Fatigue, Influenza-like symptoms, oedema (facial, extremities and generalized).

Immune system disorders: Hypersensitivity reactions, Anaphylactic and anaphylactoid reactions such as tachycardia, hypotension, circulatory collapse and anaphylactic shock.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9. Overdose

No instances of overdose with calcitonin (salmon) nasal spray have been reported and no serious adverse reactions have been associated with high doses. There is no known potential for drug abuse for calcitonin (salmon). Nausea, vomiting, flushing and dizziness are known to be dose dependent when calcitonin is administered parenterally. Such events might therefore also be expected to occur in association with an overdose of calcitonin (salmon) nasal spray. However, calcitonin (salmon) nasal spray has been administered up to 1600 IU as a single dose and up to 800 IU per day for three days without causing any serious adverse event. If symptoms of overdose appear, treatment is to be symptomatic.

There have been no reports of hypocalcemic tetany. However, the pharmacologic actions of calcitonin (salmon) nasal spray suggest that this could occur in overdose. Therefore, provisions for parenteral administration of calcium should be available for the treatment of overdose.

5. Pharmacological properties

5.1. Mechanism of Action

Calcitonin is a polypeptide hormone secreted by the parafollicular cells of the thyroid gland in the mammals and by the ultimobranchial gland of birds and fish. Calcitonin acts primarily on bone, but direct renal effects and actions on the gastrointestinal tract are recognized.

Calcitonin (salmon) appears to have actions essentially identical to calcitonins of mammalian origin, but its potency per mg is greater and it has a longer duration of action. The actions of calcitonin on bone and its role in normal human bone physiology are still not completely elucidated, although calcitonin receptors have been discovered in osteoclasts and osteoblasts. Calcitonin is a calciotropic hormone, which inhibits bone resorption by a direct action on osteoclasts. By inhibiting osteoclast activity via its specific receptors, calcitonin (salmon) decreases bone resorption. Calcitonin markedly reduces bone turnover in conditions with an increased rate of bone resorption such as osteoporosis.

The absence of mineralisation defect with calcitonin has been demonstrated by bone histomorphometric studies both in man and in animals.

In pharmacological studies calcium has been shown to have analgesic activity in animal models. Intranasal calcitonin produces a clinically relevant biological response in humans after only a single dose, as shown by an increase in the urinary excretion of calcium, phosphorus and sodium (by reducing their tubular re-uptake) and a decrease in the urinary excretion of hydroxyproline. Long term administration of intranasal calcitonin significantly suppresses biochemical markers of bone turnover such as serum C-telopeptides (sCTX) skeletal isoenzymes of alkaline phosphatase for up to 5 years of treatment.

Calcitonin (salmon) nasal spray results in a statistically significant 1-2% increase in lumbar spine Bone Mineral Density (BMD) which is evident from year 1 and is sustained for up to 5 years. Hip BMD is preserved.

5.2. Pharmacodynamic properties

Calcitonin is a polypeptide hormone secreted by the parafollicular cells of the thyroid gland in the mammals and by the ultimobranchial gland of birds and fish.

5.3. Pharmacokinetic properties

Pharmacokinetic parameters of intranasally administered calcitonin (salmon) are difficult to quantitate due to the inadequate sensitivity and uncertain specificity of the available immunoassay methods used in the studies. The bioavailability of a 200 IU dose relative to parenteral administration is between 2 and 15%. Calcitonin (salmon) nasal spray is absorbed rapidly through the nasal mucosa and peak plasma concentrations are attained within the first hour of administration. The half-life of elimination of calcitonin (salmon) has been calculated to be approximately 16 to 43 minutes. There is no evidence of accumulation of the drug observed on repeated nasal administration at 10-hour intervals for up to 15 days. Doses higher than the recommended dose result in higher blood levels (as shown by an increase in AUC) but relative bioavailability does not increase. As is the case with other polypeptide hormones, there is very little value in monitoring plasma levels of calcitonin (salmon) since these are not directly predictive of the therapeutic response. Hence, calcitonin parameters of efficacy. Plasma protein binding is 30 to 40%.

6. Nonclinical properties

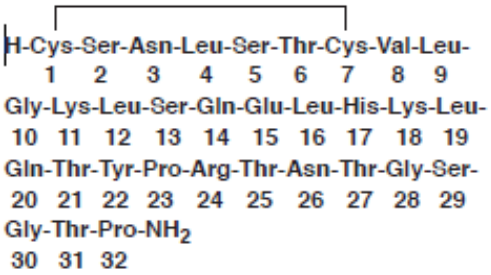
6.1. Animal Toxicology or Pharmacology

There is no data available on the nonclinical properties.

7. Description

Calcitonin is a polypeptide hormone secreted by the parafollicular cells of the thyroid gland in mammals and by the ultimobranchial gland of birds and fish.

Calcitoninis a synthetic polypeptide of 32 amino acids in the same linear sequence that is found in calcitonin of salmon origin. The molecular weight is 3431.9 g/mol. Its molecular formula is $C_{145}H_{240}N_{44}O_{48}S_2$.This is shown by the following graphic formula:



Calcitonin Salmon Nasal solution is clear solution. The excipients used are Benzalkonium Chloride, Phenyl Ethyl Alcohol, Polysorbate-80, Citric Acid Monohydrate, Sodium Chloride.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than the date of expiry.

8.3. Packaging information

Gemitrol NS Nasal Spray is available in glass bottle of 6 ml.

8.4. Storage and handing instructions.

Store unopened bottle in refrigerator at a temperature between 2°C to 8°C. Protected from light and moisture.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over the counter, vitamins, or herbal products)

10. Details of manufacturer

Biodeal Pharmaceuticals Ltd.
Vill. Saini Majra, Nalagarh Ropar
Road, Nalagarh, Distt.Solan
(H.P.) INDIA

11. Details of permission or licence number with date

Mfg Lic No. MNB/06/440 issued on 21.12.2023.

12. Date of revision

FEB-2026

MARKETED BY

TORRENT PHARMA

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