

This Patient Information summarizes the most important information about Calcitonin Salmon Nasal Solution. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Calcitonin Salmon Nasal Solution that is written for health professionals.

For more information, call 1-800-828-9393.

What are the ingredients in Calcitonin Salmon Nasal Solution?

Active Ingredients: calcitonin-salmon

Inactive Ingredients: sodium chloride, chlorobutanol (possesses a characteristic odor), hydrochloric acid (added as necessary to adjust pH), purified water and nitrogen.

How to Assemble and Use

Calcitonin Salmon Nasal Solution, USP

One Spray, Once a Day

BEFORE USING CALCITONIN SALMON NASAL SOLUTION

This package contains one bottle of Calcitonin Salmon Nasal Solution and one screw on pump.

Important Facts About Your Medication:

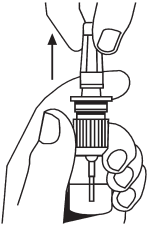
- The bottle contains the proper amount of medication — be aware that the entire bottle will not be filled with liquid.
- Before opening and assembling your medication bottle, keep it in your refrigerator between 2°C to 8°C (36°F to 46°F). Freezing is to be avoided.
- After opening and assembling a new medication bottle, keep it at room temperature between 20°C to 25°C (68°F to 77°F) in an upright position.

HOW TO USE CALCITONIN SALMON NASAL SOLUTION

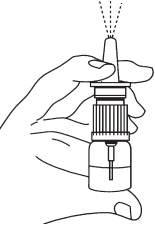
Putting the Nasal Spray Pump Unit Together

1. If your bottle and pump unit were already assembled by your pharmacist, go to step 6. If not, remove the bottle from your refrigerator and allow it to reach room temperature before assembling.
2. Keeping the bottle upright, unscrew the white cap.
3. Remove the pump from the plastic protection bag.
4. Holding the bottle upright, insert the nasal spray pump unit into the bottle. Then turn the pump clockwise, and tighten it until it is securely fastened to the bottle.

Note: Do not depress pump when it is not attached to the bottle.



Priming a New Bottle



5. Holding the bottle upright with your index finger on top of one of the two side arms of the pump, gently remove the clear protective cap from the top of the nozzle.

6. To ensure proper delivery of medication, a newly opened and assembled bottle must be primed before you use it for the **first time**.

If your pharmacist assembled the unit for you, check to see if it has already been primed by pumping the unit once. If a full spray is emitted, the unit has already been primed. If no spray is emitted, you must prime the unit. Holding the bottle upright with your index and middle fingers on the two side arms of the pump, and your thumb on the bottom of the bottle, press the arms down fully **until you see a full spray**. Now the nasal spray is ready for use.

Do not re-prime the pump before each daily use because this will waste your medication.

Using the Medication



7. The recommended dose of Calcitonin Salmon Nasal Solution is one spray once a day in one nostril.

Keep your head upright and carefully place the nozzle in one nostril. Tilt the bottle until it is in a straight line with the nasal passage.

Firmly press down on the pump once to spray the medication into your nose. It is not necessary to inhale while this is being done. Please note: Because the

mist is so fine, you may not feel it inside your nose. Also, some medication may drip out of your nose. **However,** in either case, the medication is absorbed. **IMPORTANT:** Do not “test” the spray unit or prime it before you use your daily dose because this will waste your medication.

Cleaning the Pump

Once or twice a week, wipe the nozzle with a clean, damp cloth. Dry the nozzle before replacing the dust cap.

Storing the Unit

8. Holding the bottle with two fingers **under the two side arms** of the pump, gently replace the protective cap on the nasal spray unit. **Be careful not to depress the pump** while this is being done. Once the pump is primed, the unit must be kept at room temperature between 20°C to 25°C (68°F to 77°F) in the upright position until the medication is finished.

IMPORTANT

- Do not refrigerate the unit between doses
- Do not store the unit on its side

Bottles left at room temperature (opened or unopened) for more than 35 days must be discarded.

Refrigerated bottles are good until the expiration date stamped on the bottle and box.

Alternate Nostrils Daily

The first day, start with one spray in the left nostril. The next day, use one spray in the right nostril, and so on.

It is important to receive the correct daily amount of calcium and vitamin D, as directed by your healthcare provider.

IMPORTANT

- **Use Calcitonin Salmon Nasal Solution daily.**

To ensure proper treatment, it is important to use your Calcitonin Salmon Nasal Solution daily even if you have no symptoms of postmenopausal osteoporosis.

What is the Correct Dose of Calcitonin Salmon Nasal Solution?

A single spray of Calcitonin Salmon Nasal Solution, USP contains one daily dose, which is 200 International Units of calcitonin-salmon. The fine mist is actually 0.09 mL (milliliter) of solution. Your bottle of Calcitonin Salmon Nasal Solution contains at least 30 doses. Priming the pump as described in step 6 **does not alter the total number of doses available in a bottle of Calcitonin Salmon Nasal Solution.** The bottle need only be primed once after assembly. Do not reprime or “test spray” your bottle before you use your daily dose of Calcitonin Salmon Nasal Solution. This will waste your medication.

Please see your healthcare provider for complete product information for Calcitonin Salmon Nasal Solution.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Manufactured by:
PAR PHARMACEUTICAL COMPANIES, INC.
Spring Valley, NY 10977

Revised: 08/2014

PI161-01-1-05

Gastrointestinal Tract

Some evidence from studies with injectable preparations suggests that calcitonin-salmon may have effects on the gastrointestinal tract. Short-term administration of injectable calcitonin-salmon results in marked transient decreases in the volume and acidity of gastric juice and in the volume and amylase content of pancreatic juice. Whether these effects continue to be elicited after each injection of calcitonin-salmon during chronic therapy has not been investigated. These studies have not been conducted with Calcitonin Salmon Nasal Solution.

Calcium Homeostasis

In two clinical studies designed to evaluate the pharmacodynamic response to calcitonin-salmon nasal spray, administration of calcitonin-salmon 100-1600 International Units to healthy volunteers resulted in rapid and sustained decreases within the normal range for both total serum calcium and serum ionized calcium. Single doses of calcitonin-salmon greater than 400 International Units did not produce any further biological response to the drug.

12.3 Pharmacokinetics

The bioavailability of Calcitonin Salmon Nasal Solution relative to intramuscular administration in healthy volunteers is between 3 and 5%. Calcitonin Salmon Nasal Solution is absorbed rapidly by the nasal mucosa with a mean $T_{1/2}$ of about 13 minutes. The terminal half-life of calcitonin-salmon has been calculated to be around 18 minutes and no evidence of accumulation was observed with multiple dosing.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity

The incidence of pituitary adenomas was increased in rats after one and two years of subcutaneous exposure to synthetic calcitonin-salmon. The significance of this finding to humans is unknown because pituitary adenomas are very common in rats as they age, the pituitary adenomas did not transform into metastatic tumors, there were no other clear treatment-related neoplasms, and synthetic calcitonin-salmon related neoplasms were not observed in mice after two years of dosing.

Rat findings:

The only clear neoplastic finding in rats dosed subcutaneously with synthetic calcitonin-salmon was an increase in the incidence of pituitary adenomas in male Fisher 344 rats and female Sprague Dawley rats after one year of dosing and male Sprague Dawley rats dosed for one and two years. In female Sprague Dawley rats, the incidence of pituitary adenomas after two years was high in all treatment groups (between 80% and 92% including the control groups) such that a treatment-related effect could not be distinguished from natural background incidence. The lowest dose in male Sprague Dawley rats that developed an increased incidence of pituitary adenomas after two years of dosing (1.7 International Units/kg/day) is approximately 2 times the maximum recommended intranasal dose in humans (200 International Units/day) based on body surface area conversion between rats and humans and a 20-fold conversion factor to account for decreased clinical exposure via the intranasal route. The findings suggest that calcitonin-salmon reduced the latency period for development of non-functioning pituitary adenomas.

Mouse findings:

No carcinogenicity potential was evident in male or female mice dosed subcutaneously for two years with synthetic calcitonin-salmon at doses up to 800 International Units/kg/day. The 800 International Units/kg/day dose is approximately 390 times the maximum recommended intranasal dose in humans (200 International Units) based on scaling for body surface area and a 20-fold conversion factor to account for low clinical exposure via the intranasal route.

Mutagenesis

Synthetic calcitonin-salmon tested negative for mutagenicity using *Salmonella typhimurium* (5 strains) and *Escherichia coli* (2 strains), with and without rat liver metabolic activation, and was not clastogenic in a chromosome aberration test in Chinese Hamster V79 cells. There was no evidence that calcitonin-salmon was clastogenic in the *in vivo* mouse micronucleus test.

Fertility

Effects of calcitonin-salmon on fertility have not been assessed in animals.

14 CLINICAL STUDIES

Two randomized, placebo-controlled, two-year trials were conducted in 266 postmenopausal women who were greater than 5 years postmenopause with spinal, forearm or femoral bone mineral density (BMD) at least one standard deviation below the normal value for healthy premenopausal women (T-score < -1). In both studies, a total of 144 patients received Calcitonin Salmon Nasal Solution 200 International Units or placebo daily. The intent-to-treat population comprised 139 patients who had at least one follow-up BMD measurement. In study 1, patients also received 500 mg daily calcium supplements, while in study 2, patients received no calcium supplementation. The primary endpoint for both studies was percent change in lumbar spine BMD at 2 years. Calcitonin Salmon Nasal Solution increased lumbar vertebral BMD relative to placebo in women with low bone mass who were greater than 5 years postmenopause (see Table 3 below).

Table 3. Calcitonin Salmon Nasal Solution: Lumbar Spine Bone Mineral Density in Women Greater Than 5 years Postmenopause With Low Bone Mass

| | Lumbar Spine Bone Mineral Density, Mean Change from Baseline (in %) at Month 24 | |
|--|---|--|
| | Study 1 (with calcium supplement) n (ITT)=100 | Study 2 (no calcium supplement) n (ITT)=39 |
| Calcitonin Salmon Nasal Solution 200 IU NS Daily | +1.56 | +1.02 |
| Placebo | +0.20 | -1.85 |
| Treatment Difference | +1.36 | +2.87 |
| p-value* | <0.05 | <0.005 |

ITT: Intent to Treat
IU: International Units
NS: nasal spray
*p – values by parametric testing (2 – tailed 2-sample t-test)

No effects of calcitonin salmon nasal spray on cortical bone of the forearm or hip were demonstrated.

In clinical studies of postmenopausal osteoporosis, bone biopsy and radial bone mass assessments at baseline and after 26 months of daily injectable calcitonin-salmon indicate that calcitonin therapy results in the formation of normal bone.

16 HOW SUPPLIED/STORAGE AND HANDLING

16 HOW SUPPLIED

Available as a metered dose clear solution in a 3.7 mL fill clear glass bottle. It is available in a dosage strength of 200 International Units per activation (0.09 mL/spray). A screw-on pump is provided. The pump, following priming, will deliver 0.09 mL of solution. Calcitonin Salmon Nasal Solution contains 2200 International Units/mL calcitonin-salmon and is provided in an individual box containing one glass bottle and one screw-on pump (NDC 49884-161-11).

Storage and Handling

Store unopened bottle in refrigerator between 2°C to 8°C (36°F to 46°F). Freezing is to be avoided.

Store bottle in use at room temperature between 20°C to 25°C (68°F to 77°F) in an upright position, for up to 35 days. Each bottle contains at least 30 doses.

Discard bottle after 30 doses.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information and Instructions for use).

- Instruct patients on pump assembly, priming of the pump, and nasal introduction of Calcitonin Salmon Nasal Solution. Although instructions for patients are supplied with the individual bottle, procedures for use should be demonstrated to each patient [see **DOSAGE AND ADMINISTRATION (2.2)**]. Patients should notify their healthcare provider if they develop significant nasal irritation [see **WARNINGS AND PRECAUTIONS (5.3)**].
- Inform patients of the potential increase in risk of malignancy [see **WARNINGS AND PRECAUTIONS (5.4)**].
- Advise patients to maintain an adequate calcium (at least 1000 mg elemental calcium per day) and vitamin D (at least 400 International Units per day) intake [see **DOSAGE AND ADMINISTRATION (2.3)**].
- Instruct patients to seek emergency medical help or go to the nearest hospital emergency room right away if they develop any signs or symptoms of a serious allergic reaction.
- Advise patients how to correctly store unopened and opened product [see **HOW SUPPLIED/STORAGE AND HANDLING (16)**]. Advise patients that the bottle should be discarded after 30 doses, because after 30 doses, each spray may not deliver the correct amount of medication even if the bottle is not completely empty.

Patient Information

Calcitonin Salmon Nasal Solution, USP (Calcitonin Salmon Nasal Spray)

Read this Patient Information before you start using Calcitonin Salmon Nasal Solution and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is Calcitonin Salmon Nasal Solution?

Calcitonin Salmon Nasal Solution is a prescription medicine used to treat osteoporosis in women more than 5 years after menopause. Calcitonin Salmon Nasal Solution should be used for women who cannot use other treatments or who choose not to use other treatments for osteoporosis.

It is not known if Calcitonin Salmon Nasal Solution lowers the chance of having bone fractures.

Calcitonin Salmon Nasal Solution has not been shown to be effective in women less than 5 years after menopause.

It is not known if Calcitonin Salmon Nasal Solution is safe and effective in children under 18 years of age.

Who should not use Calcitonin Salmon Nasal Solution?

Do not use Calcitonin Salmon Nasal Solution if you:

- are allergic to calcitonin-salmon or any of the ingredients in Calcitonin Salmon Nasal Solution. See the end of this leaflet for a complete list of ingredients in Calcitonin Salmon Nasal Solution.

What should I tell my healthcare provider when using Calcitonin Salmon Nasal Solution? Before you use Calcitonin Salmon Nasal Solution, tell your healthcare provider if you:

- have any other medical conditions
- have low calcium levels in your blood
- are pregnant or plan to become pregnant. It is not known if Calcitonin Salmon Nasal Solution can harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if Calcitonin Salmon Nasal Solution passes into your breast milk. You and your healthcare provider should decide if you will use Calcitonin Salmon Nasal Solution or breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Especially tell your healthcare provider if you take:

- **lithium.** Your healthcare provider may need to change your dose of lithium while you use Calcitonin Salmon Nasal Solution.

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist when you get a new medicine.

How should I use Calcitonin Salmon Nasal Solution?

- **For detailed instructions, see the Instructions for Use at the end of this Patient Information leaflet.**

- Use Calcitonin Salmon Nasal Solution exactly as your healthcare provider tells you to use it.

- **Do not use** Calcitonin Salmon Nasal Solution until your healthcare provider shows you and you understand how to use it correctly.

- Use 1 spray of Calcitonin Salmon Nasal Solution, 1 time each day, in 1 nostril (inside your nose).
 - Start with 1 spray in your **left nostril** on your first day, followed by 1 spray in your **right nostril** on the second day.
 - Continue to switch nostrils for your dose each day.
- Your healthcare provider should check your nose before you start using Calcitonin Salmon Nasal Solution and often while you are using it.
- Tell your healthcare provider if you start to have discomfort (irritation) in your nose that bothers you while you use Calcitonin Salmon Nasal Solution.
- Your healthcare provider should prescribe calcium and vitamin D to help prevent low calcium levels in your blood while you use Calcitonin Salmon Nasal Solution.
- Take your calcium and vitamin D as your healthcare provider tells you to.
- There are 30 doses (sprays) of Calcitonin Salmon Nasal Solution in each bottle. After 30 doses, each spray may not give you the right amount of medicine, even if the bottle is not completely empty. Keep track of the number of doses of medicine used from your bottle.

- If you use too much Calcitonin Salmon Nasal Solution, call your healthcare provider or go to the nearest hospital emergency room right away.

What are the possible side effects of Calcitonin Salmon Nasal Solution?

Calcitonin Salmon Nasal Solution may cause serious side effects, including:

- **allergic reactions**

Some people have had an allergic reaction when using Calcitonin Salmon Nasal Solution. Some reactions may be serious and can be life threatening. Call your healthcare provider or go to the nearest hospital emergency room right away if you have any of these symptoms of an allergic reaction.

- trouble breathing
- swelling of your face, throat or tongue
- fast heartbeat
- chest pain
- feel dizzy or faint

If you might be allergic to calcitonin-salmon, your healthcare provider should do a skin test before you use Calcitonin Salmon Nasal Solution.

- **low calcium levels in your blood (hypocalcemia)**

Calcitonin Salmon Nasal Solution may lower the calcium levels in your blood. If you have low blood calcium before you start using Calcitonin Salmon Nasal Solution, it may get worse during treatment. Your low blood calcium must be treated before you use Calcitonin Salmon Nasal Solution. Most people with low blood calcium levels do not have symptoms, but some people may have symptoms. Call your healthcare provider right away if you have any of these symptoms of low blood calcium:

- numbness or tingling in your fingers, toes, or around your mouth

Your healthcare provider should:

- do blood tests while you use Calcitonin Salmon Nasal Solution
- prescribe calcium and vitamin D to help prevent low calcium levels in your blood while you use Calcitonin Salmon Nasal Solution

Take your calcium and vitamin D as your healthcare provider tells you to.

- **nose irritation**

Irritation of your nose can happen while you are using Calcitonin Salmon Nasal Solution, especially if you are over 65 years of age. Call your healthcare provider right way if you have any of these symptoms of nose irritation:

- crusting
- dryness
- redness or swelling
- nose sores (ulcers)
- nose bleeds

Your healthcare provider may stop your treatment with Calcitonin Salmon Nasal Solution until your nose irritation symptoms go away.

- **risk of cancer**

People who use calcitonin-salmon, the medicine in Calcitonin Salmon Nasal Solution, may have an increased risk of cancer.

- **increase of certain cells (sediment) in your urine**

Your healthcare provider should test your urine often while you are using Calcitonin Salmon Nasal Solution.

The most common side effects of Calcitonin Salmon Nasal Solution include:

- back pain
- muscle aches
- headache
- runny nose

These are not all the possible side effects of Calcitonin Salmon Nasal Solution. For more information, ask your healthcare provider or pharmacist.

Tell your healthcare provider right away if you have any side effect that bothers you or does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How do I store Calcitonin Salmon Nasal Solution?

- Store open bottles of Calcitonin Salmon Nasal Solution at room temperature between 20°C to 25°C (68°F to 77°F) for 35 days.

- Store unopened bottles of Calcitonin Salmon Nasal Solution in the refrigerator between 2°C to 8°C (36°F to 46°F). Do not freeze.

- Store Calcitonin Salmon Nasal Solution bottles in an upright position.

- Safely throw away Calcitonin Salmon Nasal Solution in the trash after you have used 30 doses (sprays).

Keep Calcitonin Salmon Nasal Solution and all other medicines out of the reach of children.

General information about the safe and effective use of Calcitonin Salmon Nasal Solution.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use Calcitonin Salmon Nasal Solution for a condition for which it was not prescribed. Do not give Calcitonin Salmon Nasal Solution to other people, even if they have the same symptoms you have. It may harm them.

This Patient Information summarizes the most important information about Calcitonin Salmon Nasal Solution. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about Calcitonin Salmon Nasal Solution that is written for health professionals.

For more information, call 1-800-828-9393.

What are the ingredients in Calcitonin Salmon Nasal Solution?

Active Ingredients: calcitonin-salmon

Inactive Ingredients: sodium chloride, chlorobutanol (possesses a characteristic odor), hydrochloric acid (added as necessary to adjust pH), purified water and nitrogen.

How to Assemble and Use

Calcitonin Salmon Nasal Solution, USP

One Spray, Once a Day

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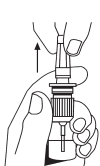
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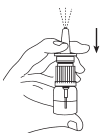
HOW TO USE CALCITONIN SALMON NASAL SOLUTION

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 2. Keeping the bottle upright, unscrew the white cap.
 3. Remove the pump from the plastic protection bag.
 4. Holding the bottle upright, insert the nasal spray pump unit into the bottle. Then turn the pump clockwise, and tighten it until it is securely fastened to the bottle.
- Note: Do not depress pump when it is not attached to the bottle.



Priming a New Bottle



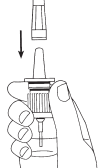
Using the Medication



Cleaning the Pump

Once or twice a week, wipe the nozzle with a clean, damp cloth. Dry the nozzle before replacing the dust cap.

Storing the Unit



IMPORTANT

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