

**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS
(PREPARATIONS) - 1986**

This medicine can be sold with a doctor's prescription only

**PecFent 100 mcg
PecFent 400 mcg**

Nasal Spray

Active ingredient:

PecFent 100: Each spray of PecFent 100 (0.1 milliliter) contains 100 mcg of *fentanyl (as citrate)*.

Each 1 ml of PecFent 100 solution contains 1000 mcg of *fentanyl (as citrate)*.

PecFent 400: Each spray of PecFent 400 (0.1 milliliter) contains 400 mcg of *fentanyl (as citrate)*.

Each 1 ml of PecFent 400 solution contains 4000 mcg of *fentanyl (as citrate)*.

Excipients: see section 6 "Additional information".

Read this entire leaflet carefully before you start using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to your doctor or pharmacist.

This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if you think that their illness is similar.

Please Note:

- **This medicine is permitted for use only if you are using other opioids.**
- **Each bottle allows only 8 medicine-releasing sprays!**
- You must read the instructions for use in order to ensure the correct manner of using the medicine.
- If your doctor has ordered a **two-spray dosage**, you must perform **one spray in each nostril and not two sprays in one nostril!** Do not exceed the recommended dose or change the dosage on your own accord.
- You must keep the medicine in a child-resistant storage container **at all times** even after use has ended or the content has been finished.
- Do not consume alcohol throughout the entire treatment period with PecFent. Alcohol consumption may cause an increase in the risk of being afflicted with serious side-effects.

Taking this medicine with benzodiazepines, other central nervous system depressants (including drugs) or alcohol may cause a feeling of deep sleepiness, breathing difficulties (respiratory depression), coma and death.

Medicines belonging to the opiates family may cause addiction, especially with prolonged use, and they have a potential for misuse and overdose. A reaction to opioid overdose can be expressed by slowed breathing and even cause death.

Make sure you know the name of your medication, your dose, how often to take it, the duration of treatment, its side effects and potential risks.

Further information can be found at the following link:

https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

1. What is the medicine intended for?

PecFent is intended for treating adult cancer patients suffering from breakthrough pain.

Breakthrough pain is a suddenly occurring pain, even when the patient is under usual treatment with opioid medicines for relieving constant pains (such as morphine, fentanyl, oxycodone, or hydromorphone).

PecFent is to be given only to adult cancer patients who are already taking other opioid medicines on a daily basis, for relieving constant pains.

How does PecFent work?

PecFent is a nasal spray. When you spray PecFent into the nose tiny gel droplets are released, the active substance is quickly absorbed through the mucosal lining of the nose into the blood stream, thus quickly relieving the breakthrough pain you are experiencing.

Therapeutic group: a powerful pain reliever that belongs to the opioid pain relievers group (narcotic).

2. Before using the medicine

Do not use this medicine if:

- you are hypersensitive (allergic) to fentanyl or to any of the other ingredients contained in this medicine (see section 6).
- you have not regularly been taking other opioid prescription medicines (such as codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine) every day as regularly scheduled, for at least a week, in order to relieve your persistent pains. If you have not been taking these medicines **do not** use PecFent, as PecFent may increase the risk of dangerously slow and/or shallow breathing, or respiratory arrest.
- you suffer from a short lasting pain that is different from breakthrough pain.
- you suffer from serious breathing or lung problems.
- you are being treated with medicines contain sodium oxybate.

If any of the above applies to you, do not use PecFent. If you are not sure, refer to your doctor or pharmacist before using PecFent.

Special warnings concerning the use of this medicine

- You must keep the medicine in a child-resistant container **at all times** even after you have finished all 8 sprays. PecFent can be life-threatening if accidentally taken by the child.
- PecFent is not approved for use in children under 18 years old.
- PecFent contains a preservative- Propyl parahydroxybenzoate (E216). This substance may cause allergic reactions (there may be delayed reactions), and very rarely, cause bronchial spasm (bronchospasm) if you use the medicine incorrectly.
- If you are an athlete, taking PecFent may result in a positive doping test result.

Before using PecFent consult with the doctor or pharmacist in the following cases:

- If for a certain time you have not taken the usual dose of daily opioid pain reliever for relieving persistent pains.
- If you suffer from breathing problems such as asthma, wheezing, or shortness of breath.
- If you have suffered a severe blow to the head.
- If you have heart problems, especially slow heart rate.
- If you have low blood pressure or a low amount of fluids in your circulation.
- If you have liver or kidney problems, as they may affect the way the body breaks down the medicine.
- If you take antidepressants or anti-psychotic medicines (please read the section "**drug interactions**").

If one of the above applies to you (or if you are unsure), refer to the doctor or pharmacist before using PecFent.

The doctor may conduct a more in-depth examination if:

- you or any of your family members have abused or been dependent on alcohol, prescription medicines or drugs ("addiction").
- you smoke.
- you have had problems related to moods (depression, anxiety, or personality disorder) or were treated by a psychiatrist for other mental illnesses.

Repeated use of PecFent may cause dependence and abuse and lead to life-threatening overdose. If you have concerns that you may be dependent on PecFent, it is important that you consult a doctor.

Consult the doctor while using PecFent if:

- you suffer from recurring nosebleeds. The doctor may be able to offer you an alternative treatment.
- you feel that PecFent is becoming less effective in treating the breakthrough pain occurrences.
- you experience pain or increased sensitivity to pain (hyperalgesia) that is irresponsive to the higher dosage of the medicine that the doctor prescribed for you.
- you think you are developing a dependence on PecFent.
- you experience a combination of the following symptoms: nausea, vomiting, loss of appetite, fatigue, weakness, dizziness and low blood pressure. Together, these symptoms may indicate a life-threatening condition known as adrenal gland insufficiency, a condition where the adrenal gland does not produce enough hormones.
- you have suffered from adrenal gland insufficiency or a deficiency in sex hormones (androgen deficiency) with opioid use in the past.

Sleep related respiratory disorders

Pecfent may cause sleep related respiratory disorders such as respiratory arrest while sleeping (sleep apnea) and low levels of oxygen in the blood while sleeping (hypoxemia while sleeping). The symptoms include stopping breathing while sleeping, waking up at night due to shortness of breath, difficulty in sleeping continuously or excessive tiredness during the day. If you or another person notices these symptoms, contact the doctor. He may consider reducing the dosage.

Drug interactions:

If you are taking, have recently taken other medicines, including non-prescription drugs and nutritional supplements, tell the doctor or pharmacist. Especially inform the doctor or pharmacist before taking PecFent if you are taking or have recently taken one of the following medicines:

- Medicines that may cause drowsiness, such as sleeping pills, tranquilizers, muscle-relaxants, anti-anxiety, such as benzodiazepines (e.g. diazepam), or medicines for allergies (anti-histamines). Use of PecFent at the same time as medicines that make you feel sleepy increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening.

Contact your doctor if you get any of these symptoms. For this reason use of PecFent, together with sedatives, should only be considered when other treatment options are not possible. However, if your doctor does prescribe PecFent together with sedative medicines the dose and length of treatment should be limited by your doctor. **Tell your doctor about all sedative medicines you are taking and follow your doctors dose instructions closely.** Inform your friends or relatives to be aware of the signs and symptoms stated above.

- Anti-depressants of the Monoamine-Oxidase Inhibitors group. Inform the attending doctor or pharmacist if you have taken medicines from this group in the last two weeks (14 days) before using PecFent. The risk of side-effects increases if you take medicines such as certain anti-depressants or anti-psychotic medicines. PecFent may interact with these medicines and you may experience a change in your mental state (such as agitation, hallucinations, coma) and other phenomena, such as a body temperature over 38°C, an increase in heart rate, unstable blood pressure and exaggeration of reflexes, muscle rigidity, lack of coordination and/or a gastrointestinal reaction (such as nausea, vomiting, diarrhea). Your doctor will inform

you whether PecFent is suitable for you.

- Nasal sprays used for treating nasal congestion (containing a decongestant, such as oxymetazoline).
- Medicines that may affect the way your body breaks down PecFent. These include:
 - Medicines for treating HIV (such as ritonavir, nelfinavir, amprenavir or fosamprenavir).
 - Medicines for treating fungal infections (such as ketoconazole, itraconazole or fluconazole).
 - Anti-bacterial infection medicines (such as troleandomycin, clarithromycin or erythromycin).
 - 'Aprepitant' - used for stopping nausea.
 - 'Diltiazem' and 'Verapamil' - used for treatment of high blood pressure or heart problems.
 - Other pain relievers known as partial agonists/antagonists such as buprenorphine, nalbuphine, pentazocine. You may experience withdrawal symptoms (nausea, vomiting, diarrhea, anxiety, chills, tremor and sweating) while using these medicines.
 - Pain relievers for neuropathic pain (gabapentin and pregabalin)

If one of the above applies to you (or if you are unsure), refer to the doctor or pharmacist before using PecFent.

Do not use any other type of nasal spray for at least 15 minutes after using PecFent.

Use of the medicine and food

Do not drink grapefruit juice throughout the entire period of using PecFent. Grapefruit juice may affect the way your body breaks down the medicine.

Use of this medicine and alcohol consumption

Do not consume alcohol throughout the entire period of using PecFent. Alcohol consumption may cause an increase in the risk of severe side effects.

Pregnancy breastfeeding and fertility

If you are pregnant or breastfeeding, may become pregnant or are planning on becoming pregnant consult the doctor or pharmacist before using the medicine.

Pregnancy:

Do not use the medicine if you are pregnant or might be pregnant unless instructed to do so by the doctor. Following prolonged use, PecFent may cause withdrawal symptoms in the newborn. Do not use PecFent during childbirth (including a caesarean section) as it passes through the placenta and may cause respiratory depression in the newborn.

Breastfeeding:

Do not use the medicine if you are breastfeeding. The medicine passes into breast milk and may cause sleepiness and respiratory arrest in the breast-fed infant. Do not breastfeed a baby for at least 5 days after taking the last dose of PecFent.

Fertility:

There is no available information about the medicine's effects on fertility.

Driving and use of machines

This medicine may affect your mental and/or physical ability to drive or operate machines. Consult with the attending doctor as to whether it would be safe for you to drive or operate equipment or machines after using the medicine.

Do not drive or operate machines if you feel sleepy, dizzy or experience problems with your eyesight or other side effects that may compromise your ability to drive or operate machines. Driving or operating dangerous equipment and machines is forbidden, as long as you do not know how the medicine will affect you.

3. How to use this medicine?

Always use according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and treatment regimen with this medicine. The dosage and treatment

regimen will be determined by the doctor only.

PecFent is available in two different strengths: PecFent 100 mcg and PecFent 400 mcg. Make sure you use the dosage prescribed for you by the doctor.

How many sprays you should use:

- The dose for treating breakthrough pain can be one or two sprays (one spray in each nostril). The doctor will instruct you on how many sprays (1 or 2) you should use to treat a breakthrough pain episode.
- **Do not exceed the dose prescribed by the doctor for each episode of breakthrough pain.**
- Do not use the PecFent more than 4 times a day.
- Wait for at least 4 hours before taking the next PecFent dose.

Initial dose:

- The initial dose is 100 mcg.
- This is a single spray into a single nostril from the PecFent 100 mcg bottle.
- See "Using the PecFent Bottle" for instructions on how to use the dose.

Finding the proper dosage:

- The doctor will help you find the proper dosage to relieve breakthrough pain. It is very important that you follow the doctor's instructions.
- Tell the doctor about your pain and how the medicine affects you. The doctor will decide whether the dosage ought to be changed.
- Do not change the dosage on your own accord!

After finding the proper dosage:

- Tell the doctor if the PecFent Dosage does not relieve the breakthrough pain. The doctor will decide whether the dosage ought to be changed. **Do not change the dosage of PecFent or the other pain relievers on your own accord.**
- Tell the doctor immediately if you experience more than 4 breakthrough pain episodes a day. The doctor may change your medicine for the persistent pain. Once the persistent pain is under control, the doctor may change your dosage of PecFent.

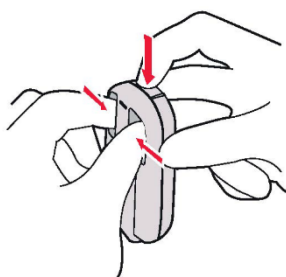
If you are not sure about the proper dosage or how many sprays of PecFent to use, refer to the doctor.

Do not exceed the recommended dosage. Do not swallow.

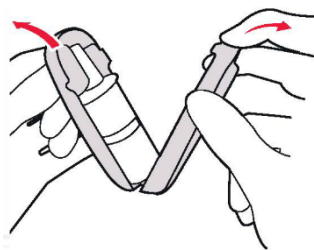
Using the PecFent bottle:

Instructions on how to open and close the child resistant container:

open

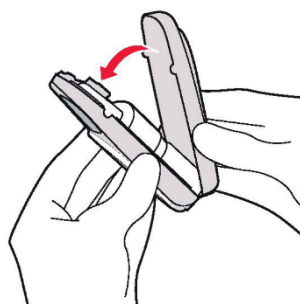


A



B

close



C

- A. Insert fingers into rear cavities and squeeze while pushing down top button.
- B. Open.
- C. Close (listen for confirmation click).

Preparing the PecFent bottle for use

Before using a new bottle of PecFent it should be prepared for use (primed), as follows:

1. On the new PecFent bottle two red lines will appear in the counting window, located on the bottle's white plastic top (see figure 1 and figure 3a).
2. Remove the clear plastic protective cap from the nozzle (figure 1).
3. Aim the spray in a direction away from you (and from other people).
4. Hold the PecFent bottle upright with your thumb at the bottom of the bottle and with the index and middle fingers on both sides of the nozzle, in the place intended for the fingers (finger grips) (figure 2).
5. Press firmly with the fingers until a "click" is heard, and then release the fingers (figure 2). An additional "click" sound will be heard and one wide red bar will appear in the counting window (figure 3b).
6. Repeat the action described in step 5 three times. Each time you repeat step 5, the red bar in the counting window will become narrower until a green bar appears in the counting window (figure 3b-e). The appearance of the green bar in the counting window signifies that PecFent is ready for use.
7. Wipe the spray nozzle with a tissue and flush the tissue down the toilet.
8. If you do not intend to use the spray immediately, close the nozzle with the protective cap. Afterwards, put the PecFent bottle into the child-resistant storage container. If PecFent has not been used for 5 days, the spray should be prepared for use by spraying once. If the PecFent Spray has not been used for 60 days since the spray was prepared for use (primed), dispose of the bottle and start using a new bottle.

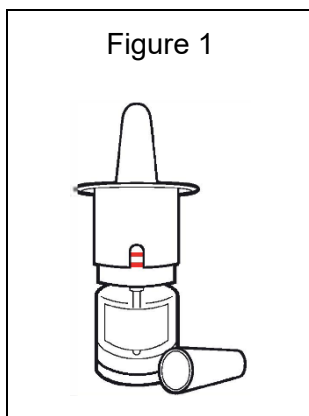


Figure 1



Figure 2

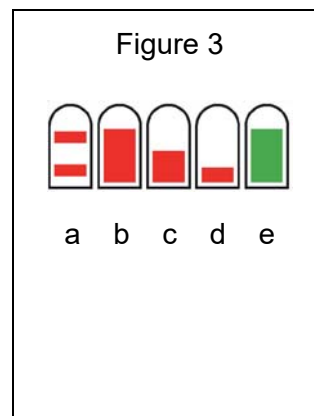


Figure 3

Using PecFent:

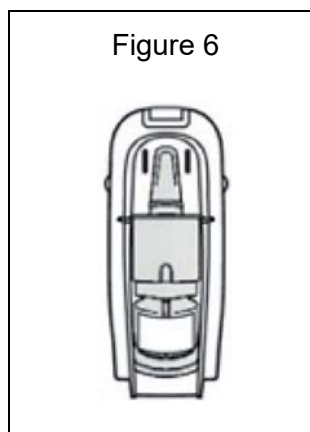
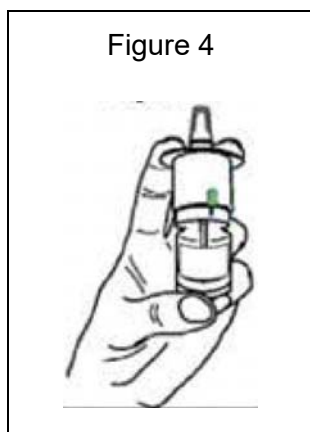
PecFent is only to be used by spraying into your nostril.

1. Check that a green bar or number appears in the counting window (figure 4): this indicates that the priming of the spray (preparation for use) was done successfully (see "preparing the PecFent bottle for use").
2. Blow your nose if you feel a need to do so.
3. Sit down and keep your head upright.
4. Remove the protective cap from the nozzle.
5. Hold the PecFent bottle with your thumb at the bottom of the bottle and the index and middle fingers on the finger grips on both sides of the nozzle (figure 4).
6. Insert the nozzle about 1 cm deep into the nostril. Aim the nozzle inwards towards the inner wall of the nostril. This action will cause a slight change in the bottle's tilting angle (figure 5).
7. Close the other nostril with the finger of the other hand (figure 5).
8. Press down firmly on the finger grips on both sides of the nozzle in order to cause spraying of the spray into the nostril. When a "click" sound is heard, let go of the grips.
Note: you may not feel any change inside your nose - this does not mean the spray has not worked. Trust the "click" sound and the number in the counting window.
9. Inhale gently through the nose and exhale through the mouth.
10. The number in the counting window will increase after each use and will signify the number of sprays that have already been performed.
11. If the doctor has prescribed two sprays of the spray, repeat the actions in section 5 to 9 while

using **the other nostril**.

Do not take a higher dose than the one prescribed by the doctor for treating any single episode of breakthrough pain.

12. Put the bottle back into the child-resistant container after every use. Keep the medicine out of the reach and sight of children (figure 6).
13. Remain seated for at least one minute after using the spray.



The number of sprays in a PecFent bottle:

Each bottle of PecFent Spray contains 8 full sprays.

- After the first spray, the number "1" will appear in the counting window. The number will increase with each additional spray.
- When you see a red number "8" in the counting window this means that the preparation is finished and you can no longer get a full spray from it.

How to dispose of PecFent spray that has not been used:

If a number other than "8" appears in the counting window, it means that you have not used all 8 sprays of the bottle.

You must empty the remaining PecFent doses from the bottle by aiming the spray away from you (and other people) and spraying repeatedly until a red number "8" appears in the counting window.

When you see the number "8" in the counting window, there is still medicine inside the bottle and it should be emptied out.

- You must press down and release the finger grips 4 more times while the nasal spray is directed away from you (and other people).
- You will feel a slightly increased resistance while pressing and the finger grips will only move down slightly.
- You will **not** hear a "click" sound while pressing down.
- In the counting window the number "8" will remain unchanged.
- Close the spray bottle with the protective cap.
- Put the spray bottle into the child-resistant container.
- Consult the pharmacy on how to dispose of empty bottles (see "How to store PecFent").

If the PecFent nasal spray is blocked or is not working properly:

If the PecFent nasal spray is blocked, aim the spray away from you (and other people) and press down firmly on the pump. This action will release the blockage.

If your nasal spray is still not working properly, dispose of it and start using a new one. Tell the doctor about the incident. **Never try to fix or dismantle the spray by yourself** because the product may then give you an incorrect dose of the medicine.

Dispose of the PecFent bottle and use a new bottle if:

It has been 60 days or more since you prepared the PecFent bottle for use or used your bottle

for the first time.

If you have accidentally taken a higher dosage or if a child has accidentally swallowed the medicine, proceed immediately to a hospital emergency room, and bring the package of the medicine with you.

In case of an overdose you may experience drowsiness, nausea, dizziness, slow or shallow breathing or additional side effects to the ones specified in section 4, or experience the specified side effects in a more serious manner. In severe cases taking too much PecFent may lead to coma. **If you feel extremely dizzy, extremely drowsy or if you have a slow or shallow breathing, you must call an MDA ambulance or seek other emergency assistance.**

Do not induce vomiting without an explicit order from a doctor!

If you have forgotten to take this medicine at the required time, do not take a double dose. Consult the doctor.

If you stop using the medicine:

If you no longer experience breakthrough pain episodes consult with the doctor before stopping use of the medicine and follow the doctor's orders. In any case, you must continue taking the other opioid medicine to relieve persistent pains. The doctor may need to check the dosage.

You may experience withdrawal symptoms similar to the possible side effects when discontinuing the medicine. If you experience withdrawal symptoms, you should contact the doctor.

The doctor will decide whether you need to take a medicine to treat the withdrawal symptoms.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like all medicines, using PecFent can cause side effects in some users. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

You must immediately call an MDA ambulance or ask someone else to call one if:

- You feel very dizzy or faint
 - You feel very sleepy
 - Your breathing is slow or shallow (slight movement in the chest while breathing)
 - Your skin is cold and clammy, you look pale, you have a weak pulse or other signs of shock.
- If you or your caregiver notices one of the aforementioned side effects, immediately call MDA.

Common side effects (may affect up to 1 in 10 people):

- Not knowing where you are (disorientation)
- A change in taste
- Feeling dizzy
- Feeling or being sick
- Feeling sleepy, headache
- Nosebleed, discomfort in the nose (such as burning in the nose), runny nose
- Constipation
- Itchy skin

Uncommon side effects (may affect up to 1 in 100 people):

- Chest infection
- Pain, sensitivity or inflammation in the throat or nose
- Coughing, sneezing, runny nose or cold, change in the fluid secreted by the nose

- Allergic reactions, rash
- Decrease or increase in appetite, weight gain
- Dehydration, thirst
- Misuse of the medicine
- Seeing or hearing things that are not really there (hallucinations/delirium), feeling confused
- Feeling depressed, worried, slow or nervous
- Lack of concentration or increased activity
- Memory loss
- A feeling of euphoria
- Decreased awareness or responsiveness, loss of consciousness
- Convulsions
- Muscle spasms or trembling
- Loss of sense of taste, loss or change in sense of smell
- Difficulty speaking
- Blue skin color
- Vertigo, falling over, malaise
- Heat and circulation that is not working properly, feverish skin or flush, chills, excessive sweating
- Swelling of soft tissues
- Low blood pressure
- Obstruction of windpipe
- Shortness of breath
- Vaginal bleeding
- A tear in the intestine or inflammation in the stomach lining
- Numbness or tingling in the mouth, tongue or nose or other tongue problems, mouth ulcers, dry mouth
- Diarrhea
- Retching, stomach aches, indigestion
- Pain or sensitivity in the joints
- Difficulty or inability to urinate
- Chest pain
- Fatigue, weakness, problems with movement
- Changes in blood cells (detected by laboratory tests)
- Increased blood sugar
- Protein in the urine

Side effects of an unknown frequency (it is not possible to estimate the frequency of the available data):

- Severe breathing problems
- Flushing
- Insomnia
- Withdrawal symptoms (can be manifested by the following side effects: nausea, vomiting, diarrhea, anxiety, chills, tremor and excessive sweating).
- Drug dependence (addiction)
- Drug abuse

Prolonged treatment with PecFent during pregnancy may cause withdrawal symptoms in the newborn which can be life-threatening (see section 2).

If a side effect appears, if any of the side effects worsens, or if you suffer from a side effect that is not mentioned in this leaflet, consult the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the "Reporting side effects following drug treatment" link found on the Ministry of Health homepage (www.health.gov.il) that

directs you to the online form for reporting side effects or at the following link:

<https://sideeffects.health.gov.il>

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Do not use the nasal spray after 60 days from the first use. Write down the date of first use or priming of the PecFent bottle on the label of the child-resistant container.

If the nasal spray has not been used for more than 5 days, it must be re-primed by spraying once.

Storage conditions:

Store at a temperature below 25°C. Do not freeze!

Keep the spray in the child-resistant container in order to protect from the light. The PecFent spray should be kept in the child-resistant container throughout the entire period of use and even after the medicine has been finished.

PecFent that has expired or that is no longer needed, may still contain a sufficient amount of medicine to be harmful to other people and especially children. Do not dispose of the medicine via wastewater or household waste. Medicine that is no longer needed should be disposed of as soon as possible following the instructions specified under the "**How to dispose of PecFent spray that has not been used**" section. All empty bottles must be returned into the child-resistant container.

6. Additional information

In addition to the active ingredient, this medicine also contains:

mannitol, pectin, sucrose, propyl parahydroxybenzoate, phenylethyl alcohol, purified water, hydrochloric acid or sodium hydroxide.

This medicine contains sucrose at a concentration of 5 mg/ml and the preservatives Propyl parahydroxybenzoate and Phenylethyl alcohol.

What the medicine looks like and contents of the pack:

The medicine is clear to nearly clear and colorless solution. It is contained in a clear glass bottle, fitted with a measuring pump. The pump has a dose counter that "clicks", so you can hear as well as see in the counting window that the dose has been given. The spray is closed with a clear protective cap. After preparing the PecFent bottle for use, it contains 8 full sprays.

Each PecFent bottle is marketed in a child-resistant container and is packed in a carton box.

A carton box contains 1 or 4 bottles of PecFent.

PecFent Nasal Spray is available in two dosages: 100 mcg and 400 mcg.

Registration holder and address: Medison Pharma Ltd., 10 Hashiloach St., P.O. Box 7090, Petach Tikva.

Manufacturer's name and address: Kyowa Kirin Holdings B.V., The Netherlands
Bloemlaan 2, 2132NP Hoofddorp, The Netherlands

Revised in May 2022 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

PecFent 100: 152 59 33975

PecFent 400: 152 60 33978

PECFENT-PIL-10/2019-V4