

PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

Fentamed 100 mcg Fentamed 200 mcg Fentamed 300 mcg Fentamed 400 mcg Fentamed 600 mcg Fentamed 800 mcg

Sublingual tablets

Composition:

Each sublingual tablet contains:

The active ingredient and its quantity:

Fentamed 100 mcg: Fentanyl (as citrate) micronized 100 mcg

Fentamed 200 mcg: Fentanyl (as citrate) micronized 200 mcg

Fentamed 300 mcg: Fentanyl (as citrate) micronized 300 mcg

Fentamed 400 mcg: Fentanyl (as citrate) micronized 400 mcg

Fentamed 600 mcg: Fentanyl (as citrate) micronized 600 mcg

Fentamed 800 mcg: Fentanyl (as citrate) micronized 800 mcg

For a list of inactive and allergenic ingredients in the preparation: see section 6 "Further Information" and section 2 "Important information about some of the ingredients of the medicine".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar. This medicine is intended for adults above the age of 18.

- Taking this medicine with benzodiazepines or other medicines that suppress the central nervous system (including recreational drugs) or alcohol may result in a sensation of profound sleepiness, breathing difficulties (respiratory depression), coma and death.
- Opioids could cause addiction, mainly in prolonged use, and may potentially lead to abuse and overdose. A reaction to an overdose can manifest itself in slow breathing and even lead to death. Make sure you know the name of the medicine, the dosage you are taking, administration frequency, duration of treatment, and the potential side effects and risks. Additional information related to the risk of dependence and addiction can be found at the link: https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

1. WHAT IS THE MEDICINE INTENDED FOR?

Fentamed is intended for the treatment of breakthrough pain in oncological patients who are being treated with strong pain-relief medicines (opioids) regularly. Breakthrough pain is pain which occurs suddenly, even though you are using your opioid pain-relief medicine on a continuous basis.

Therapeutic group: The active ingredient in Fentamed sublingual tablets is fentanyl. Fentanyl belongs to a group of strong narcotic pain-relief medicines called opioids.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient, fentanyl, or any of the additional ingredients contained in the medicine (listed in section 6 "Further Information" and section 2 "Important information about some of the ingredients of the medicine").
- You suffer from severe breathing problems.
- You have not been using a prescribed opioid medicine on a continuous basis every day at fixed times for at least a week to control your persistent pain (e.g., opioids such as: codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine). If you are not using a medicine of this type, **you must not** use Fentamed because it may increase the risk of dangerously slow and/or shallow breathing, or even cessation of breathing.
- You suffer from short-term pain that is different than breakthrough pain.
- You are being treated with medicines that contain sodium oxybate.

Special warnings regarding use of the medicine

Before treatment, tell your doctor or pharmacist if you suffer or have suffered in the past from any of the following conditions, as your doctor will need to take this into account when adjusting your dosage:

- A head injury, because Fentamed may mask the seriousness of the injury.
- Breathing problems or if you suffer from myasthenia gravis (a disease that weakens your muscles).
- If you suffer from heart problems, especially if you suffer from a slow heart rate.
- Low blood pressure.
- Liver or kidney disease, your doctor may need to adjust your dosage more carefully.
- Brain tumor and/or increased intracranial pressure (increased pressure in the brain causing severe headaches, nausea/vomiting and blurred vision).
- Ulcers in your mouth or oral mucositis (swelling and redness in the oral cavity).
- If you take antidepressants or antipsychotics, please carefully read the section below, "Drug interactions".
- If you have ever developed adrenal insufficiency or lack of sex hormones (androgen deficiency) with opioid use.

During treatment with Fentamed, inform your doctor or dentist that you are taking this medicine if:

- You are due to undergo any surgery.
- You experience pain or increased sensitivity to pain (hyperalgesia) which does not respond to a higher dosage of your medicine as determined by the doctor.
- You suffer from a combination of the following symptoms: nausea, vomiting, anorexia, fatigue, weakness, dizziness and low blood pressure. This combination of symptoms may be a sign of a potentially life-threatening condition called adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones.

Your doctor may need to check you more carefully if:

- You or any of your family members have ever abused or suffered from dependence on alcohol, prescription medicines or illicit drugs ("addiction").
- You smoke.
- If you have suffered from mood problems (depression, anxiety or personality disorder) or have been treated by a psychiatrist due to other mental illnesses.

Repeated use of Fentamed may lead to dependence and abuse, which may lead to a life-threatening overdose. It is important to consult with a doctor if you are concerned that you may develop Fentamed dependence.

Sleep-related breathing problems

Fentamed may cause sleep-related breathing problems, such as sleep apnea (breathing cessations while sleeping) and hypoxemia during sleep (low blood oxygen level). Possible symptoms are: breathing cessations while sleeping, awakening at night due to shortness of breath, difficulty staying asleep or increased drowsiness during daytime. If you or anyone else have noticed these symptoms, contact the doctor. The doctor may consider reducing the dosage.

Drug interactions

If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Some medicines may increase or decrease the effects of Fentamed. You should therefore tell the doctor if you are starting, changing the dosage of or stopping treatment with the following medicines, as the doctor may need to adjust your dosage of Fentamed:

- Antifungal medicines used to treat fungal infections, e.g., ketoconazole or itraconazole.
- Antibiotics of the macrolides group used to treat infections, e.g., erythromycin.
- Antiviral medicines of the protease inhibitors class used to treat infections caused by viruses, e.g., ritonavir.
- Rifampin or rifabutin (medicines used to treat bacterial infections).
- Carbamazepine, phenytoin or phenobarbital (medicines used to treat convulsions/seizures).
- Herbal medicines containing St. John's wort (*Hypericum perforatum*).
- Medicines containing alcohol.
- Medicines of the monoamine-oxidase inhibitors (MAOI) class, which are used to treat severe depression and Parkinson's disease. Tell your doctor if you have taken this type of medicine within the last two weeks.
- Certain types of strong pain killers, called partial agonists/antagonists, e.g., buprenorphine, nalbuphine and pentazocine. You may experience symptoms of withdrawal syndrome (e.g., nausea, vomiting, diarrhea, anxiety, chills, tremor, and sweating) while using these medicines.

Fentamed may enhance the anesthetic effect of the following medicines (sedatives) and in addition increase the risk of respiratory depression and decrease in blood pressure:

- Other strong pain-relief medicines (medicines of the opioid class for relief of pain or cough)
- Painkillers for nerve pain (gabapentin and pregabalin)
- General anesthetics (intended for anesthesia during surgery)
- Muscle relaxants
- Medicines to induce sleep
- Medicines used to treat:
 - ▶ Depression
 - ▶ Allergies (sedating antihistamines H1 blockers)
 - ▶ Anxiety and psychosis (medicines of the barbiturate class, benzodiazepines, e.g., diazepam, sleep-inducing medicines or antianxiety medicines)
- Medicines containing clonidine (used to treat hypertension)

Use of Fentamed at the same time as using medicines that make you feel sleepy (sedatives) such as benzodiazepines, increases the risk of drowsiness, breathing difficulties (respiratory depression), coma, and may be life-threatening. Therefore, use of Fentamed together with sedatives should be considered only when there are no other treatment options.

However, if the doctor still decides to use Fentamed together with sedatives, the dosage and treatment duration should be limited by the doctor.

Please tell the doctor about any sedatives you are taking and carefully follow the dosage recommended by the doctor. It may be useful to inform your friends or relatives to make them aware of the signs and symptoms detailed above. Contact the doctor upon experiencing such symptoms.

The risk of certain other side effects increases if you are taking medicines such as antidepressants or antipsychotics, since there may be a drug interaction that manifests itself in changes in your mental state [e.g., agitation (restlessness), hallucinations, coma] and other effects such as high fever above 38°C, increase in heart rate, unstable blood pressure and enhanced reflexes, muscular rigidity, lack of coordination and/or digestive system effects (e.g., nausea, vomiting, diarrhea). In this case, the doctor will advise you whether Fentamed is suitable for you.

Use of the medicine with food and drink

Grapefruit juice may increase the risk of side effects of Fentamed; therefore do not drink grapefruit juice while being treated with Fentamed.

Use of the medicine and alcohol consumption

Fentamed may cause drowsiness in some patients. Do not consume alcohol while being treated with the medicine without consulting the doctor, as it may cause excessive drowsiness.

Pregnancy and breastfeeding

Do not use Fentamed if you are pregnant, unless you have been explicitly told otherwise by the doctor, since fentanyl may cause withdrawal symptoms in the newborn and endanger its life.

Do not breastfeed during treatment with Fentamed, and do not start breastfeeding before at least 5 days have passed since the last dose of Fentamed. Fentanyl can pass into breast milk and may cause sleepiness and respiratory depression in the breastfed infant.

If you are pregnant or breastfeeding, consult with a doctor or pharmacist before using medicines.

Driving and using machinery

Fentamed may impair your mental and/or physical ability to perform potentially hazardous tasks such as driving or operating machinery.

If you feel sleepy, drowsy or have blurred vision when using Fentamed, **do not drive a car or operate machinery.**

Important information about some of the ingredients of the medicine

Fentamed contains sodium

This medicine contains less than 23 mg sodium per tablet, and is therefore considered sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

Before starting treatment with Fentamed, your doctor will explain how Fentamed should be taken to effectively relieve your breakthrough pain.

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

The preparation is intended to be used **only** by you according to your doctor's instructions. **The preparation must not be used by anybody other than yourself, as it could present a grave danger to health, especially in children.**

Fentamed is different from other medicines you may have taken in the past to treat breakthrough pain. **You must always take Fentamed at the dosage prescribed by your doctor** – this dosage may be different from the dosage of other medicines you have taken in the **past** to treat breakthrough pain.

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:

Starting treatment – finding the most appropriate dosage

For Fentamed to work effectively, the doctor will need to identify the most appropriate dosage for treating your breakthrough pain. Fentamed is available in several dosages. You may need to try different dosages of Fentamed over a number of episodes of breakthrough pain to find the most appropriate dosage for you.

Your doctor will help you with this and will instruct you on finding the most appropriate tablet strength.

If you do not feel adequate pain relief after one dose, your doctor may instruct you to take an additional dose to treat an episode of breakthrough pain.

Do not take an additional dose, unless your doctor tells you to, as this may result in overdose.

Your doctor may instruct you to take a dose which consists of more than one tablet at a time. **Only do this if explicitly directed by the doctor.**

Wait at least 2 hours after taking your last dose of Fentamed before taking the next dose to treat another episode of breakthrough pain.

Maintenance dose (continuing treatment) – once you have found the most appropriate dosage for you

Once you and your doctor have found a dose of Fentamed that controls your breakthrough pain, you should take this dose no more than four times a day. **A dose of Fentamed may consist of more than one tablet.**

Wait at least 2 hours after taking your last dose of Fentamed before taking the next dose to treat another episode of breakthrough pain.

If you think that the dose of Fentamed that you are taking is not controlling your breakthrough pain satisfactorily, tell your doctor, as the dose may need to be adjusted.

Do not change the dosage of Fentamed unless explicitly told to do so by the doctor. **Do not exceed the recommended dose.**

Directions for use:

Fentamed is intended for sublingual use. Place the tablet under the tongue, where it dissolves rapidly, and thus the active ingredient, fentanyl, will be absorbed by the oral mucosa. Once absorbed, fentanyl starts to relieve the pain.

When you experience an episode of breakthrough pain, take the dose prescribed by your doctor as follows:

- If your mouth is dry, take a sip of water to moisten it. You may spit out or swallow the water.
- Remove the tablet from the blister pack **immediately** before use as follows:
 - ▶ Separate one of the tray (blister) squares by tearing along the perforated lines (keep the remaining tray [blister] squares together).
 - ▶ Peel back the edge of the aluminum foil in the direction of the marked arrow, and carefully remove the tablet. Do not try to push a tablet through the foil top, as this may damage it.
- Place the tablet under your tongue as far back as you can until it completely dissolves.
- Fentamed will dissolve rapidly under the tongue and will be absorbed in order to relieve the pain.

Do not suck, halve, crush, chew or swallow the tablet.

Place the entire tablet under your tongue.

Do not eat or drink until the tablet has completely dissolved under your tongue.

If you accidentally took a higher dosage:

- Remove any remaining medicine from your mouth.
- Tell your caregiver or another person what has happened.
- Refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you. The person accompanying the patient should keep the patient alert by talking to him or shaking him now and then.

Symptoms of overdose include:

- Extreme drowsiness
- Slow and shallow breathing
- Coma

If these symptoms occur, summon emergency medical help immediately.

If an adult or child has accidentally taken the medicine, they must be immediately referred to a doctor or hospital emergency room, and bring the package of the medicine.

Adhere to the treatment regimen as recommended by the doctor.

If you stop taking the medicine

If you no longer suffer from breakthrough pain, you may stop using Fentamed, but you must continue using your regular opioid pain-relief medicine to treat your persistent pain as instructed by your doctor.

If you stop taking Fentamed, you may suffer from withdrawal symptoms similar to the side effects of Fentamed.

If you suffer from withdrawal symptoms or if you are concerned about your pain relief, consult the doctor. The doctor will consider whether you need a medicine to treat the withdrawal symptoms.

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

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

4. SIDE EFFECTS

As with any medicine, use of this medicine may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

If you feel extremely or unusually drowsy or your breathing becomes slow or shallow, refer immediately to a doctor or proceed to the nearest hospital for emergency treatment (see also section 3 If you accidentally took a higher dosage).

Very common side effects – effects that occur in more than 1 user in 10:

- Nausea

Common side effects – effects that occur in 1-10 in 100 users:

- Dizziness, headache, excessive drowsiness
- Shortness of breath
- Inflammation of the oral cavity, vomiting, constipation, dry mouth
- Sweating, lethargy/tiredness/lack of energy

Uncommon side effects – effects that occur in 1-10 in 1,000 users:

- Allergic reactions, tremor, disturbed or blurred vision, slowing or speeding up of heart rate, low blood pressure, memory loss
- Depression, suspicious thoughts or feeling afraid for no reason, feeling confused, feeling disoriented, feeling anxious/restless/unhappy, feeling unusually happy (euphoria), mood swings
- Feeling full persistently, abdominal pain, indigestion
- Mouth ulcers, problems with tongue, pain in mouth or throat, tightness in throat, lip or gum ulcers
- Loss of appetite, loss of or change in sense of taste/smell
- Difficulty falling asleep or sleep disturbances, lack of attention/being easily distracted, lack of energy/weakness
- Skin disorders, rash, itchiness, night sweats, decreased sensitivity to touch, bruising easily
- Joint pain or stiffness, muscle stiffness
- Drug withdrawal symptoms (e.g., nausea, vomiting, diarrhea, anxiety, chills, tremor, sweating), taking an accidental overdose, in males: an inability to achieve and/or maintain an erection, feeling generally unwell.

Side effects of unknown frequency (effects whose frequency has not yet been determined):

- Swollen tongue, severe breathing problems, falls, flushing, feeling extremely warm, diarrhea, seizures (convulsions), swelling of the arms or legs, seeing or hearing things that are not really there (hallucinations), fever, drug dependence (addiction), drug overuse, reduced level or loss of consciousness, itchy rash and delirium (symptoms may include a combination of agitation, restlessness, disorientation, confusion, fear, seeing or hearing things that are not really there, sleep disturbances, nightmares).

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

Reporting side effects

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects may be reported to the Ministry of Health by clicking the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the following link: <https://sideeffects.health.gov.il>

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! **Fentamed is a very strong pain-relief medicine which may be life-threatening if accidentally taken by a child.** Therefore, this medicine and any other medicine, should be kept in a safe **locked** 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 the doctor.
- **It is recommended to keep this medicine in a locked place.**
- Do not use the medicine after the expiry date (exp. date) that appears on the exterior package and on the blister tray. The expiry date refers to the last day of that month.
- **Storage Conditions:** Store below 25°C.

How to dispose of unused tablets? If you have Fentamed tablets that you no longer need, give them to the nearest pharmacy so that they can be destroyed safely, thus protecting the environment. Medicines should not be disposed of via wastewater or household waste.

6. FURTHER INFORMATION

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

Mannitol, silicified microcrystalline cellulose, magnesium stearate, croscarmellose sodium.

• What the medicine looks like and the contents of the package:

Fentamed is a small white sublingual tablet. The tablet comes in a range of different strengths and shapes. Your doctor will prescribe the strength and number of tablets suitable for you.

- Fentamed 100 mcg tablet is a white round tablet
- Fentamed 200 mcg tablet is a white oval-shaped tablet
- Fentamed 300 mcg tablet is a white triangle-shaped tablet
- Fentamed 400 mcg tablet is a white diamond-shaped tablet
- Fentamed 600 mcg tablet is a white "D"-shaped tablet
- Fentamed 800 mcg tablet is a white capsule-shaped tablet

Fentamed is marketed in packs of 30 tablets. The tablets are packaged in trays (blister packs).

• **Registration holder and its address:** Inovamed Pharma Ltd., POB 2349, Bnei Brak.

• **Manufacturer and its address:** Kern Pharma, S.L., Terrassa, Barcelona, Spain.

Revised in July 2023 according to MOH guidelines.

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

- Fentamed 100 mcg 173-43-36706
- Fentamed 200 mcg 173-44-36707
- Fentamed 300 mcg 173-45-36708
- Fentamed 400 mcg 173-46-36709
- Fentamed 600 mcg 173-47-36710
- Fentamed 800 mcg 173-48-36711