

Package leaflet: Information for the user

Instanyl 50 micrograms nasal spray, solution in single-dose container
Instanyl 100 micrograms nasal spray, solution in single-dose container
Instanyl 200 micrograms nasal spray, solution in single-dose container
fentanyl

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Instanyl is and what it is used for
2. What you need to know before you use Instanyl
3. How to use Instanyl
4. Possible side effects
5. How to store Instanyl
6. Contents of the pack and other information

1. What Instanyl is and what it is used for

Instanyl contains the active substance fentanyl and belongs to a group of strong painkillers called opioids. Opioids act by blocking the pain signals to the brain.

Instanyl acts rapidly and is used for relieving breakthrough pain in adult cancer patients already treated with opioids for their usual pain. Breakthrough pain is an additional sudden pain that occurs despite you having taken your usual opioid pain relieving medicines.

2. What you need to know before you use Instanyl

Do not use Instanyl:

- if you are allergic to fentanyl or any of the other ingredients of this medicine (listed in section 6).
- if you are not regularly using a prescribed opioid medicine (e.g., codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine), every day on a regular schedule, for at least a week, to control your persistent pain. If you have not been using these medicines you must not use Instanyl, because it may increase the risk that breathing could become dangerously slow and/or shallow, or even stop.
- if you are taking a medicine which contains sodium oxybate.
- if you suffer from short-term pain other than breakthrough pain.
- if you have serious difficulties breathing or suffer from a serious obstructive lung disease.
- if you have previously received facial radiotherapy.
- if you suffer from recurrent episodes of nose bleeding.

Warnings and precautions

Store this medicine in a safe and secure place, where other people cannot access it (see section 5. How to store Instanyl for more information).

Talk to your doctor or pharmacist before using Instanyl, especially:

- if you suffer from a long-term obstructive lung disease, your breathing may be impaired by Instanyl.
- if you have problems with your heart especially slow heart rate, low blood pressure or low blood volume.
- if you have problems with your liver or kidneys.
- if you have problems with your brain function, e.g., due to a brain tumour, a head injury or increased intracranial pressure.
- if you have ever developed adrenal insufficiency or lack of sex hormones (androgen deficiency) with opioid use.
- if you take sedative medicines such as benzodiazepines or related drugs (please also refer to the section 'Other medicines and Instanyl').
- if you take antidepressants or antipsychotics, (please also refer to the section 'Other medicines and Instanyl').
- if you take medicines called partial agonist/antagonists, e.g., buprenorphine, nalbuphine and pentazocine (medicines for treatment of pain) as you may experience symptoms of withdrawal syndrome. Please refer to the section '*Other medicines and Instanyl*' for more information.
- if you use other nasal spray products, e.g., for common cold or allergy.

Sleep-related breathing disorders

Instanyl can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

If you experience difficulties breathing while being treated with Instanyl, it is very important that you contact your doctor or hospital immediately.

Consult your doctor while using Instanyl, if:

Long-term use and tolerance

This medicine contains fentanyl which is an opioid medicine. Repeated use of opioid painkillers can result in the drug being less effective (you become accustomed to it, known as drug tolerance). You may also become more sensitive to pain while using Instanyl. This is known as hyperalgesia. Increasing the dose of Instanyl may help to further reduce your pain for a while, but it may also be harmful. If you notice that your medicine becomes less effective, talk to your doctor. Your doctor will decide whether it is better for you to increase the dose or to gradually decrease your use of Instanyl.

Dependence and addiction

Repeated use of Instanyl can also lead to dependence, abuse and addiction which may result in life-threatening overdose. The risk of these side effects can increase with a higher dose and longer duration of use. Dependence or addiction can make you feel that you are no longer in control of how much medicine you need to use or how often you need to use it. You might feel that you need to carry on using your medicine, even when it doesn't help to relieve your pain.

The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent or addicted on Instanyl if:

- you or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs ("addiction").
- you are a smoker.
- you have ever had problems with your mood (depression, anxiety or a personality disorder) or have been treated by a psychiatrist for other mental illness.

If you notice any of the following signs whilst using Instanyl, it could be a sign that you have become dependent or addicted.

- you need to use the medicine for longer than advised by your doctor
- you need to use more than the recommended dose
- you are using the medicine for reasons other than prescribed, for instance, ‘to stay calm’ or ‘help you sleep’
- you have made repeated, unsuccessful attempts to quit or control the use of the medicine
- when you stop taking the medicine you feel unwell (e.g. nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating), and you feel better once using the medicine again (‘withdrawal effects’)

If you notice any of these signs, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to stop safely.

- you experience pain or increased sensitivity to pain (hyperalgesia) which does not respond to a higher dosage of your medicine as prescribed by your doctor.
- you experience a combination of the following symptoms: nausea, vomiting, anorexia, fatigue, weakness, dizziness and low blood pressure. Together these 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.

If you experience recurrent nose bleeding or nasal discomfort whilst being treated with Instanyl, you must contact your doctor, who will consider alternative treatment for your breakthrough pain.

Children and adolescents

Instanyl should not be used in children and adolescents under 18 years of age.

Other medicines and Instanyl

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.

Instanyl may affect or be affected by other medicines.

Special care should be taken if you are treated with any of the following medicines:

- other medicines for pain and some painkillers for nerve pain (such as gabapentin and pregabalin).
- any medicines which might normally make you sleepy (have a sedative effect) such as sleeping pills, sedative medicines such as benzodiazepines or related medicines, medicines to treat anxiety, antihistamines, or tranquillisers, skeletal muscle relaxants and gabapentinoids (gabapentin and pregabalin). The use of such other medicines at the same time as Instanyl, may cause risk of drowsiness, deep sedation and affect your ability to breathe (respiratory depression), which may lead to coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However if your doctor does prescribe Instanyl together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedative medicines you are taking, and follow your doctor’s dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.
- any medicines that might have an effect on the way in which your body breaks down Instanyl, such as:
 - ritonavir, nelfinavir, amprenavir, and fosamprenavir (medicines that help control HIV infection);
 - CYP3A4 inhibitors such as ketoconazole, itraconazole, or fluconazole (used for treatment of fungal infections);
 - troleandomycin, clarithromycin, or erythromycin (medicines for treatment of bacterial infections);

- aprepitant (used to treat severe nausea);
 - diltiazem and verapamil (medicines for treatment of high blood pressure or heart diseases).
- medicines called Monoamine Oxidase Inhibitors (MAOI) used for severe depression, even if you have been treated with one in the past 2 weeks.
 - The risk of side effects increases if you are taking medicines such as certain antidepressants or antipsychotics. Instanyl may interact with these medicines and you may experience mental status changes (e.g., agitation, hallucinations, coma), and other effects such as body temperature above 38 °C, increase in heart rate, unstable blood pressure, and exaggeration of reflexes, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea). Your doctor will tell you whether Instanyl is suitable for you.
 - medicines called partial agonist/antagonists e.g., buprenorphine, nalbuphine and pentazocine (medicines for treatment of pain). You could experience symptoms of withdrawal syndrome (nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating).
 - other medicines taken via the nose, especially oxymetazoline, xylometazoline and similar medicines, which are used for relief of nose congestions.

Instanyl with food, drink and alcohol

Do not drink alcohol whilst being treated with Instanyl, as it can increase the risk of experiencing dangerous side effects.

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby ask your doctor or pharmacist for advice before taking any medicine.

Instanyl should not be used during pregnancy unless you have discussed this with your doctor.

Instanyl should not be used during childbirth because fentanyl may cause serious breathing problems in the new-born child.

Fentanyl can get into breast milk and may cause side effects in the breast-fed infant. Do not use Instanyl if you are breast-feeding. You should not start breast-feeding until at least 5 days after the last dose of Instanyl.

Driving and using machines

You should not drive or use machinery whilst being treated with Instanyl. Instanyl can cause dizziness, drowsiness and visual disturbances, which may affect your ability to drive or use machines.

3. How to use Instanyl

Before starting treatment and regularly during treatment, your doctor will also discuss with you what you may expect from using Instanyl, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also section 2).

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

The dose of Instanyl is independent of your usual cancer pain treatment.

When you first start using Instanyl, your doctor will work with you to find the dose that will relieve your breakthrough pain.

The initial dose is one puff of 50 micrograms in one nostril each time you have an episode of breakthrough pain. During the determination of your right dose, your doctor may instruct you to change to a higher dose.

If your breakthrough pain is not relieved after 10 minutes, you may use only one puff more for this episode.

Generally, you should wait 4 hours before treating another episode of breakthrough pain. On exceptional occasions where a new episode occurs earlier, you can use Instanyl to treat it but you must wait at least 2 hours before doing so. If you regularly have breakthrough pain episodes that are less than 4 hours apart, contact your doctor as your usual cancer pain treatment may have to be changed.

You can use Instanyl to treat up to four episodes of breakthrough pain per day.

If you experience more than four episodes of breakthrough pain per day, contact your doctor, as your usual cancer pain treatment may have to be changed.

Do not change the dose of Instanyl or your other pain medicines on your own. Change in dose must be done together with your doctor.

Instanyl is for nasal use.

Please read the instruction for use at the end of this leaflet to learn how to use Instanyl.

If you use more Instanyl than you should or if you think someone has accidentally used Instanyl

You should contact your doctor, hospital or emergency room for assessment of the risk and for advice if you have taken more Instanyl than you should.

Symptoms of overdose are:

Sleepiness, drowsiness, dizziness, reduced body temperature, slow heart beat, difficulties coordinating arms and legs.

In serious cases taking too much Instanyl may cause coma, sedation, convulsions or severe breathing difficulties (very slow or shallow breathing). An overdose may also result in a brain disorder known as toxic leukoencephalopathy.

If you feel any of the above symptoms you should seek immediate medical assistance.

Note to carers

If you see the person taking Instanyl suddenly acting slowly, having difficulties breathing or if you have difficulties waking the person up:

- you should immediately call for emergency help.
- while waiting for the emergency help, you must try to keep the person awake by talking to or gently shaking the person every now and then.
- if the person has difficulty breathing, you should prompt the person to breathe in every 5-10 seconds.
- if the person has stopped breathing, you should attempt to resuscitate her/him until emergency help arrives.

If you think someone has accidentally taken Instanyl, please seek immediate medical assistance. Try to keep the person awake until emergency help arrives.

If someone has accidentally taken Instanyl, they may have the same symptoms as described above for overdose.

If you forget to use Instanyl

If the breakthrough pain is still ongoing, you may take Instanyl as prescribed by your doctor. If the breakthrough pain has stopped, do not take Instanyl until the next episode of breakthrough pain occurs.

If you stop using Instanyl

You should discontinue Instanyl when you no longer have any breakthrough pain. You should however continue to take your usual pain relieving medicine to treat your cancer pain. Contact your doctor to confirm the correct dose of your usual medicine if you are not sure.

You may experience withdrawal symptoms similar to the possible side effects of Instanyl when discontinuing Instanyl. If you experience withdrawal symptoms, you should contact your doctor. Your doctor will evaluate if you need medicine to reduce or eliminate the withdrawal symptoms.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects will often stop or reduce in intensity with continued use of the product.

Discontinue the treatment and contact your doctor, hospital or emergency room immediately, if you:

- experience sudden, severe allergic reaction with breathing difficulty, swelling, lightheadedness, fast heartbeat, sweating or loss of consciousness.
- experience severe breathing difficulties.
- have a rattling sound when you breathe in.
- have convulsive pain.
- experience extreme dizziness.

These side effects can be very serious.

Other side effects reported after use of Instanyl:

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

Sleepiness, dizziness even with difficulties keeping balance, headache, irritation of the throat, nausea, vomiting, flushing, feeling very warm, excessive sweating.

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

Sleeplessness, drowsiness, convulsive muscle contractions, abnormal sensation of the skin even unpleasant, change of taste, motion sickness, low blood pressure, severe breathing problems, nose bleeds, nasal ulcer, runny nose, constipation, inflammation of the mouth, dry mouth, skin pain, itching of the skin, fever.

Not known (frequency cannot be estimated from the available data):

Allergic reaction, fall, diarrhoea, convulsions (fits), loss of consciousness, swelling of arms or legs, seeing or hearing things that are not really there (hallucinations), delirium (symptoms may include a combination of agitation, restlessness, disorientation, confusion, fear, seeing or hearing things that are not really there, sleep disturbance, nightmares), drug tolerance, drug dependence (addiction), drug abuse (see section 2), fatigue, malaise, withdrawal syndrome (may manifest by the occurrence of the following side effects nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating), shortness of breath.

There have also been reports of patients developing a hole in the septum of the nose – the structure, which separates the nostrils.

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

You should tell your doctor if you experience recurrent episodes of nose bleeding or nasal discomfort.

Reporting of side effects

If you get any side effects talk to your doctor. This includes any side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help provide more information on the safety of this medicine.

5. How to store Instanyl

The pain-relieving medicine in Instanyl is very strong and can be life-threatening to children. Instanyl must be kept out of reach and sight of children.

Store this medicine in a safe and secure place, where other people cannot access it. It can cause serious harm and be fatal to people who may take this medicine by accident, or intentionally when it has not been prescribed for them.

Do not use Instanyl after the expiry date which is stated on the carton and the single-dose container after EXP. The expiry date refers to the last day of that month.

Store below 30 °C. Keep the blister in the outer carton. Keep stored upright.

Instanyl can be harmful to other people, especially children. Do not throw away any medicines via wastewater or household waste. Any unused single-dose containers should be returned systematically and suitably in the child-resistant blister and discarded according to local requirements or returned to the pharmacy. Ask your pharmacist how to dispose of medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Instanyl contains

The active substance is fentanyl. The content is:

50 micrograms: 1 dose (100 microlitres) contains fentanyl citrate equivalent to 50 micrograms fentanyl.

100 micrograms: 1 dose (100 microlitres) contains fentanyl citrate equivalent to 100 micrograms fentanyl.

200 micrograms: 1 dose (100 microlitres) contains fentanyl citrate equivalent to 200 micrograms fentanyl.

The other ingredients are sodium dihydrogen phosphate dihydrate, disodium phosphate dihydrate, and water for injections.

What Instanyl looks like and contents of the pack

Instanyl is a nasal spray, solution in a single-dose spray container. The solution is clear and colourless.

The single-dose container contains 1 dose of Instanyl and is supplied in a child-resistant blister. Instanyl comes in different pack sizes of 2, 6, 8 and 10 single-dose containers.

Not all pack sizes may be marketed.

The labelling of the three Instanyl strengths is differentiated by colour:

50 micrograms labelling is orange.

100 micrograms labelling is purple.

200 micrograms labelling is greenish-blue.

Marketing Authorisation Holder

Istituto Gentili S.r.l.

Via San Giuseppe Cottolengo 15

20143 Milan

Italy

Manufacturer

Curida AS

Solbærvegen 5

NO-2409 Elverum

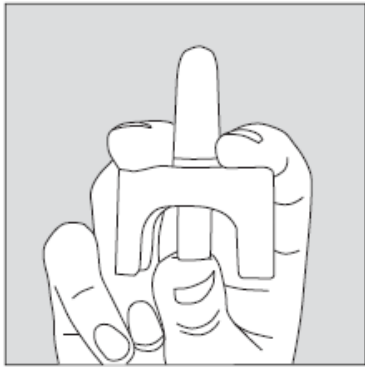
Norway

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INSTRUCTIONS FOR USE OF INSTANYL SINGLE-DOSE NASAL SPRAY

Please read the following instructions carefully to learn how to use Instanyl single-dose nasal spray:

- Each single-dose container is sealed in a child-resistant blister. Do not open the blister before you are ready to use the spray. Each single-dose container contains only one dose of Instanyl. Do not test before use.
- To open cut with scissors along the line (above the scissors symbol) on the blister. Hold the edge of the foil, peel the foil back and take the nasal spray out.
- Blow your nose if it feels blocked or you have a cold.
- Gently hold the single-dose container with your thumb supporting it at the plunger at the bottom and your index and middle finger on either side of the spray tip (see drawing). Do not press the plunger yet.



- Block one nostril by placing your other index finger against the side of your nose and insert the spray tip into the other nostril (approximately 1 cm). It does not matter which nostril you use. If you have to take a second dose after 10 minutes to get sufficient pain relief, this dose should be taken in the other nostril.



- Keep your head upright
- Press the plunger upwards firmly to release the dose with your thumb while inhaling gently through the nose and then remove the spray container from the nose. You may not feel the dose in your nose, but you have received it when the plunger has been pressed up.

Your single-dose container is now empty.