

PHYSICIAN'S GUIDE
TO PRESCRIBING
INSTANYL® ▼



IMPORTANT INFORMATION:

INSTANYL[®] NASAL SPRAY FOR BREAKTHROUGH CANCER PAIN

Dear Prescriber,

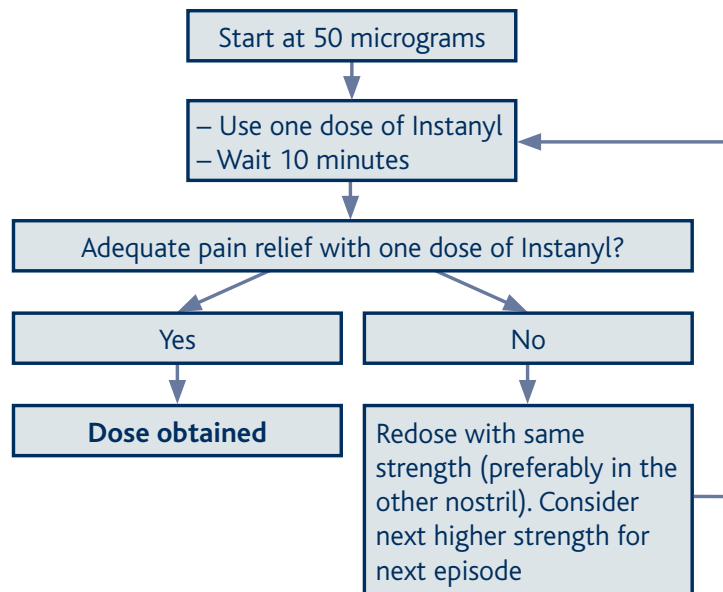
Before prescribing Instanyl please read and assimilate the following information:

INDICATION

- ▶ Instanyl should only be prescribed by physicians who are knowledgeable and skilled in the use of opioids to treat cancer pain
- ▶ Instanyl prescribers must select patients according to the strict criteria listed below and ensure that they are carefully monitored
- ▶ Instanyl is indicated for the management of breakthrough pain in adults already receiving maintenance opioid therapy for chronic cancer pain. Breakthrough pain is a transitory exacerbation of pain that occurs on a background of otherwise controlled persistent pain
- ▶ Patients receiving maintenance opioid therapy are those who are taking at least 60 mg of oral morphine daily; at least 25 µg of transdermal fentanyl/hour; at least 30 mg oxycodone daily; at least 8 mg of oral hydromorphone daily; or an equianalgesic dose of another opioid daily, for a week or longer
- ▶ Do not use Instanyl to treat any other type of pain
- ▶ Patients who take Instanyl must already have "constant or continuous pain of long duration" treated with round-the-clock opioids

DOSING & TITRATION

- ▶ Do not calculate Instanyl dose strengths based on comparison with other fentanyl products the patient is already on
- ▶ To optimise breakthrough cancer pain treatment with Instanyl, please make use of the titration flow chart on the following page or for more information please see the Summary of Product Characteristics
- ▶ Monitor and re-evaluate patients' pain status when renewing prescriptions or during visits. Consider adjusting the baseline pain treatment if the patient experiences more than four breakthrough pain episodes a day (24 hours)



MANDATORY ACTIONS

- ▶ Before prescribing, ensure that you and all other staff able to prescribe opioids, are familiar with the Instanyl Summary of Product Characteristics
- ▶ Please familiarise yourself with the Instanyl instructions for use and ensure you are able to demonstrate the correct handling and use of the Instanyl nasal spray to patients:
 - ▶ Please take patients through the comprehensive Patient Brochure (“How to Use Your Instanyl”) and make sure they take a copy with them
- ▶ Please make use of the checklist for prescribers:
 - ▶ Approved indications fulfilled
 - ▶ Instructions for using the nasal spray fulfilled
 - ▶ Patient advised on package leaflet inside the Instanyl® child-resistant box
 - ▶ Patient familiarised with the Patient Brochure and the dose monitoring cards
 - ▶ Patient advised on signs of fentanyl overdose and the need for immediate medical assistance
 - ▶ Patient advised on secure storage (out of the reach and sight of children; return of the nasal spray after use to the child-resistant box)
 - ▶ Patient educated on the opening and closing of the child-resistant box (as described in the folding label on the outside on the child-resistant box and the Patient Brochure)
 - ▶ Patient advised on the correct disposal of Instanyl® nasal spray

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STORAGE & SAFETY

- ▶ Instanyl should only be handled by patients or their carers. Advise them never to let anyone else handle or use the product
- ▶ After administration, Instanyl must be placed back in the child-resistant box for storage
- ▶ Misuse and diversion (misappropriation by others) should be avoided by safely storing Instanyl in a suitably secure place
- ▶ Please ensure patients understand that in order to prevent theft and misuse, they should store Instanyl in a suitably secure place.

WARNINGS

- ▶ Unintentional exposure to Instanyl is considered a medical emergency and a potentially life-threatening event
- ▶ If a child is accidentally exposed to the product, seek prompt medical attention as it can result in medical emergencies
- ▶ Please bear in mind the potential for abuse of the product
- ▶ Ensure your staff are aware of the signs of fentanyl overdose and the appropriate protocol for its management
 - ▶ Signs of toxicity are:
 - Deep sedation
 - Lethargy
 - Ataxia
 - Miosis
 - Convulsions
 - Respiratory depression
 - ▶ Any of these events require immediate medical assistance
 - ▶ Patients and carers should be made aware of these signs, understand their potential seriousness and be appropriately advised on what to do in the event of an emergency

DISPOSAL

- ▶ Instanyl nasal spray must be disposed of properly, in accordance with local regulations and systems. All unused/ partly used/ empty nasal sprays that are no longer required should be returned to your local pharmacist for proper disposal in accordance with the local regulations

INSTANYL[®] PRESCRIBING CHECKLIST

Required actions before Instanyl[®] is prescribed

- Approved indication fulfilled
- Patient instructed on how to use the nasal spray
- Patient familiarised with the package leaflet
- Patient advised on the Patient Brochure provided
- Patient given the dose monitoring cards and instructed on their use
- Patient advised on the signs of fentanyl overdose and the need for immediate medical assistance
- Secure storage explained (out of the reach and sight of children; return of the nasal spray after use to the child-resistant box)
- Patient educated on the opening and closing of the child-resistant box
- Patients advised on the proper disposal of Instanyl nasal spray

Please note

- ▶ Patient Brochure ("How to Use Your Instanyl") and dose monitoring cards have been developed for patients
- ▶ A Pharmacist's Guide to Dispensing & Checklist has also been developed

These materials can be requested from the Nycomed Medical Information Department:

Tel: +44 (0)800 633 5797

Fax: +44 (0) 1628 646534

Email: medinfo@nycomed.com

PRESCRIBING INFORMATION

Instanyl® ▼ 50, 100 and 200 mcg/dose nasal spray, solution (fentanyl)

Prescribing Information (refer to Summary of Product Characteristics for full information).

Presentation: Each 100 microlitre dose of the nasal spray contains 50, 100 or 200 micrograms of the active ingredient fentanyl. The nasal spray also contains sodium dihydrogen phosphate dihydrate, disodium phosphate dihydrate and purified water.

Indications: Management of breakthrough pain (BTP) in adults already receiving maintenance opioid therapy for chronic cancer pain. Patients receiving maintenance opioid therapy are those who are taking at least 60 mg of oral morphine daily, at least 25 micrograms of transdermal fentanyl per hour, at least 30 mg oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.

Dosage and administration: Intended for nasal use only. Treatment should be initiated by and remain under the supervision of a physician experienced in the management of opioid therapy in cancer patients. Physicians should keep in mind the potential of abuse of fentanyl. Patients should be individually titrated to the dose that provides adequate analgesia with tolerable adverse drug reactions. Patients must be carefully monitored during the titration process. Titration to a higher dose necessitates contact with the health care professional. Maximum daily dose: Treatment of up to four breakthrough pain episodes, each with no more than two doses separated by at least 10 minutes. Patient should wait at least 4 hours before treating another BTP episode with Instanyl during both titration and maintenance therapy. *Adults:* Initially one dose of 50 micrograms in one nostril, titrating upwards as necessary. If adequate analgesia is not obtained redosing of the same strength may be administered at the earliest after 10 minutes. Each titration step (dose strength) should be evaluated in several episodes. Once the dose has been established the patient should be maintained on this strength. Generally, the maintenance strength of Instanyl should be increased when a patient requires more than one dose per breakthrough pain episode for several consecutive episodes. Dose adjustment of the background opioid therapy may be required if the patient consistently present with more than four breakthrough pain episodes per 24 hours. Recommended to sit or stand in upright position when administering Instanyl. Cleaning of the nasal spray tip is required after each use. *Children and adolescents:* Not recommended in children and adolescents below 18 years of age. *Elderly:* Limited data available for the use of Instanyl in patients above >65 years of age. Elderly patients may have a reduced clearance, a prolonged half-life and higher sensitivity to fentanyl than younger patients. In clinical trials elderly tend to titrate to a lower effective strength than patients less than 65 years of age therefore caution when titrating. *Hepatic and renal impairment:* Administer with caution to patients with moderate to severe hepatic or renal impairment (see section 4.4 of full SmPC).

Contraindications: Hypersensitivity to fentanyl or any of the excipients. Use in opioid-naïve patients. Severe respiratory depression or severe obstructive lung conditions. Previous facial radiotherapy. Recurrent episodes of epistaxis.

Warnings and precautions: Patients and carers must be instructed to keep Instanyl out of the reach and sight of children. Ensure patients and carers follow instructions for use and know what action to take in case of overdose. Monitor closely during titration process. Ensure maintenance opioid therapy stabilised before Instanyl therapy starts. Clinically significant respiratory depression may occur with fentanyl, and patients must be observed for effects. In patients with chronic obstructive pulmonary diseases, fentanyl may have more severe adverse reactions. Administer with caution to patients with moderate to severe hepatic or renal impairment. Use with caution in patients with evidence of increased intracranial pressure, impaired consciousness or coma. Use with caution in patients with cerebral tumour or head injury. Administer with caution to patients with bradyarrhythmias, hypotonia and/or hypovolaemia. If the patient experiences recurrent episodes of epistaxis or nasal discomfort while taking Instanyl, an alternative administration form for treatment of breakthrough pain should be considered. Tolerance and physical/psychological dependence may develop upon repeated administration of opioids such as fentanyl. Withdrawal symptoms may be precipitated by administration of substances with opioid antagonist activity.

Interactions: Fentanyl is metabolised by CYP3A4. Concomitant use of agents that induce CYP3A4 activity may reduce the efficacy of Instanyl. Use with strong inhibitors of the cytochrome P450 3A4 system (e.g. ritonavir, ketoconazole, itraconazole, troleandomycin, clarithromycin and nelfinavir) or moderate inhibitors (amprenavir, aprepitant, diltiazem, erythromycin, fluconazole, fosamprenavir and verapamil) may result in increased fentanyl plasma concentrations. Concomitant use of other central nervous system depressants, including other opioids, sedatives or hypnotics, general anaesthetics, phenothiazines, tranquilisers, skeletal muscle relaxants, sedating antihistamines and alcohol may produce additive depressant effects. Concomitant use of partial opioid agonists/antagonists e.g. buprenorphine, nalbuphine and pentazocine is not recommended. Concomitant use of oxymetazoline or other nasal decongestants should be avoided. Not recommended for use within 14 days of use of monoamine oxidase (MAO) inhibitors.

Pregnancy and Lactation: Studies in animals have shown reproductive toxicity (see Section 5.3 of full SmPC). The potential risk to humans is not known. Should not be used in pregnancy unless clearly necessary. Long-term treatment may cause withdrawal in the new-born infant. Do not use during labour and delivery, including caesarean section, since fentanyl passes through the placenta and may cause respiratory depression in the foetus. If administered, an antidote for the child should be available. Fentanyl is excreted into human milk and may cause sedation and respiratory depression in the breast-fed infant. Fentanyl should only be used by breastfeeding women if benefits outweigh the risks for both mother and child.

Driving, etc: Opioid analgesics are known to impair the mental and/or physical ability required for driving or operating machinery. Patient should be advised not to drive or operate machinery if they experience somnolence, dizziness, visual disturbances or other adverse reaction which can impair their ability to drive and operate machinery.

Undesirable effects: Typical opioid side effects are to be expected. The most serious adverse reactions are respiratory depression, circulatory depression, hypotension and shock and all patients should be closely monitored for these. The most commonly reported adverse reactions are somnolence, dizziness, headache, vertigo, flushing, hot flush, throat irritation, nausea, vomiting and hyperhydrosis. Please refer to full summary of product characteristics for other undesirable effects.

Overdose: Immediate countermeasures should be started including physical or verbal stimulation of the patient. A patent airway should be established and maintained and ventilatory support if necessary. Adequate body temperature and fluid intake should be maintained. Consider the use of opioid antagonists.

Pack size and Basic NHS Price: Instanyl 50µg/dose nasal spray (10 dose) £59.50, Instanyl 50µg/dose nasal spray (20 dose) £119.00, Instanyl 100µg/dose nasal spray (10 dose) £59.50, Instanyl 100µg/dose nasal spray (20 dose) £119.00, Instanyl 200µg/dose nasal spray (10 dose) £59.50, Instanyl 200µg/dose nasal spray (20 dose) £119.00

Legal Category: CD (Schedule 2), POM

Marketing Authorisation Number(s): EU/1/09/531/001-002, 004-005, 007-008

Marketing Authorisation holder: Nycomed Danmark ApS, Langeberg 1, DK-4000 Roskilde, Denmark.

Marketed by: Nycomed UK Ltd, Three Globeside Business Park, Fieldhouse Lane, Marlow, Buckinghamshire, SL7 1HZ.

Further information is available on request from Nycomed UK Ltd Tel 0800 633 5797 Email medinfo@nycomed.com

Date of PI preparation: Sept 2009

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk.
Adverse events should also be reported to Nycomed UK Ltd on 0800 633 5797

Intranasal fentanyl SPRAY
INSTANYL®



