PHARMACIST'S GUIDE FOR DISPENSING INSTANYL® SINGLE DOSE NASAL SPRAY

Introduction

This guide is designed to help you understand the proper dispensing of Instanyl ® (fentanyl nasal spray) for patients experiencing breakthrough cancer pain. Please read this guide carefully before dispensing Instanyl® and keep it for future reference. The pharmacist dispensing checklist should be reviewed before dispensing the product.Encourage patients to communicate all medication-related issues to their prescriber.

Note: Instanyl® nasal spray should only be initiated/supervised by physicians who are experienced, knowledgeable and qualified in the management of cancer pain using opioid therapy. Special care should be taken when patients transition from the hospital to home-based care. Pharmacists play an important role in supervising the provision and use of Instanyl®.

The following materials are also available:

- A Patient's Guide to the safe use of Instanyl® Single Dose Nasal Spray
- Training video for patients about breakthrough cancer pain and the use of Instanyl® (to be confirmed)
- A Physician's Guide for Prescribing Instanyl

This Pharmacist's Guide (and the other materials listed above) can be viewed or downloaded from www.medicines.ie or requested from the Takeda Medical Information Department. Tel: 1800 937970, Email: medinfoemea@takeda.com.

Reporting Side Effects

Healthcare Professionals are asked to report any suspected adverse events to HPRA Pharmacovigilance, Website: www.hpra.ie.

Alternatively, suspected adverse events should be reported to Takeda Products Ireland Ltd on 1800 937 970 or AE.GBR-IRL@takeda.com

WHAT IS INSTANYL®?

Instanyl® for the treatment of cancer breakthrough pain

Instanyl® is an intranasal solution of fentanyl, an opioid analgesic. Instanyl® is indicated for the treatment of breakthrough cancer pain (BTP) in adults who are already receiving background opioid therapy for their chronic cancer pain. [1]

Instanyl® is suitable for adult patients with BTP who have been receiving basic opioid therapy for at least a week, consisting of:

- At least 60 mg of oral morphine daily, **or**
- At least 25 micrograms of transdermal fentanyl per hour, **or**
- At least 30 mg of oxycodone daily, **or**
- At least 8 mg of oral hydromorphone daily, **or**
- An equianalgesic dose of another opioid daily. [1]

Breakthrough Cancer Pain (BTP)

- BTP is when a patient suffers temporary (non-permanent) pain episodes that are of greater intensity than their background pain or the pain they normally experience during stable opioid treatment. [2.3]

BTP is usually of medium to high intensity. Episodes start quickly and are short-lived (about 30 minutes long). [3] Continuous cancer pain is treated with a number of management strategies, including around-the-clock opioids, other analgesics, and non-pharmacological approaches, but BTP generally requires rapid- or short-acting opioids.[3]

HOW IS INSTANYL® USED?

Left untreated, BTP can have serious negative effects on a patient's quality of life.
As a pharmacist, you should talk to patients before dispensing Instanyl® to ensure they understand how to use Instanyl® correctly, according to the Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL):

One puff of Instanyl® per BTP episode, with the possibility of administering one extra puff after at least 10 minutes if the BTP is not relieved.[1]

It is important to explain to the patient that there should generally be at least 4 hours between each treatment of a BTP episode, highlighting the risks associated with more frequent use. [1]

- In exceptional cases, if a new episode of pain occurs earlier, patients can use Instanyl® to treat it, but a minimum of at least 2 hours must have passed between treated episodes of BTP.
- Dose adjustment of the patient's background opioid should be considered if the patient frequently presents with BTP episodes that are less than 4 hours apart, or with more than four BTP episodes per 24 hours.

No more than four BTP episodes should be treated per day. [1]

Please note that Instanyl® nasal spray is not interchangeable with other Fentanyl products.

WARNINGS

Overdose

Unintentional exposure to Instanyl® is considered a medical emergency and a potentially life-threatening event. Make sure that you and your staff know the signs of fentanyl overdose/toxicity and the need for urgent medical attention.

The most serious signs of overdose/toxicity are:

- Deep sedation that can lead to loss of consciousness
- Hypotension
- Respiratory depression, which can lead to respiratory failure
- Convulsions
- Coma

Any of these symptoms require immediate medical attention, as these can lead to death without proper medical treatment. Patients or their caregivers should therefore immediately call the **emergency number (112)** in the event of an overdose or the appearance of the symptoms mentioned.

- Please ensure that patients and caregivers are made aware of the signs of fentanyl overdose/toxicity described above, understand the potential seriousness and have been adequately instructed on what to do in an emergency.
- Watch for signs that the patient may not be using the product as prescribed, and be aware of the serious risk of abuse, medication errors, overdose, and dependence.
- Ensure that the patient is aware of the potential for abuse, dependence and addiction associated with Instanyl®.

Safety, Storage and disposal

Remind the patient of the following important storage instructions:
• Store Instanyl® below 30°C.
• Instanyl® should only be handled by patients or their carers. Please advise the patient to never let anyone else handle or use the product.
• Keep Instanyl® and its packaging in the outer carton until use. Store the bottle upright.
• The Instanyl® single-dose nasal spray must not be taken out of the child-resistant blister pack until right before the patient intends to use it.
• The particular danger to children if exposed to Instanyl®.
• Please ensure patients understand that in order to prevent theft, diversion (misuse for illegal purposes), and other misuse of the drug, they should store Instanyl® in a suitably secure place. Fentanyl, the active constituent of Instanyl®, is a target for people who abuse

narcotic medicines or other street drugs and therefore the storage instructions must be closely followed.[1]

Please counsel patients on these additional safety and disposal instructions:
• Instructions for opening the blister pack for the single-dose nasal spray (Patient Information Leaflet)
• Appropriate disposal of Instanyl® single-dose nasal spray - all unused devices or empty containers should be returned systematically according to local regulations.[1]

RISKS ASSOCIATED WITH OFF-LABEL USE OF INSTANYL®

Importance of preventing off-label use

- The use of Instanyl® in any way other than that described in the approved SmPC is considered off-label use (OLU). If you are concerned that OLU may be taking place, please contact the prescriber to discuss your concerns.
- OLU can take many forms, including prescribing:
  - For an indication other than BTP in cancer patients, including any other type of pain, acute or chronic.
  - If the patient does not receive opioid therapy for their background pain.
  - More frequent dosing than licensed.
  - To someone who is under 18-years old.
- Each of these OLUs poses a **risk** to the patient. At worst , it can lead to **dependence, addiction, overdose, and death**. Side effects are generally increased with OLU.

Medication errors are particularly important to avoid when prescribing an opioid.

Medication errors include:
- Unintentional drug prescribing error.
- Drug administration error.
- Drug dispensing error.
- Incorrect dosage administered.
- Use of an incorrect route of administration.

In order to minimize the risk of medication errors, all Instanyl® labels are color-coded differently for each of the strengths of action.

RISKS ASSOCIATED WITH "OPIOID USE DISORDER" (OUD)

What is OUD?

- OUD is a "problematic pattern of opioid use that leads to clinically significant impairment or exposure" (DSM-5). [4]
- The diagnostic criteria for OUD include taking too much of the opioid, inability to cut down use, craving, negative effects on work, home, or social life, use in hazardous situations, use despite knowledge of negative effects, tolerance, and withdrawal. [4]
- The severity of OUD is determined by the number of diagnostic criteria that the patient meets. [5]
- Patients will require monitoring for signs of drug-seeking behaviour (e.g. too-early requests for prescriptions). Monitoring also should include a review of prescription frequency for concomitant opioids and psychoactive drugs (such as benzodiazepines).

Who is at risk of OUD?

The following patients may have an increased risk of developing OUD*:*

- Patients who switch from hospital-based to home care*.*
- Patients with a personal or family history (parents or siblings) of substance use disorder, including alcohol abuse*.* [6]
- Patients who smoke.
- Patients with other medical challenges.
- Personal history of other mental health problems (e.g. severe depression, anxiety, and personality disorders). .

It is important to pay careful attention to the signs of OUD, as detection will ultimately help the patient. For example, tolerance (the need for more drugs to achieve the same effect) and withdrawal are criteria associated with OUD. A patient with withdrawal symptoms may complain of nausea and vomiting, anxiety, insomnia, hot and cold flushes, sweating, muscle cramps, watery discharge from the eyes and nose, and/or diarrhea. [7]

Most importantly: *If you believe that a patient might have an issue with their treatment, discuss your concerns immediately with the patient's prescribing physician. Encourage the patient to regularly talk to their doctor about how their treatment is going. Report any known OLU, misuse or abuse via* ***HPRA Pharmacovigilance website: www.hpra.ie.*** *Alternatively, suspected adverse events should be reported to Takeda Products Ireland Ltd on 1800 937 970 or AE.GBR-IRL@takeda.com*

CHECKLIST FOR DISPENSING INSTANYL®

- ☐ Ensure that all the criteria of the approved indication are fulfilled. Instanyl® should only be prescribed for breakthrough pain (BTP) in adults who are already receiving opioid maintenance therapy for background cancer pain. If you are unsure about a difference between the label and a prescribers request, please contact the prescriber for clarification
- ☐ Give the patient and/or caregiver instructions on how to use the nasal spray
- ☐ Advise the patient/caregiver of the single-use nature of the nasal spray (each nasal spray contains only one dose and the plunger should only be pressed once the spray tip is inserted into the nose; it should not be tested before use)
- ☐ Make sure the patient/caregiver reads the Patient Information Leaflet inside the Instanyl® single-dose package
- ☐ Supply the patient/caregiver with the Instanyl® patient guide
- ☐ Instruct the patient/caregiver on how to open the child-resistant blister as described in the Patient Guide
- ☐ Explain the risks of using more than the recommended amount of Instanyl®
- ☐ Advise the patient/caregiver of signs of fentanyl overdose and the need for immediate medical assistance
- ☐ Explain secure storage and the need to keep Instanyl® out of the reach and sight of children
- ☐ Explain the correct process for disposal of Instanyl®
- ☐ Encourage the patient/caregiver to discuss background and breakthrough cancer pain and the patient's use of opioids with their doctor.

References:
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5. National Institute on Drug Abuse (NIDA). The science of drug use and addiction: the basics. Last updated July 2018. https://www.drugabuse.gov/publications/media-guide/science-drug-use-addiction-basics. Accessed on 31 March 2020.
6. Klimas J, Gorfinkel L, Fairbairn N, et al. Strategies to identify patient risks of prescription opioid addiction when initiating opioids for pain: a systematic review. *JAMA Netw Open*. 2019 May 3;2(5):e193365. doi:10.1001/jamanetworkopen.2019.3365.
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