Abstral (fentanyl citrate) sublingual tablet

Pharmacist Guide

Important risk minimisation information for healthcare professionals

Content

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INTRODUCTION

This brochure will provide you with important safety information on Abstral and points to consider when dispensing to your patients. Before dispensing Abstral, please read this Guide and retain it for future reference. A dispensing checklist is also provided within the Guide. The Guide should be used in conjunction with the product Summary of Product Characteristics (SmPC).

The following documents are also available for download at hpra.ie and medicines.ie:

- Patient/Carer Guide
- Physician Guide, including a prescribing checklist
- Summary of Product Characteristics (SmPC).

A digital copy of this brochure, as well as other educational materials are available and downloadable by scanning this QR code:

www.grunenthalhealth.ie/fentanyl-rmm

Chapter 1: What is Abstral?

- **Definition**: Abstral is a sublingual tablet containing fentanyl.
- **Indication:** The product is **ONLY** indicated for the management of breakthrough pain in adult patients using opioid therapy for chronic (background) cancer pain. It is not indicated to treat any other type of pain.
- **Cancer Breakthrough Pain (CBTP)**: CBTP is a sudden onset, transient exacerbation of pain (usually of moderate to severe intensity) experienced by cancer patients that occurs on a background of otherwise controlled persistent pain despite being on maintenance opioid therapy.[1]
- The tablet should only be administered to patients who are considered tolerant to their opioid therapy for persistent cancer pain. Patients can be considered opioid tolerant if they are taking at least 60 mg of oral morphine daily, at least 25 mcg of transdermal fentanyl per hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily or an equianalgesic dose of another opioid for a week or longer.

Chapter 2: What are the opioid-specific risks associated with the fentanyl sublingual tablet?

- **Opioid use disorder (OUD)**: OUD is defined as the problematic pattern of opioid use leading to clinically significant distress or impairment.[2] Symptoms of OUD include an overpowering desire to use opioids, increased opioid tolerance, and withdrawal syndrome when opioids are discontinued.[3] OUD is classified in DSM-4 as opioid abuse and dependence, however, in the DSM-5, these two categories were merged into a single diagnosis called "opioid use disorder".[4]
    - **Opioid abuse** is the intentional and non-therapeutic use of opioids with the aim of achieving the desired psychological or physiological effect.[5]
    - **Dependence** refers to physical or psychological dependence. Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs after abrupt discontinuation. Psychological dependence refers to a state in which individuals have impaired control over drug use based on the rewarding properties of the drug.[3]
- **Addiction**: A chronic and recurrent use disorder characterised by compulsive drug-seeking behaviour and continuous use despite harmful consequences.[6]
- **Off-label use:** The use of a drug for an unapproved indication or in an unapproved age group, dosage, or route of administration. The off-label use of Abstral include:
    - Use for all other indications (including use for other pain therapy) other than CBTP
    - Use in patients not already receiving maintenance opioid therapy
    - More frequent dosing than recommended
    - Use in persons under the age of 18 years.

  Please note that different fentanyl formulations have different indications. Make sure that you are familiar with the specific indication of this medicine before dispensing. The use of this medicine for indications other than their approved indication increases the risk of misuse, abuse, medication error, overdose, addiction and death.

- **Overdose:** Intake of a dose higher than the maximal recommended dose in the product SmPC or PIL. Signs of overdose are described in the warnings section below with the most serious effects being cardiorespiratory arrest and death.
- **Misuse:** Situations where a drug is intentionally and inappropriately used not in accordance with the authorized product information. The tablets should not be used for purposes of seeking effects other than analgesic effects such as for sedation or to ‘get high’. Misuse of a drug may increase the risk of drug dependence.
- **Medication error:** A medication error is an unintended failure in the drug treatment process that leads to or has the potential to lead to, harm to the patient. This might be related to administering the drug by a wrong dose, wrong route, wrong frequency, to a wrong person, or

for a wrong duration. Medication errors are also particularly important to avoid. Types of medication errors include:

- Unintentional errors in prescribing a drug
- Error in administration of a drug
- Error in dispensing a drug
- Administration of an incorrect dose
- Using an incorrect route of administration.

Chapter 3: Points to consider when dispensing the fentanyl tablets

- Before dispensing the tablets ensure that you are familiar with the product SmPC/PIL, this Guide and the Patient/Carer Guide.
- Please make use of the dispensing checklist that can be found at the end of this Brochure (refer to Chapter 5).
- Ensure patients are familiar with the Abstral Patient/Carer Guide.

Indication

- This medicine is only to be prescribed for the management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain.
- It should be initiated, prescribed and supervised by a physician experienced in the management of opioid therapy for cancer patients, in particular regarding transition from hospital to home.
- Abstral is not interchangeable with other fentanyl products.

Opioid use disorder

- Explain to patients the risks of abuse and dependence associated Patients at risk of abuse and misuse need to be identified and monitored before and during treatment to identify the key features of opioid use disorder (OUD) distinguishing features of opioid-related side effects versus that of OUD.
- Tools such as the DSM-V diagnostic criteria table for opioid use disorder (refer to Chapter 4), the Opioid Risk Tool (ORT) and the Prescription Opioid Misuse Index (POMI) can be used to detect patients with OUD.
- The prescribing physician should be notified if OUD is recognized.
- Cases of off-label use, misuse, abuse, addiction, and overdose should be reported to responsible competent authorities.

Signs of overdose

- Patients and carers should be made aware of the signs of fentanyl overdose, understand the potential seriousness and be advised on what to do in the event of an emergency. The most common serious signs of opioid overdose are:
  - Altered mental status
  - Myosis
  - Respiratory depression potentially leading to respiratory distress and respiratory failure which could lead to death.

  Other symptoms of opioid overdose include
  - Deep sedation potentially leading to loss of consciousness/coma
  - Hypotension
  - Convulsions
  - Cases of Cheyne-Stokes respiration have been observed in cases of fentanyl overdose, particularly in patients with a history of heart failure
  - Cardiorespiratory arrest.

  Opioid overdose without medical intervention could lead to death.

Any of the above events require immediate medical assistance.

Instructions for use and monitoring

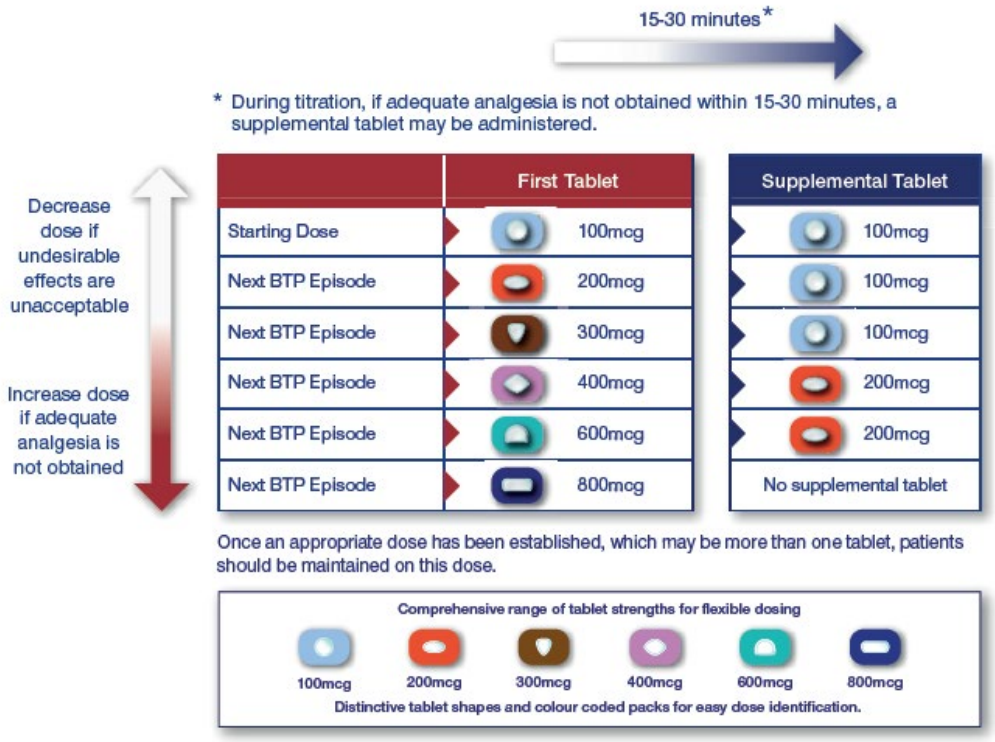
- Ensure that the patient understands how to use the tablets correctly.
- Patients should be instructed not to use two different short-acting formulations of fentanyl concurrently for the treatment of CBTP when switching to Abstral.
- Patients should be informed about the child-resistant blister, the different strengths of the product which are available, and how to differentiate the strengths according to the colour-coded packaging.
- The number of tablet strengths available to the patient at any time should be minimized to prevent confusion and reduce the risk of overdose.
- The prescribed dosing instructions must be strictly adhered to by the patient.
- Patients should be instructed never to share their medication with anyone or use it for a different purpose.
- Patients must be aware of the need for recurrent visits to the prescribing physician to perform periodic check-ups.
- Patients should be encouraged to report any issues they encounter during their treatment.

Abstral is available in different strengths. The different strength tablets have different shapes and come in colour-coded boxes to avoid confusion.

Initial dose

The starting dose of the product is 100 micrograms (mcg) in all cases, titrating upwards as shown in the table below. Patients should be monitored during the titration process. The initial dosing applies even for patients switching from other fentanyl-containing products for their cancer breakthrough pain (CBTP).

Titration



- During titration, patients can be instructed to use multiples of 100 microgram tablets and/or 200 microgram tablets for any single dose.
- The total dose for a single episode of BTP during the titration phase includes the first tablet(s) taken plus the supplemental tablet(s), if required.
- No more than four (4) tablets should be used at any time.
- No more than 4 episodes of BTP should be treated in any 24 hour period, once the dose of Abstral that controls the BTP has been reached.
- Patients should wait at least 2 hours before treating another episode of BTP with this medicine.
- If adequate analgesia is achieved at the higher dose, but undesirable effects are considered unacceptable, an intermediate dose (using the 100 microgram tablet where appropriate) may be administered.
- In order to minimise the risk of opioid-related adverse reactions and to identify the appropriate dose, it is imperative that patients be monitored closely by health professionals during the titration process.

If after titration, patients do not experience relief for their BTP episodes, they should first be reassessed so that their pain management strategy can be reviewed and modified as appropriate. Following continued monitoring, patients who continue to receive inadequate pain relief should be referred to a pain or palliative care specialist.

<u>Discontinuation</u>

Monitor and re-evaluate the patient's pain status when renewing prescriptions or during visits. The tablets should be discontinued immediately if the patient no longer experiences CBTP episodes. The treatment for the persistent background pain should be kept as prescribed. If discontinuation of all opioid therapy is required, the patient must be closely monitored to avoid the possibility of abrupt withdrawal effects. Refer to section 4.2 of the SPC for further information about stopping treatment with the tablets.

Safe-keeping and disposal

The fentanyl sublingual tablet can cause life-threatening breathing difficulties if ingested by individuals, especially children, for whom it was not prescribed. Additionally, there is a risk of the medication being stolen by individuals who misuse prescription medications. Therefore patients should be advised about the importance of correct storage/disposal of this medicine, as inappropriate storage/disposal could put someone else (not the patient) at risk of accidental opioid-naïve use, or drug diversion.

- Inform the patients that in order to prevent theft and misuse of the tablets they have to keep it in a safe place to avoid misuse and diversion.
- Unintentional exposure to fentanyl is considered a medical emergency and a potentially life-threatening event.
- If a child is accidentally exposed to the product, seek immediate medical attention as this is considered to be a medical emergency and may, without proper professional treatment, cause death.
- Tablets should be stored in a safe and secure place, such as a locked storage space, out of the reach and sight of children and inaccessible to other people, to avoid risk of serious harm and/or death.
- Tablets must be kept in the original blister pack to protect them from moisture.
- Patients should not dispose of unused or expired tablets through sewage or household waste.
- Any partly used or unused tablets should be returned to the pharmacy where they will be disposed in accordance with national and local requirements.

Administration

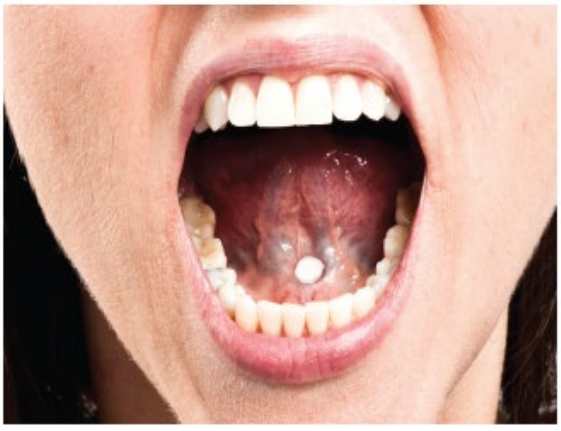
The fentanyl sublingual tablet is a very strong opioid and must never be taken by anyone but the person it is prescribed for.

• The patient should sip some water before taking the tablet, if their mouth is dry.

• The tablet should be placed under the tongue, as far back as possible, and let to dissolve completely.

• The patient should not bite, chew, suck, or swallow the tablet or it will not work properly.

• The patient should not eat or drink anything until the tablet has completely dissolved.



NB. For more information on how to take Abstral, please read the “Patient Information Leaflet” which can be found in the product pack.

Chapter 4: What are the risks associated with opioid use disorder?

Who is at risk of OUD?

Repeated use of fentanyl may lead to opioid use disorder. Patient's physician should be contacted if OUD is recognised.The risk of developing OUD is increased in patients with a personal or family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users, or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

Table 1: Diagnostic Criteria for opioid use disorder (DSM-5)[7]

1	Opioids are often taken in larger amounts or over a longer period of time than intended.
2	There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3	A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4	Craving, or a strong desire to use opioids.
5	Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home.
6	Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7	Important social, occupational or recreational activities are given up or reduced because of opioid use.
8	Recurrent opioid use in situations in which it is physically hazardous
9	Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.
10	Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of an opioid.
11	Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms.

This table lists the main diagnostic criteria for opioid use disorder. The number of criteria met signifies the severity of the opioid use disorder: Mild: 2-3 symptoms. Moderate: 4-5 symptoms. Severe: 6 or more symptoms.

How to detect adverse effects associated with OUD?

- Pay attention to patients who are exposed to significant risks: some of the risk factors for OUD include e.g. personal and family history of substance abuse, psychological stress, trauma or disease; history of substance abuse treatment, history of legal problems; young age, smokers, exaggeration of pain and unclear etiology of pain.[8] For patients with signs and symptoms of opioid addiction, a consultation with an addiction specialist should be considered.
- Review the diagnostic criteria for opioid use disorder and look for patients that meet the criteria.
- Recognise the symptoms of addiction and withdrawal.
- Communicate with your patients: ask questions about their overall well-being and determine if the problems discussed are related to primary diagnosis, pain medications or other factors.

Chapter 5: Dispensing checklist

This checklist is a reminder of actions to be taken when dispensing Abstral:

- ☐ Check that the indication is in line with the approved indication: management of breakthrough pain in adult patients using opioid therapy for chronic cancer pain.
- ☐ Supply the patient/carer with the Abstral Patient/ Carer Guide which covers the topics of:
    - Cancer and Pain.
    - Abstral. What is it? How do I use it?
    - Risk of misuse.
- ☐ Advise patients of the risks of misuse and signs of overdose and the need for immediate medical assistance.
- ☐ Advise the patient/carer to read the PIL inside the product box or package.
- ☐ Explain the administration instructions, including how to open the child-resistant blister, the different strengths of the product that are available, and the color-coded packaging for each strength.
- ☐ Check that the patient understands the titration steps.
- ☐ Advise the patient/carer on the risks of using more than the recommended dose of the fentanyl tablet.
- ☐ Explain the use of the dose monitoring card.
- ☐ Advise the patient/carer about safe storage and the need to keep the medicine out of reach and sight of children.
- ☐ Advise the patient/carer on the correct product disposal.
- ☐ Remind the patient/carer to ask their doctor or pharmacist if they have any questions or concerns about this medicine, its administration or the associated risks of misuse, abuse and addiction.

Chapter 6: Dose monitoring card

- This dose monitoring card serves to keep a record of how many doses of the tablets patients have taken. Patients need to be reminded that it is not safe to treat more than four breakthrough pain episodes per day.
- Patients need to fill in the correct dose strength in the dose monitoring card.
- Each time patients take the tablet, they need to make sure they, or their carers, fill it in the card with the date and time the medicine was taken.
- Remind patient to always take the card to their doctor's visit.
- If the patients cannot use the dose monitoring card, advise them to contact their doctor or pharmacist for help on how to keep a record of their use of the tablets.

Sample (Can be modified)

Abstral

100/200/300/400/600/800 micrograms (mcg) sublingual tablets

Doses Monitoring Card: Below is an example of the first three doses taken during initial titration.

Dose (Date and Time)	Amount of tablets taken
21.04.2023, 10:00 am	1
21.04.2023, 10:15 am	1
21.04.2023, 4:00 pm	1

Chapter 7: References

1. Brząkała, J., & Leppert, W. (2019). The role of rapid onset fentanyl products in the management of breakthrough pain in cancer patients. Pharmacological reports : PR, 71(3), 438–442.
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6. National Institute on Drug Abuse (NIDA). The science of drug use and addiction: the basics. Last updated July 2018. https://www.druga buse.gov/publications/media-guide/science-drug-use-addiction-basics. Accessed 18 April 2024.
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Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, website: www.hpra.ie.

Adverse events should also be reported to the company: drugsafety.IE@grunenthal.com