Abstral
Prescriber and Pharmacist Guide

paladin

Abstral™
fentanyl citrate sublingual tablets

Introduction

The Abstral Prescriber and Pharmacist Guide is designed to support health-care professionals in the diagnosis of breakthrough cancer pain, and in the initiation, administration and dose titration of Abstral. This document should be referred to in conjunction with important information contained within the Abstral Product Monograph and the Abstral Prescribing Information at the back of this book.

ABSTRAL PRESCRIBER AND PHARMACIST GUIDE

1. BACKGROUND CANCER PAIN
   - Background Cancer Pain Medication

2. BREAKTHROUGH CANCER PAIN
   - Defining Breakthrough Cancer Pain
   - Diagnosing Breakthrough Cancer Pain
   - Managing Breakthrough Cancer Pain

3. AN INTRODUCTION TO ABSTRAL
   - Product Overview
   - Selecting the Abstral Patient
   - Route of Administration

4. TITRATING TO THE CORRECT DOSE
   - Necessity of Titrating
   - Dose Titration
   - Switching Medication
   - Referring Patients

5. IMPORTANT CONSIDERATIONS
   - Adverse Effects

6. PROVIDING GUIDANCE FOR PATIENTS & CAREGIVERS
   - Correct Treatment Administration & Adherence
   - Monitoring Effectiveness
   - Monitoring Side Effects
   - Action in the Event of an Accidental Overdose
   - Safe Keeping, Dispensing & Disposal

1. Background Cancer Pain

- Pain is a common experience among patients with cancer[1]
- One type of pain that occurs is background pain
- This is a persistent pain that occurs for a number of different reasons and can be controlled using specific pain medication

Background Cancer Pain Medication

There are a range of pharmacological and non-pharmacological treatments that can be used to help control background cancer pain. However, the most commonly prescribed forms of cancer pain medication are opioids. These should be prescribed in long-acting form and be taken regularly by patients in order to provide effective relief from background cancer pain.

Options for the Treatment of Uncontrolled Background Cancer Pain

- Increase medication dosing
- Change medication
- Add another medication to existing one
- Explore non-pharmacological treatments

If a patient's persistent background cancer pain is being adequately controlled, but there are still complaints of severe pain, this may indicate breakthrough cancer pain. This is explained in more detail in the next section.

2. Breakthrough Cancer Pain

- Breakthrough cancer pain is characterized by a short episode of severe pain that occurs **in addition** to persistent background pain in cancer patients
- It is a common problem in cancer patients, either as a direct or indirect result of cancer or cancer treatment[1]
- Engaging with patients is a vital part of supporting them in the management of their breakthrough pain, from diagnosis through to treatment and assessment

Defining Breakthrough Cancer Pain

While there is no universally accepted definition for breakthrough cancer pain, the European Association for Palliative Care guidelines quotes a helpful working definition of breakthrough pain taken from *Breakthrough pain: definition, prevalence, and characteristics by Portenoy RK, Hagen NA (Pain* 1990*)*. Breakthrough pain is defined as:

> "[The] transitory exacerbation of pain that occurs in addition to otherwise stable persistent pain."[2]

Types and Triggers of Breakthrough Cancer Pain

- **PREDICTABLE** – incident breakthrough cancer pain[1]
  - Voluntary – triggered by movement such as walking
  - Involuntary – triggered by reflex movement such as coughing
  - Procedural – related to a therapeutic intervention e.g. wound dressing

- **UNPREDICTABLE** – spontaneous breakthrough cancer pain[1]
  – unrelated to any identifiable action

Diagnosing Breakthrough Cancer Pain

Before making a diagnosis of breakthrough cancer pain it is important first to take the following steps:

(i) Assess whether a patient's complaint of pain is due to inadequately controlled background cancer pain

(ii) Optimize background cancer pain medication as necessary (described in **Options for the Treatment of Uncontrolled Background Cancer Pain** in section 1) to help ameliorate the breakthrough cancer pain episodes[1]

If the patient continues to experience severe pain despite receiving effective relief for their background cancer pain, ask them to describe and explain the nature of this pain. You can use the following questions and diagnostic markers to form part of the assessment of breakthrough cancer pain.

Diagnosing Breakthrough Cancer Pain

Questions for the patient	Breakthrough cancer pain diagnostic markers
1. Can you describe the pain?	1. Severe pain in addition to controlled background pain[1]
2. Does the pain coincide with movement, e.g., walking or coughing?	2. Yes (predictable, incident breakthrough cancer pain) No (spontaneous breakthrough cancer pain)
3. Does the pain occur at or around the time that your regular pain medicine is due?	3. Does not coincide with regular pain medication dosing

Managing Breakthrough Cancer Pain

Once diagnosed, it is important to discuss with the patient how they wish to proceed in managing their breakthrough cancer pain. Breakthrough cancer pain can be treated using medications that belong to the opioid class of drugs. There are a variety of formulations and ways of administering these medications, e.g., oral, sublingual, transmucosal, subcutaneous, nasal.

3. An Introduction to Abstral

Product Overview

Abstral is a sublingual fentanyl tablet indicated only for the management of breakthrough pain in patients with cancer, 18 years of age and older, who are already receiving, and who are tolerant to, opioid therapy for their persistent baseline cancer pain.[3]

Abstral should be prescribed and administered in accordance with the approved information contained within the Abstral Product Monograph. Abstral should not be used for any indication other than that for which it is approved.

Selecting the Abstral Patient

In all cases, reference should be made to the relevant sections of the Abstral Product Monograph to ensure appropriate selection of patients. Abstral should only be administered to adult patients who are considered tolerant to their opioid therapy for persistent baseline cancer pain. Patients can be considered opioid tolerant if they take at least 60 mg oral morphine per day, or 25 micrograms transdermal fentanyl per hour, 30 mg oral oxycodone per day, 8 mg oral hydromorphone per day, 25 mg oral oxymorphone per day, or an equianalgesic dose of another opioid for a week or longer. Abstral is contraindicated for use in opioid non-tolerant patients including those using opioids intermittently, on an as needed basis. Fentanyl products which are designed to manage breakthrough pain, including Abstral, should not be used in patients who are receiving partial opioid agonists such as buprenorphine or agents with some opioid effects such as tramadol, as the safety of their concomitant use has not been established. Abstral is contraindicated in the management of acute or postoperative pain, including headache/migraine, dental pain, or use in the emergency room.

In selecting suitable patients for Abstral it is also important to assess whether they have demonstrated an addiction, or may be at risk of addiction, to their background pain medication. In turn, patients should be informed about the risk of addiction (other side effects are discussed in a later section) associated with the opioid class of treatments, including Abstral, in order to engage them fully in the selection process. It is also important to assess whether the patient might be at risk from accidental overdose or intentional suicide.

Route of Administration

Patients selected to use Abstral for the management of their breakthrough cancer pain should be given the following important information about administering their medication:

1. Take tablet at onset of breakthrough cancer pain episode
2. Place tablet directly under the tongue at the deepest part
3. Do not swallow, chew or suck the tablet
4. Allow the tablet to dissolve
5. Do not consume anything until the tablet has completely dissolved

4. Titrating to the correct dose

Necessity of Titrating

Patients using Abstral must be individually titrated until they achieve the optimal dose.

Dose titration

The object of dose titration is to identify an optimal maintenance dose for ongoing treatment of breakthrough pain episodes. This optimal dose should provide adequate analgesia with an acceptable level of adverse reactions.

The optimal dose of Abstral will be determined by upward titration, on an individual patient basis. Several doses are available for use during the dose titration phase. **The initial dose of Abstral used must be 100 micrograms,** titrating upwards as necessary through the range of available dosage strengths.

Patients should be carefully monitored until an optimal dose is reached.

Direct switching from other fentanyl containing products to Abstral must not occur without re-titration because of differences in pharmacokinetic profiles, different absorption profiles and individual variability. If patients are switched from another fentanyl containing product, a new dose titration with Abstral is required and must be started on **no greater than 100 micrograms of Abstral.**

When prescribing, do not switch patients from any other fentanyl product to Abstral as Abstral is not equivalent on a mcg per mcg basis with any other fentanyl product.

Start all patients with a single 100 mcg tablet.

- If adequate analgesia is obtained within 30 minutes of administration of the 100 mcg tablet, continue to treat subsequent episodes of breakthrough pain with this dose.
- Patients must wait at least 2 hours before treating another episode of breakthrough pain with ABSTRAL.

Subsequent Dose/Titration

The following dose titration regimen is recommended, however in all cases the physician should take into account the clinical need of the individual patient, age, co-existing illness or medical condition, and concomitant medications.

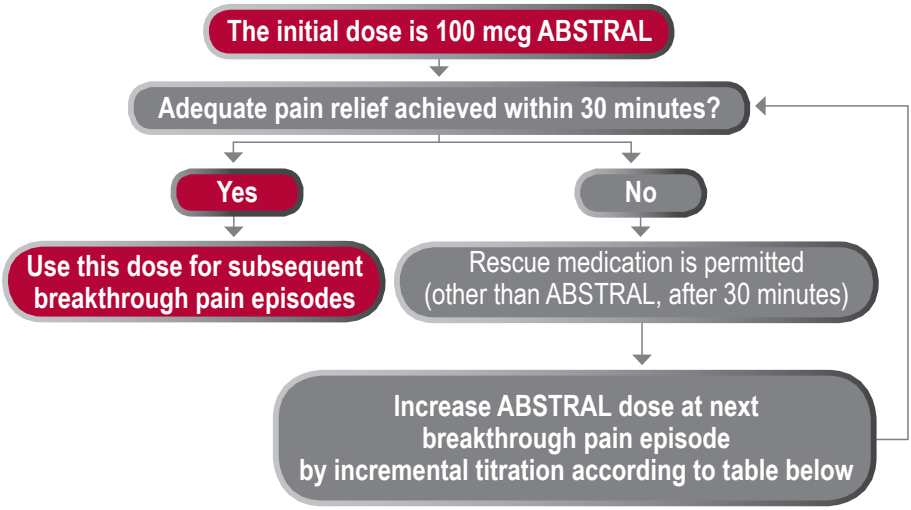
If adequate analgesia was not obtained with the first 100 mcg dose, continue dose escalation in a stepwise manner over consecutive breakthrough episodes until adequate analgesia with tolerable side effects is achieved. Increase the dose by 100 mcg multiples up to 400 mcg as needed. If adequate analgesia is not obtained with a 400 mcg dose, the next titration step is 600 mcg. If adequate analgesia is not obtained with a 600 mcg dose, the next titration step is 800 mcg. During titration, patients can be instructed to use multiples of 100 mcg tablets and/or 200 mcg tablets for any single dose. Instruct patients not to use more than 4 tablets at one time. **Doses above 800 mcg Abstral should not be used.**

Once adequate pain relief *is achieved* with a dose between 100 and 800 mcg Abstral, the patient should get a prescription for Abstral of the dose determined by titration (i.e. 100, 200, 300, 400, 600 or 800 mcg) to treat subsequent episodes.

Single doses should be separated by at least 2 hours. Abstral should only be used once per breakthrough cancer pain episode, i.e. Abstral should not be redosed within an episode.

During any episode of breakthrough cancer pain, if adequate pain relief is *not achieved* after Abstral, the patient may use a rescue medication (other than Abstral, after 30 minutes) as directed by their healthcare provider.

ABSTRAL TITRATION PROCESS



ABSTRAL dosing for a subsequent episode should be separated by at least 2 hours

Abstral Dose	Using
200 mcg	2 x 100 mcg tablets, or 1 x 200 mcg tablet
300 mcg	3 x 100 mcg tablets, or 1 x 300 mcg tablet
400 mcg	4 x 100 mcg tablets, or 2 x 200 mcg tablets, or 1 x 400 mcg tablet
600 mcg	3 x 200 mcg tablets, or 1 x 600 mcg tablet
800 mcg	4 x 200 mcg tablets, or 1 x 800 mcg tablet

In order to minimise the risk of opioid–related adverse reactions and to identify the appropriate dose, it is imperative that patients be supervised closely by health professionals during the titration process.

Maintenance therapy:

Once an appropriate dose for pain management has been established, instruct patients to use only one ABSTRAL tablet of the appropriate strength per dose. Maintain patients on this dose.

If adequate analgesia is not obtained after use of ABSTRAL, the patient may use rescue medication other than Abstral (after 30 minutes) as directed by their health care provider. No more than one dose of ABSTRAL may be used to treat an episode of breakthrough pain.

Patients must wait at least 2 hours before treating another episode of breakthrough pain with ABSTRAL.

Dose Re-Adjustment

If the response (analgesia or adverse reactions) to the titrated ABSTRAL dose markedly changes, an adjustment of dose may be necessary to ensure that an optimal dose is maintained.

During maintenance treatment, if the prescribed dose no longer adequately manages the breakthrough cancer pain episode for several consecutive episodes, increase the dose of Abstral as described in Dose Titration. Once a successful dose is determined, each episode is treated with a single tablet. Use of Abstral should be limited to four episodes of breakthrough pain per day, and administration of Abstral must be separated by at least 2 hours.

If more than four episodes of breakthrough pain are experienced per day, then the dose of the long-acting opioid used for persistent underlying cancer pain should be re-evaluated. If the long-acting opioid or dose of long-acting opioid is changed, then the ABSTRAL dose should be re-evaluated and re-titrated as necessary to ensure the patient is on an optimal dose.

It is imperative that any dose re-titration of any opiate analgesic is monitored carefully by a health professional.

Switching Medication

1. Switching to Abstral from another opioid for breakthrough cancer pain
    - Different treatments are not equivalent,[3] so **always start titration of Abstral with a dose of 100 micrograms**
    - Refer to Abstral Product Monograph for further important information about initiating treatment with Abstral

2. Switching from Abstral to another opioid for breakthrough cancer pain
    - First assess whether the patient has been titrated to the correct dose (and re-titrate as necessary) before considering a switch of breakthrough cancer pain medication

3. Stopping Abstral altogether
    - For patients no longer requiring any opioid therapy, the Abstral dose should be taken into consideration before a gradual downward titration of opioids, to minimise possible withdrawal effects, such as anxiety, tremor, sweating, paleness, nausea and vomiting.
    - In patients who continue to take their chronic opioid therapy for persistent pain, but no longer require treatment for breakthrough pain, Abstral therapy may usually be discontinued immediately.

Referring Patients

Patients who do not experience adequate pain relief for their breakthrough cancer pain episodes despite titration should first be reassessed so that their pain management strategy can be reviewed and modified as appropriate. If, after continued monitoring, patients continue to receive inadequate pain relief they should be referred to a pain or palliative care specialist with an interest in breakthrough cancer pain.

5. Important Considerations

Treatment with opioid-based formulations can be associated with adverse effects. However, the risk of serious adverse effects is reduced if these medications are used under the following conditions:

- In the right patient (as outlined in the section entitled 'Selecting the Abstral Patient')
- Within the parameters of the titration schedule (refer to Section 4 'Titrating to the Correct Dose')
- In accordance with the approved product indications and information (refer to Abstral Product Monograph)

Adverse Effects

The most serious adverse reactions associated with all opioids including Abstral are respiratory depression (potentially leading to apnea or respiratory arrest), circulatory depression, hypotension and shock.[3] Prescribers should therefore monitor for early evidence of respiratory depression throughout the titration and treatment process. Other very commonly reported adverse reactions include nausea, headache, constipation and somnolence/fatigue.[3] Further information on adverse reactions can be found in the Abstral Product Monograph.

To avoid risk of addiction or accidental overdosing, patients who have reached their optimal dose of Abstral following titration should be limited to a maximum of four Abstral doses per day.[3]

6. Providing Guidance for Patients and Caregivers

In addition to referring patients and caregivers to the Abstral Patient Information leaflet, and ensuring they are aware of and understand the information contained within that, patients receiving Abstral or their caregivers should be given the following instructions by the physician:

1. Patients should be informed that accidental use by individuals (including children) other than the patient for whom it was originally prescribed, may lead to severe, even fatal, consequences.

2. Patients should be advised that ABSTRAL contains fentanyl, an opioid pain medicine similar to morphine, hydromorphone, methadone, oxycodone and oxymorphone.

3. Patients should be advised that ABSTRAL should be taken as directed by the physician and the dose of ABSTRAL should NEVER be adjusted without the prescribing physician's instruction.

    a. The dose of ABSTRAL will be adjusted until the physician finds the right dose for the patient that achieves adequate analgesia with tolerable side effects.
    b. ABSTRAL should be used only one time for each episode of breakthrough cancer pain. Doses of Abstral should be separated by at least 2 hours.
    c. ABSTRAL should not be used for more than four episodes of breakthrough cancer pain in one day. If the patient has more than four episodes of breakthrough pain each day, the dose of the opioid pain medicine for the persistent baseline cancer pain may need to be changed.
    d. Once the right dose for the patient has been found, the patient should not change the dose of ABSTRAL unless directed by their physician.

4. ABSTRAL comes in individually sealed child-resistant blister packages. Patients should be advised not to open the package until ready to use. Once opened, the entire ABSTRAL sublingual tablet should be used right away. Instructions for opening the blister package are included in the Consumer Information.

5. Patients should be advised not to eat or drink anything until the ABSTRAL sublingual tablet is completely dissolved under their tongue and they can no longer feel it in their mouth.

6. Patients should be advised to never chew, suck or swallow this medication, as this will decrease its activity.

7. Patients should be advised that ABSTRAL may impair mental and/or physical ability required for the performance of potentially hazardous tasks (e.g., driving, operating machinery).

8. Patients should be advised that ABSTRAL should not be combined with alcohol or other CNS depressants (e.g. sleep medications, tranquilizers) because dangerous additive effects may occur, resulting in serious injury or death.

9. Patients should be advised to consult their physician or pharmacist if other medications are being or will be used with ABSTRAL.

10. Patients should be advised that ABSTRAL contains fentanyl, a drug with high potential for abuse. Patients, family members and caregivers should be advised to protect ABSTRAL from theft or misuse in the work or home environment.

11. Patients should be instructed to keep ABSTRAL in a secure place out of the reach of children due to the high risk of fatal respiratory depression.

12. When ABSTRAL is no longer needed, the unused ABSTRAL sublingual tablets should be removed from their blister units and dropped into the toilet. The toilet should be flushed after all tablets are dropped in it. Blister packages and cartons should not be dropped in the toilet. ABSTRAL rapidly and completely disintegrates on administration. If for any reason a tablet is removed from the mouth before it has completely disintegrated, it should be disposed of in accordance with the instructions provided above.

13. Patients should be informed that accidental exposure or misuse may lead to death or other serious medical problems.

14. Patients should be advised to report episodes of uncontrolled breakthrough pain and adverse experiences occurring during therapy. Individualization of dosage is essential to make optimal use of this medication.

15. Patients should be advised of the most common adverse reactions that may occur while taking ABSTRAL: nausea, constipation, somnolence and headache.

16. Patients should be advised that ABSTRAL should never be given to any one other than the individual for whom it was prescribed.

17. Women of childbearing potential who become or are planning to become pregnant should be advised to consult a physician prior to initiating or continuing therapy with ABSTRAL. Women who are breast-feeding or pregnant should not use ABSTRAL.

Monitoring Effectiveness

- The patient should continually monitor the effectiveness of Abstral during the titration phase in providing relief for their breakthrough cancer pain and report the following back to their healthcare professional:
  - Did they achieve pain relief at the prescribed dose?
  - How long did it take to achieve pain relief?

Monitoring Side Effects

- The patient and caregiver should continually monitor for any adverse reactions and report these to their healthcare professional at their next visit, or immediately if serious

Action in the Event of an Accidental Overdose

- Extreme drowsiness and shallow breathing may indicate that the patient has exceeded their agreed optimal dosage. Patients and caregivers should take the following action in the event of an overdose:
  - Seek emergency medical help by contacting the regional poison control centre or by calling 911 immediately
  - Remove the tablet or any parts of it still remaining in the mouth
  - Alert their caregiver to what is happening
  - The caregiver should try to keep the patient conscious

Safe Keeping, Dispensing & Disposal

- Tablets must be stored in a locked storage space out of the reach of children to avoid risk of death
- Tablets must be kept in the original blister pack to protect them from moisture[3]
- Any unused tablets should be returned to the pharmacy and disposed of in accordance with national and local requirements[3] or,
- Unopened Abstral blisters can also be disposed by flushing them down the toilet as follows:
    1. Remove the Abstral tablet from its blister package.
    2. Drop the Abstral tablet into the toilet.
    3. Repeat steps 1 and 2 for each Abstral blister. Flush the toilet after all unneeded blisters have been put into the toilet.

    Do not flush the Abstral blister packages or cartons down the toilet.

Further Information/Advice

For further information please contact the sponsor, Paladin Labs Inc., at 1-888-550-6060.