Prescriber's guide for prescribing EFFENTORA® (fentanyl) buccal tablets

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions *via* HPRA Pharmacovigilance, www.hpra.ie.

Adverse events may also be reported to Teva Pharmaceuticals Ireland *via* email to medinfo@tevauk.com or *via* phone on +44 (0) 207 540 7117.

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INTRODUCTION

This guide is designed to help you understand the proper prescribing of EFFENTORA® (fentanyl) buccal tablets for patients with breakthrough cancer pain.

Please read this guide carefully before prescribing EFFENTORA® and keep it for future reference. This guide should be read in conjunction with the EFFENTORA® Summary of Product Characteristics. Critically, select patients based upon labelled information and use the Prescriber's Checklist provided.

Encourage patients to talk about all medication-related issues and inform them that you will need to review their Effentora medication on a periodic basis.

EFFENTORA® buccal tablets may only be prescribed by physicians who are experienced, knowledgeable, and qualified in the use of opioid therapy in cancer patients. Special care should be taken when patients transition from hospital to home-based care.

The following materials are also available:

- A Patient/Carer Guide to the safe use of EFFENTORA® buccal tablets
- A Pharmacist's Guide for dispensing EFFENTORA® buccal tablets

This Physician's Guide (and the other materials listed above) can be viewed or downloaded from the Health Products Regulatory Authority Website at: https://www.hpra.ie (enter 'EFFENTORA' in Find a Medicines Search Area. Click *'EdM' under the 'Documents' column for the relevant EFFENTORA product).

*For a full list of medicines that have Educational Materials use the advanced search option and click on 'Only Medicines with Educational Materials'.

Reporting Side Effects

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WHAT IS EFFENTORA®?

EFFENTORA® for the treatment of cancer breakthrough pain

EFFENTORA® is a transmucosal form of fentanyl, an opioid analgesic. EFFENTORA® is indicated for management of breakthrough pain in patients already receiving maintenance opioid therapy for chronic cancer pain.[1]

EFFENTORA® is suitable for adult patients with breakthrough pain who have been receiving maintenance opioid therapy for at least a week, consisting of:

- At least 60 mg of oral morphine daily, **or**
- At least 25 mg 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.[1]

Off-label use would include the following prescriptions:

- All indications except breakthrough pain, including any other pain therapy.
- Patients who do not already receive maintenance opioid therapy.
- More frequent dosing than recommended.
- Patients under 18 years of age.

What are the risks associated with off-label use of EFFENTORA®?

Importance of preventing off-label use

The use of EFFENTORA® outside the approved indication is considered off-label use. **Please note that different fentanyl formulations have different indications.** Make sure that you are familiar with the specific indication for EFFENTORA® before prescribing. The use of EFFENTORA® for indications other than those approved increases the risk of misuse, abuse, medication error, overdose, addiction and death.

HOW IS EFFENTORA® USED?

Correct use of EFFENTORA®.

Important: The treatment of cancer pain must be initiated by, and remain under the supervision of, a physician who has sufficient knowledge and experience in the management of opioid therapy in cancer patients.

As a prescriber, you must ensure your patient is appropriate for treatment with EFFENTORA® and that they understand how to use the medication. Specifically:

1 buccal tablet	One tablet of EFFENTORA® per breakthrough pain episode, with the option of taking a second EFFENTORA® tablet of the same strength after at least 30 minutes, during the titration period, if breakthrough pain is not relieved.
4 Hours	It is important to explain to the patient that there should be at least 4 hours between each treatment of a breakthrough pain episode, highlighting the risks associated with more frequent use.[1]
No more than 4 tablets	Dose readjustment of the background opioid therapy may be required if patients consistently present with more than four breakthrough pain episodes per 24 hours.[1]

Medication errors are also particularly important to avoid when prescribing EFFENTORA®.

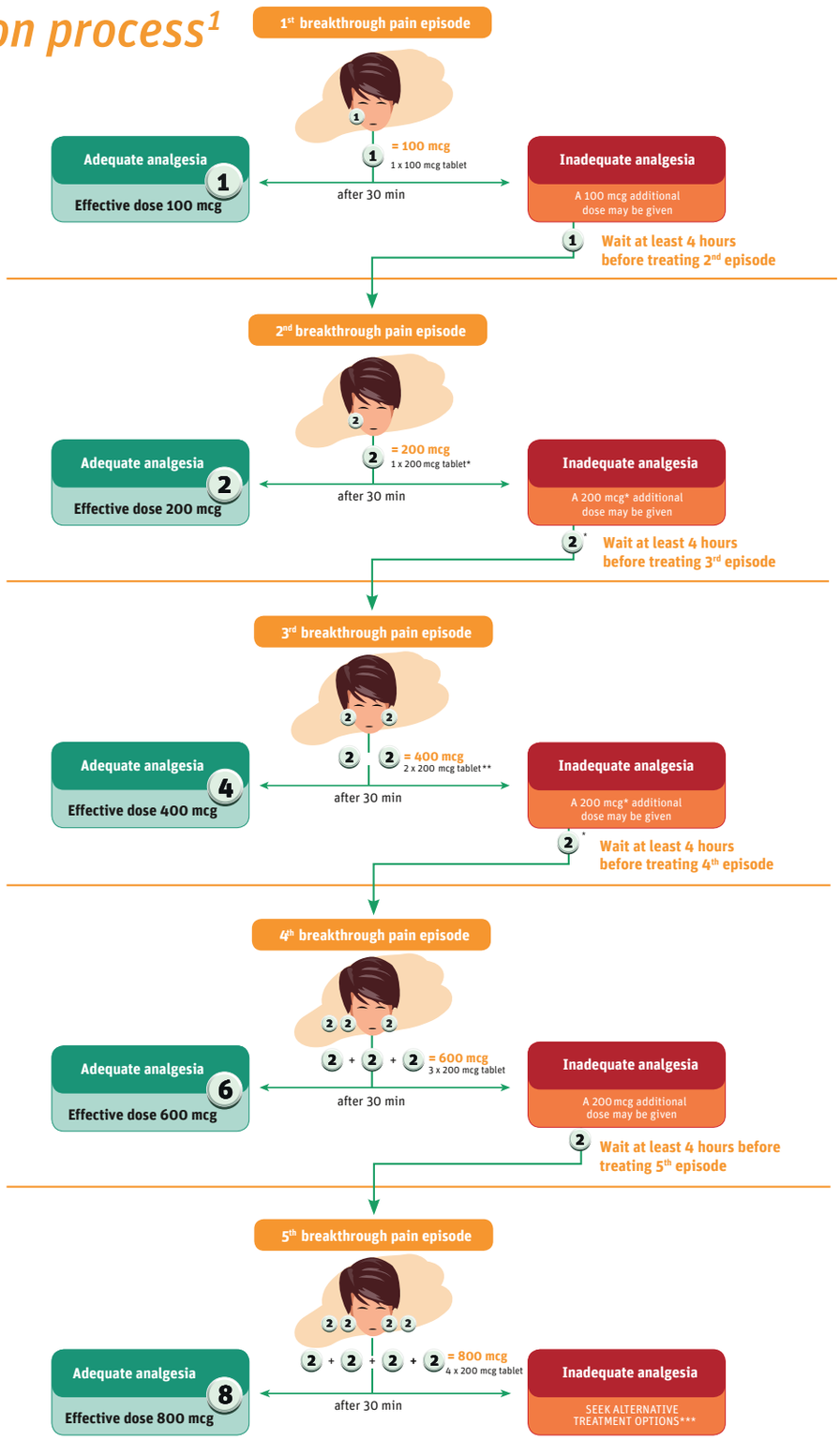
In order to minimise the risk of medication errors, all EFFENTORA® labels are color-coded differently for each of the strengths of action as follows:

- 100 mcg – Blue
- 200 mcg - Orange
- 400 mcg – Green
- 600 mcg – Purple

Dosage and titration

- ➔ Do not compare EFFENTORA® buccal tablets strengths with those of other fentanyl-containing products. Dose only according to the SmPC.
- ➔ To optimise breakthrough pain treatment, please make use of the titration tool below with stepwise titration through the appropriate doses until adequate analgesia is achieved.
- ➔ The initial dose of EFFENTORA® should be 100 micrograms, titrating upwards as necessary through the range of available tablet strengths (200 mcg, 400 mcg & 600 mcg).
- ➔ During titration, if adequate analgesia is not obtained within 30 minutes after the start of administration of a single tablet EFFENTORA®, a second EFFENTORA® tablet of the same strength may be used.
- ➔ If treatment of a breakthrough pain episode requires more than one tablet, an increase in dose to the next higher available strength should be considered to treat the next breakthrough pain episode.

Titration process[1]



* 2x 100 mcg can be used here as an alternative to 1x 200mcg
** 4x 100 mcg can be used here as an alternative to 2x 200mcg
*** Doses above 800 mcg EFFENTORA® have not been evaluated in clinical trials

Maintenance therapy

- Once an effective dose has been established during titration patients should continue to take this dose as a single tablet of that given strength.
- Breakthrough pain episodes may vary in intensity and the required EFFENTORA® dose might increase over time due to progression of the underlying cancer disease. In these cases, a second tablet of the same strength may be used. If a second tablet of EFFENTORA® was required for several consecutive times, the usual maintenance dose is to be readjusted.
- Patients should wait at least 4 hours before treating another breakthrough pain episode with EFFENTORA® during maintenance therapy.[1]

Dose re-adjustment

- The maintenance dose of EFFENTORA® should be increased when a patient requires more than one tablet per breakthrough pain episode for several consecutive breakthrough pain episodes.
- Dose readjustment of the background opioid therapy may be required if a patient consistently presents with more than four breakthrough pain episodes per 24 hours.
- In absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered.[1]

Discontinuation of therapy

- EFFENTORA® should be discontinued immediately if the patient no longer experiences breakthrough pain episodes. The treatment for persistent background pain should be kept as prescribed.
- If discontinuation of all opioid therapy is required, the patient must be closely followed by the doctor in order to manage the risk of abrupt withdrawal effects.

Overdose and Unintentional exposure

Unintentional exposure to EFFENTORA® is considered a medical emergency and a potentially life-threatening event.

If a child is accidentally exposed to EFFENTORA®, it is considered a medical emergency and may, without professional treatment, cause death.

Make sure that both yourself and colleagues likely to come into contact with patients on fentanyl therapy are aware of the signs of fentanyl overdose/toxicity and the appropriate protocol for its management. Ensure medications such as naloxone are readily accessible and staff are trained in their use.[1]

Please ensure that your patients and their carers are aware of the signs of fentanyl overdose/toxicity and understand the need to seek urgent medical attention.

Patients should be monitored for signs that they are not using EFFENTORA® as prescribed and should be made aware of the serious risks associated with misuse, abuse, overdose, and addiction.[1]

Safety, Storage, and disposal

- ➔ EFFENTORA® should only be handled by the patient or their carers. Effentora® should never be shared with friends and family members. Please advise the patient never to allow anyone else to handle or use the product.
- ➔ Store EFFENTORA® in the original package in order to protect from moisture. The tablet should not be stored once removed from the blister package as the tablet integrity cannot be guaranteed and a risk of accidental exposure to a tablet can occur.
- ➔ Please draw the attention of patients and their carers to the danger if children are exposed to EFFENTORA®.
- ➔ Please ensure that patients understand that in order to prevent theft, diversion (i.e., misuse for illegal purposes) or other misuse, fentanyl should be stored in a suitably secure place. Fentanyl, the active ingredient in EFFENTORA® is a target for people who abuse narcotic medicines or other street drugs, and therefore storage instructions must be closely followed.
- ➔ Information about proper disposal: Patients and carers must be advised to dispose of any unopened tablets remaining from a prescription as soon as they are no longer needed. Any used or unused but no longer required medicinal product or waste material should be disposed of in accordance with local requirements.

RISKS ASSOCIATED WITH "OPIOID USE DISORDER" (OUD)

How to recognise abuse-related side effects and OUD

The following considerations may help you identify patients who have developed OUD. In patients where OUD is strongly suspected, a consultation with an addiction specialist should be considered.

1. **Pay particular attention to patients who have an increased risk of OUD before and during therapy.**
   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 and in patients with a personal history of other mental health problems (e.g. depression, anxiety and personality disorders).

2. **Carefully monitor prescription requests and recognise the symptoms of addiction and withdrawal.**
   Patients must be observed for signs of drug-seeking behavior (e.g. desire for early follow-up prescriptions). This includes monitoring concomitant use of other opioids and other psychoactive drugs (such as benzodiazepines).

   Withdrawal symptoms are one of the criteria associated with OUD. The context of withdrawal symptoms must be accurately assessed. A patient suffering from withdrawal symptoms may complain of nausea and vomiting, anxiety, insomnia, heat and cold flushes, excessive sweating, muscle cramps, watery discharge from the eyes and nose, and/or diarrhoea.[3]

   Some OUD criteria may be difficult to distinguish from behaviors that are frequently observed in cancer patients receiving opioid pain therapy. Some classical opioid withdrawal symptoms are also "normal" side effects that have been reported after the use of EFFENTORA® (e.g. flushing, insomnia, sweating).[1]

WHAT TO DO IF YOU SUSPECT THAT YOUR PATIENT IS SUFFERING FROM OUD?

A patient suffering from OUD can still receive cancer treatment and have their pain relieved. For patients with signs and symptoms of OUD, consultation with an addiction specialist should be considered. Several treatment options for patients with OUD can be considered and tailored to individual needs.[5]

A combination of behavioral and pharmacotherapeutic approaches (so-called drug-assisted therapy) has proven to be the most successful in helping patients overcome OUD.[2] If you do not feel qualified to offer effective behavioral and/or pharmacotherapeutic treatment for OUD, please refer your patient to an appropriately qualified specialist.

Report any known off-label use, misuse, abuse, addiction, and overdose via:

HPRA Pharmacovigilance, www.hpra.ie.

Adverse events should also be reported to Teva Pharmaceuticals Ireland *via* email at medinfo@tevauk.com or *via* phone on +44 (0) 207 540 7117.

OTHER IMPORTANT POINTS ABOUT EFFENTORA®

Please counsel the patient on the following points from the EFFENTORA® SmPC:

1. **The following adverse reactions have been reported with EFFENTORA® and/or other fentanyl-containing compounds during clinical studies and post-marketing experience:** dyspnoea, drug dependence (addiction), drug abuse, neonatal withdrawal syndrome, loss of consciousness. (See SmPC Section 4.8.)

2. **Hyperalgesia:** As with other opioids, in case of insufficient pain control in response to an increased dose of fentanyl, the possibility of opioid-induced hyperalgesia should be considered. Fentanyl dose reduction or discontinuation of fentanyl treatment or treatment review may be indicated. (See SmPC Section 4.2 and 4.4.)

3. **Concomitant use of medicinal products containing sodium oxybate and fentanyl is contraindicated.** (See SmPC Sections 4.3 and 4.5.)

4. **Co-administration of fentanyl with other central nervous system depressants**, including other opioids, sedatives or hypnotics, (including benzodiazepines), general anaesthetics, phenothiazines, tranquillisers, skeletal muscle relaxants, sedating antihistamines, gabapentinoids (gabapentin and pregabalin) and alcohol can produce additive depressant effects, which may result in a fatal outcome. (See SmPC Section 4.5.)

5. **Pregnancy:** There is no adequate data from the use of fentanyl in pregnant women. Studies in animals have shown reproductive toxicity (see SmPC Section 5.3). The potential risk for humans is unknown. EFFENTORA® should not be used in pregnancy unless clearly necessary. (See SmPC Section 4.6.)

CHECKLIST FOR PRESCRIBING EFFENTORA®

- [ ] Ensure that all the criteria of the approved indication are fulfilled. EFFENTORA® should only be prescribed for breakthrough pain in adults who are already receiving opioid maintenance therapy for background cancer pain
- [ ] Give the patient and/or carer instructions on how to use the EFFENTORA®
- [ ] Make sure the patient/carer reads the Package Leaflet inside the EFFENTORA® package
- [ ] Supply the patient/carer with the EFFENTORA® patient/carer guide and explain the use of the dose monitoring card
- [ ] Instruct the patient/carer on how to open the blister packaging as described in the Patient/Carer Guide
- [ ] Explain the risks of using more than the recommended amount of EFFENTORA®
- [ ] Advise the patient/carer of signs of fentanyl overdose and the need for immediate medical assistance
- [ ] Explain secure storage and the need to keep EFFENTORA® out of the reach and sight of children
- [ ] Explain the correct process for disposal of EFFENTORA®
- [ ] Encourage the patient/carer to discuss their maintenance opioid therapy, breakthrough pain, and their use of opioids with you
- [ ] Remind the patient and/or caregiver that they should ask their doctor if they have any questions or concerns about how to use EFFENTORA® or about the associated risks of misuse and abuse.

NOTES

Teva Pharmaceuticals Ireland.
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