

Effentora® therapeutic indication

Effentora® is indicated for the treatment of Breakthrough Cancer Pain (BTcP) in adults who are already receiving maintenance opioid therapy* for chronic cancer pain. BTcP is a transitory exacerbation of pain that occurs on a background of otherwise controlled persistent pain¹.

Before initiating Effentora® treatment for the first time in a new BTcP patient, ensure that:

	YES	NO
1/ The patient is suffering from cancer pain	✓	Not indicated
2/ The patient has been receiving around-the-clock (ATC) medication for persistent pain	✓	Not indicated
→ For at least 1 week	✓	Not indicated
→ *ATC therapy:		
<ul style="list-style-type: none"> oral morphine ≥ 60 mg/day, or transdermal fentanyl ≥ 25 µg/hour, or oxycodone ≥ 30 mg/day, or oral hydromorphone ≥ 8 mg/day, or an equianalgesic dose of another opioid 		
3/ The patient is experiencing transitory exacerbations of pain (i.e. BTcP)	✓	Not indicated
4/ The patient is experiencing a maximum of 4 BTcP episodes/day	✓	Re-assess and adapt ATC therapy
5/ The patient has no contraindications to the use of Effentora	✓	Re-assess
<ul style="list-style-type: none"> Hypersensitivity to the active substance or to any of the excipients Severe respiratory depression or severe obstructive lung conditions 		

Effentora® can be prescribed to your patients when all answers are positive

UK PRESCRIBING INFORMATION:

Effentora® 100 micrograms, 200 micrograms, 400 micrograms, 600 micrograms, 800 micrograms fentanyl buccal tablet (fentanyl). Please refer to Summary of Product Characteristics (SmPC) before prescribing.

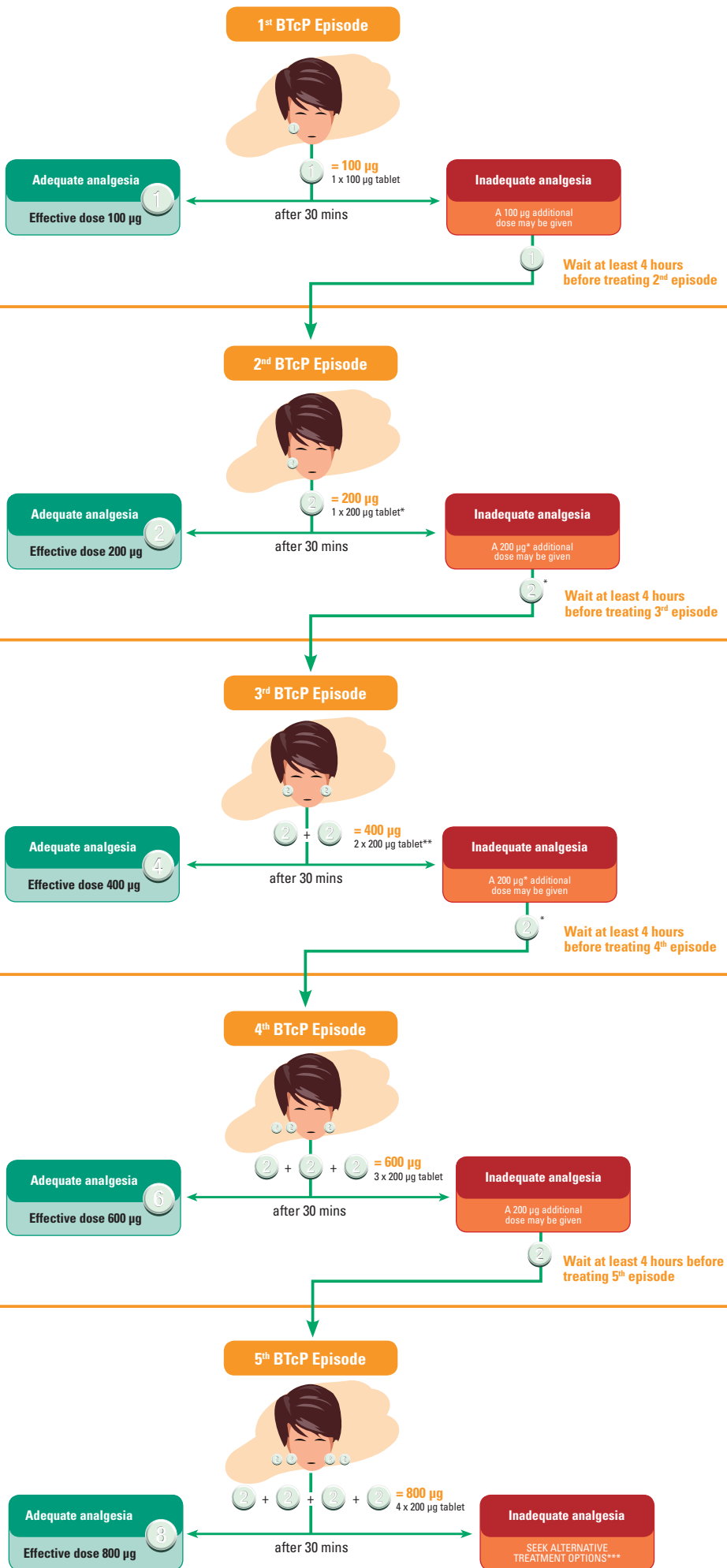
Presentation: Effentora buccal tablet containing 100 micrograms, 200 micrograms, 400 micrograms, 600 micrograms and 800 micrograms fentanyl. **Indications:** Treatment of breakthrough pain (BTP) in adults with cancer who are already receiving maintenance opioid therapy for chronic cancer pain. Patients 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 of 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:** See SmPC for full information. **Method:** Patient should remove the tablet from the blister unit and immediately place the entire tablet in the upper portion of the buccal cavity (above an upper rear molar between the cheek and gum) and retain for a period sufficient to allow disintegration of the tablet which usually takes approximately 14-25 minutes. The Effentora tablet should not be sucked, chewed or swallowed, as this will result in lower plasma concentrations. **Adult:** Treatment should be individually titrated by and remain under the guidance of a physician experienced in the management of opioid therapy in cancer patients. The Physician should keep in mind the potential abuse of fentanyl. Effentora should be individually titrated to an "effective" dose that provides adequate analgesia and minimises undesirable effects. Once an effective dose has been established, the patient should continue to take this dose as a single tablet of that given strength. Patients should wait at least 4 hours before treating another BTP episode with Effentora during maintenance therapy. **Children and adolescents:** Effentora is not recommended for use in patients below 18 years of age due to a lack of data on safety and efficacy. **Elderly:** In clinical studies patients older than 65 years tended to titrate to a lower effective dose than younger patients. **Hepatic and renal impairment:** Effentora should be administered with caution to patients with moderate to severe hepatic or renal impairment. Please see section 4.4 of SmPC for more information. **Xerostomia:** Patients experiencing xerostomia are advised to drink water to moisten the buccal cavity prior to administration of Effentora. If this recommendation does not result in an adequate disintegration, then a switch of therapy may be advised. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. Patients not on maintenance opioid therapy (see SmPC section 4.1) as there is an increased risk of respiratory depression. Severe respiratory depression or severe obstructive lung conditions. **Warnings and Precautions:** Patients and their carers must be instructed to keep all Effentora tablets out of the reach and sight of children. To minimise the risks of opioid-related undesirable effects it is imperative that patients be monitored closely during

the titration process and that the maintenance opioid therapy has been stabilised before Effentora therapy begins. As with all opioids, there is a risk of clinically significant respiratory depression associated with the use of fentanyl. Dosage increase should be done with caution. Particular caution should be used when titrating patients with chronic obstructive pulmonary disease or other medical conditions predisposing them to respiratory depression. Extreme caution should be exercised in patients who may be particularly susceptible to the intracranial effects of CO₂ retention, such as those with evidence of increased intracranial pressure or impaired consciousness. Effentora should be used with caution in patients with pre-existing bradyarrhythmias, with hepatic or renal impairment. Careful consideration should be given to patients with hypovolaemia and hypotension. **Interactions:** Fentanyl is metabolised mainly via the human cytochrome P450 3A4 isoenzyme system (CYP3A4), therefore potential interactions may occur when Effentora is given concurrently with agents that affect CYP3A4 activity. Coadministration with agents that induce 3A4 activity may reduce the efficacy of Effentora. The concomitant use of Effentora with strong CYP3A4 inhibitors (e.g., ritonavir, ketoconazole, itraconazole, troleanandomycin, clarithromycin, and neflavinir) or moderate CYP3A4 inhibitors (e.g., amprenavir, aprepitant, diltiazem, erythromycin, fluconazole, fosamprenavir, grapefruit juice, and verapamil) may result in increased fentanyl plasma concentrations, potentially causing serious adverse drug reactions including fatal respiratory depression and patients should be carefully monitored for an extended period of time. The concomitant use of other central nervous system depressants, including other opioids, sedatives or hypnotics may produce additive depressant effects (please refer the SmPC for full list). Effentora is not recommended for use in patients who have received Monoamine Oxidase Inhibitors (MAOIs) within 14 days. The concomitant use of partial opioid agonists/antagonists (e.g. buprenorphine, nalbuphine, pentazocine) is not recommended as they partially antagonise the analgesic effect of fentanyl and may induce withdrawal symptoms in opioid dependant patients. **Pregnancy and lactation:** Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk for humans is unknown and Effentora should not be used in pregnancy unless clearly necessary. Following prolonged treatment, fentanyl may cause withdrawal in the new-born infant. It is advised not to use fentanyl during labour and delivery (including caesarean section) because fentanyl passes through the placenta and may cause respiratory depression in the foetus. If Effentora is administered, an antidote for the child should be readily available. Fentanyl passes into breast milk and may cause sedation and respiratory depression in the breast-fed child and

should only be used if the benefits outweigh the potential risks for both mother and child. Effects on ability to drive and use machines: Opioid analgesics impair the mental and/or physical ability required for the performance of potentially dangerous tasks (e.g., driving a car or operating machinery). If affected patients should be advised not to drive or operate machinery while taking Effentora and not to drive or operate machinery until they know how they react. **Undesirable effects:** Please see the SmPC for complete list of adverse effects. Typical opioid undesirable effects are to be expected with Effentora. However, the most serious adverse reactions are respiratory depression (potentially leading to apnoea or respiratory arrest), circulatory depression, hypotension and shock and all patients should be closely monitored for these. Application site reactions including pain, ulcer, irritation, paraesthesia, anaesthesia, erythema, oedema, swelling and vesicles. Very common effects (>10%) – nausea and dizziness. Common (>1% - 10%) – Dysgeusia, Somnolence, Lethargy, Headache, Tremor, Sedation, Vomiting, Constipation, Stomatitis, Dry mouth, Diarrhoea, Pruritus, Hyperhidrosis, Fatigue, Disorientation and Euphoric mood. **Overdose:** See SmPC for full information. **Immediate management of opioid overdose** includes removal of the Effentora, ensuring a patent airway, physical and verbal stimulation, assessment of the level of consciousness, ventilatory and circulatory assessment, and ventilatory support if necessary. **Basic UK NHS Costs:** Effentora all strengths x4 £20.56. **Legal Category:** CD (Sch2), POM. **Marketing Authorisation Numbers:** EU/1/08/441/001-010. **Marketing Authorisation Holder:** Cephalon Europe 5 rue Charles Martigny F-94700 Maisons-Alfort France. **Date of SmPC:** April 2008. Information, including SmPC, is available from Cephalon UK Limited, 1 Albany Place, Hyde Way, Welwyn Garden City, Hertfordshire, AL7 3BT Medical Information ukmedinfo@cephalon.com. Free phone: UK 0800 783 4869

Adverse events should be reported. Reporting forms and information can be found at www.yellowcard.gov.uk. Adverse events should also be reported to Cephalon UK Ltd on 0800 783 4869 or ukmedinfo@cephalon.com

Date of Prescribing Information: 19 June 2009
 Code number: CE/FE-09087



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

Why titrate?

Effentora® should be individually titrated to an effective dose that provides adequate analgesia and minimises undesirable effects.

In clinical studies, the effective dose of Effentora® was not predictable from the daily dose of maintenance opioid therapy¹.

Patients should start with the lowest strength of Effentora® (100 µg), increasing as necessary through the range of available tablet strengths (100 µg, 200 µg, 400 µg, 600 µg, 800 µg) until an effective dose is reached.

When switching from another oral fentanyl citrate product, independent dose titration is required as bioavailability between products differs significantly. However, in these patients, a starting dose higher than 100 µg may be considered.

Before initiating treatment with Effentora® it is important to note that:

1. Effentora® is indicated for the treatment of breakthrough pain (BTcP) in adults with cancer who are already receiving maintenance opioid therapy for chronic cancer pain.
2. 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 per hour, at least 30 mg of oxycodone daily, at least 8 mg of oral hydromorphone daily an equianalgesic dose of another opioid for a week or longer.
3. Patients should experience a maximum of 4 BTcP episodes per day.
4. Patients should take Effentora® when the pain starts.
5. Presence of pain, efficacy of treatment and the necessity of BTcP treatment should be regularly assessed.
6. As with any opioid drug, there is a potential risk of misuse, abuse and diversion with Effentora®. Healthcare professionals should pay particular attention to the patient's maintenance opioid therapy and potential accidental exposure.

Reference: 1. Effentora® SmPC April 2008