Package leaflet: Information for the user

Effentora® 100 micrograms buccal tablets
Effentora® 200 micrograms buccal tablets
Effentora® 400 micrograms buccal tablets
Effentora® 600 micrograms buccal tablets
Effentora® 800 micrograms buccal tablets
fentanyl

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Effentora is and what it is used for

The active substance of Effentora is fentanyl citrate. Effentora is a pain-relieving medicine known as an opioid, which is used to treat breakthrough pain in adult patients with cancer who are already taking other opioid pain medicines for their persistent (around-the-clock) cancer pain.
Breakthrough pain is additional, sudden pain that occurs in spite of you having taken your usual opioid pain-relieving medicines.

2. What you need to know before you use Effentora

Do NOT use Effentora if you:
- are not regularly using a prescribed opioid medicine (e.g codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine), every day on a regular schedule, for at least a week, to control your persistent pain. If you have not been using these medicines you **must not** use Effentora, because it may increase the risk that breathing could become dangerously slow and/or shallow, or even stop.
- are allergic to fentanyl or any of the other ingredients of this medicine (listed in section 6)
- suffer from severe breathing problems or severe obstructive lung conditions
- suffer from short-term pain other than breakthrough pain
- are taking a medicine which contains sodium oxybate.

Warnings and precautions
Keep using the opioid pain medicine you take for your persistent (around-the-clock) cancer pain during your Effentora treatment.
Whilst you are being treated with Effentora, do not use other fentanyl treatments previously prescribed for your breakthrough pain. If you still have some of these fentanyl treatments at home, contact your pharmacist to check how to dispose of them.

Store this medicine in a safe and secure place, where other people cannot access it (see section *5. How to store Effentora* for more information).

Talk to your doctor or pharmacist **BEFORE** using Effentora if:
- your other opioid pain medicine taken for your persistent (around-the-clock) cancer pain is not stabilised yet
- you are suffering from any condition that has an effect on your breathing (such as asthma, wheezing, or shortness of breath)
- you have a head injury
- you have an exceptionally slow heart rate or other heart problems
- you have liver or kidney problems, as these organs have an effect on the way in which your system breaks down the medicine
- you have low amount of fluid in the circulation or low blood pressure
- you are over 65 years old - you may need a lower dose and any dose increase will be reviewed very carefully by your doctor
- you have problems with your heart especially slow heart rate
- you use benzodiazepines (see section 2 under "Other medicines and Effentora"). Using benzodiazepines can increase the chances of getting serious side effects including death
- you use antidepressants or antipsychotics (selective serotonin reuptake inhibitors [SSRIs], serotonin norepinephrine reuptake inhibitors [SNRIs], monoamine oxidase (MAO) inhibitors; see section 2 under "Do not use Effentora" and "Other medicines and Effentora"). The use of these medicines with Effentora can lead to a **serotonin syndrome a potentially life-threatening condition** (see section 2 under "Other medicines and Effentora")
- you have ever developed adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones or lack of sex hormones (androgen deficiency) with opioid use (see section 4 under "Serious side effects")
- you have ever abused or been dependent on opioids or any other drug, alcohol or illegal drugs
- you drink alcohol; please refer to section Effentora with food, drink and alcohol.

Consult your doctor **WHILE** using Effentora if:
- you experience pain or increased sensitivity to pain (hyperalgesia) which does not respond to a higher dosage of your medicine as prescribed by your doctor
- you experience a combination of the following symptoms: nausea, vomiting, anorexia, fatigue, weakness, dizziness and low blood pressure. Together these symptoms may be a sign of a potentially life-threatening condition called adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones
- sleep-related breathing disorders: Effentora can cause sleep-related breathing disorders such as sleep apnoea (breathing pauses during sleep) and sleep related hypoxemia (low oxygen level in the blood). The symptoms can include breathing pauses during sleep, night awakening due to shortness of breath, difficulties to maintain sleep or excessive drowsiness during the day. If you or another person observe these symptoms, contact your doctor. A dose reduction may be considered by your doctor.

Long-term use and tolerance
This medicine contains fentanyl which is an opioid medicine. Repeated use of opioid painkillers can result in the drug being less effective (you become accustomed to it, known as drug tolerance). You may also become more sensitive to pain while using Effentora. This is known as hyperalgesia. Increasing the dose of Effentora may help to further reduce your pain for a while, but it may also be harmful. If you notice that your medicine becomes less effective, talk to your doctor. Your doctor will decide whether it is better for you to increase the dose or to gradually decrease your use of Effentora.

Dependence and addiction

This medicine contains fentanyl, which is an opioid. It can cause dependence and/or addiction.

Repeated use of Effentora can also lead to dependence, abuse and addiction which may result in life-threatening overdose. The risk of these side effects can increase with a higher dose and longer duration of use. Dependence or addiction can make you feel that you are no longer in control of how much medicine you need to use or how often you need to use it. You might feel that you need to carry on using your medicine, even when it doesn't help to relieve your pain.
The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent or addicted on Effentora if you:
- or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs ("addiction")
- are a smoker
- have ever had problems with your mood (depression, anxiety or a personality disorder) or have been treated by a psychiatrist for other mental illness.

If you notice any of the following signs whilst using Effentora, it could be a sign that you have become dependent or addicted.
- you need to use the medicine for longer than advised by your doctor
- you need to use more than the recommended dose
- you are using the medicine for reasons other than prescribed, for instance, 'to stay calm' or 'help you sleep'
- you have made repeated, unsuccessful attempts to quit or control the use of the medicine
- when you stop taking the medicine you feel unwell (e.g nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating), and you feel better once using the medicine again ('withdrawal effects').

If you notice any of these signs, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to stop safely.

Seek **URGENT** medical advice if:
- you experience symptoms such as difficulty in breathing or dizziness, swelling of the tongue, lip or throat while using Effentora. These might be early symptoms of a serious allergic reaction (anaphylaxis, hypersensitivity; see section 4 under "Serious side effects").

What to do if someone accidentally takes Effentora
If you think someone has accidentally taken Effentora please seek immediate medical assistance. Try to keep the person awake until emergency help arrives.

If someone has accidentally taken Effentora, they may have the same side effects as described in the section 3 "If you use more Effentora than you should".

Children and adolescents
Do not give this medicine to children and adolescents below18 years of age.

Other medicines and Effentora
Tell your doctor or pharmacist before starting Effentora if you are taking or have recently taken or might take any of the following medicines:
- Concomitant use of Effentora and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible. However if your doctor does prescribe Effentora together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor. Please tell your doctor about all sedative medicines you are taking (such as sleeping pills, medicines to treat anxiety, some medicines to treat allergic reactions (antihistamines), or tranquillisers) and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.
- Some muscle relaxants - such as baclofen, diazepam (see also section "Warnings and precautions".
- Any medicines that might have an effect on the way in which your body breaks down Effentora, such as ritonavir, nelfinavir, amprenavir, and fosamprenavir (medicines that help control HIV infection) or other so-called CYP3A4 inhibitors such as ketoconazole, itraconazole, or fluconazole (used for treatment of fungal infections), troleandomycine, clarithromycine, or erythromycine (medicines for treatment of bacterial infections), aprepitant (used for severe nausea) and diltiazem and verapamil (medicines for treatment of high blood pressure or heart diseases).
- Medicines called monoamine-oxidase (MAO) inhibitors (used for severe depression) or have done so in the past 2 weeks.
- Certain type of strong pain killers, called partial agonist/antagonists e.g. buprenorphine, nalbuphine and pentazocine (medicines for treatment of pain). You could experience symptoms of withdrawal syndrom (nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating) while using these medicines.
- Some painkillers for nerve pain (gabapentin and pregabalin).
- The risk of side effects increases if you are taking medicines such as certain antidepressants or antipsychotics. Effentora may interact with these medicines and you may experience mental status changes (e.g. agitation, hallucinations, coma), and other effects such as body temperature above 38°C, increase in heart rate, unstable blood pressure, and exaggeration of reflexes, muscular rigidity, lack of coordination and/or gastrointestinal symptoms (e.g nausea, vomiting, diarrhoea). Your doctor will tell you whether Effentora is suitable for you.

Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

Effentora with food, drink and alcohol
- Effentora may be used before or after, but not during, meals. You may drink some water before using Effentora to help moisten your mouth, but you should not drink or eat anything while taking the medicine.
- You should not drink grapefruit juice while using Effentora because it may affect the way your body breaks down Effentora.
- Do not drink alcohol while using Effentora. It can increase the risk of experiencing serious side effects including death.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Pregnancy
Effentora should not be used during pregnancy unless you have discussed this with your doctor.
If Effentora is used for a long time during pregnancy, there is also a risk of the new-born child having withdrawal symptoms which might be life-threatening if not recognized and treated by a doctor.

You should not use Effentora during childbirth because fentanyl may cause respiratory depression in the new-born child.

Breast-feeding
Fentanyl can get into breast milk and may cause side effects in the breast-fed infant. Do not use Effentora if you are breast-feeding. You should not start breast-feeding until at least 5 days after the last dose of Effentora.

Driving and using machines
You should discuss with your doctor whether it is safe for you to drive, or operate machinery after taking Effentora. Do not drive or operate machinery if you: are feeling sleepy or dizzy; have blurred or double vision; or have difficulty in concentrating. It is important you know how you react to Effentora before driving or operating machinery.

Effentora contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per buccal tablet, that is to say essentially 'sodium-free'.

3. How to use Effentora

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Before starting treatment and regularly during treatment, your doctor will also discuss with you what you may expect from using Effentora, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also section 2).

Dosage and frequency
When you first start using Effentora, your doctor will work with you to find the dose that will relieve your breakthrough pain. It is very important that you use Effentora exactly as the doctor tells you. The initial dose is 100 micrograms. During determination of your right dose, your doctor may instruct you to take more than one tablet per episode. If your breakthrough pain is not relieved after 30 minutes, use only 1 more tablet of Effentora during the titration period.

Once the right dose has been determined with your doctor, use 1 tablet for an episode of breakthrough pain as a general rule. In the further course of treatment your requirement for analgesic therapy may change. Higher doses may be necessary. If your breakthrough pain is not relieved after 30 minutes, use only 1 more tablet of Effentora during this dose-readjustment period.
Contact your doctor if your right dose of Effentora does not relieve your breakthrough pain. Your doctor will decide if your dose needs to be changed.

Wait at least 4 hours before treating another episode of breakthrough pain with Effentora.

You must let your doctor know immediately if you are using Effentora more than four times per day, as a change may be required to your treatment regimen. Your doctor may change the treatment for your persistent pain; when your persistent pain is controlled again, your doctor may need to change the dose of Effentora. If your doctor suspects Effentora-related increased sensitivity to pain (hyperalgesia), a reduction of your Effentora dose may be considered (see section 2 under "Warnings and precautions"). For the most effective relief, let your doctor know about your pain and how Effentora is working for you, so that the dose can be changed if needed.

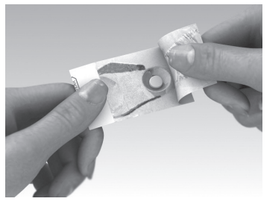
Do not change doses of Effentora or your other pain medicines on your own. Any change in dosage must be prescribed and monitored by your doctor.

If you are not sure about the right dose, or if you have questions about taking this medicine, you should contact your doctor.

Method of administration
Effentora buccal tablets are for oromucosal use. When you place a tablet in your mouth, it dissolves and the medicine is absorbed through the lining of your mouth, into the blood system. Taking the medicine in this way allows it to be absorbed quickly to relieve your breakthrough pain.

Taking the medicine
- Open the blister only when you are ready to use the tablet.

The tablet must be used immediately once removed from the blister.
- Separate one of the blister units from the blister card by tearing apart at the perforations.
- Bend the blister unit along the line where indicated.
- Peel the blister backing to expose the tablet. Do NOT attempt to push the tablet through the blister, because this can damage the tablet.



- Remove the tablet from the blister unit and **immediately** place the entire tablet near a molar tooth between the gum and the cheek (as shown in the picture). Sometimes, your doctor may tell you to place the tablet under your tongue instead.
- Do not attempt to crush or split the tablet.

- Do not bite, suck, chew, or swallow the tablet, as this will result in less pain relief than when taken as directed.
- The tablet should be left between the cheek and gum until dissolved, which usually takes approximately 14 to 25 minutes.
- You may feel a gentle bubbling sensation between your cheek and gum as the tablet dissolves.
- In case of irritation, you may change the placement of the tablet on the gum.
- After 30 minutes, if pieces of the tablet remain, they may be swallowed with a glass of water.

If you use more Effentora than you should
- The most common side effects are feeling sleepy, sick or dizzy. If you begin to feel very dizzy, or very sleepy before the tablet is completely dissolved, rinse your mouth with water and spit the remaining pieces of the tablet into a sink or toilet right away.
- A serious side effect of Effentora is slow and/or shallow breathing. This can occur if your dose of Effentora is too high or if you take too much Effentora. In severe cases taking too much Effentora may also lead to coma. If you feel very dizzy, very sleepy or have slow or shallow breathing, If this occurs, please seek immediate medical assistance.
- An overdose may also result in a brain disorder known as toxic leukoencephalopathy.

If you forget to use Effentora
If the breakthrough pain is still ongoing, you may take Effentora as prescribed by your physician. If the breakthrough pain has stopped, do not take Effentora until the next breakthrough pain episode.

If you stop using Effentora
You should discontinue Effentora when you no longer have any breakthrough pain. You must however continue to take your usual opioid pain relieving medicine to treat your persistent cancer pain as advised by your doctor. You may experience withdrawal symptoms similar to the possible side effects of Effentora when discontinuing Effentora. If you experience withdrawal symptoms or if you are concerned about your pain relief, you should contact your doctor. Your doctor will evaluate if you need medicine to reduce or eliminate the withdrawal symptoms.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. If you notice any of these, contact your doctor.

Serious side effects

- **The most serious side effects are shallow breathing, low blood pressure and shock. Effentora like other fentanyl products can cause very severe breathing problems which can lead to death. If you become very sleepy or have slow and/or shallow breathing, you or your carer should contact your doctor immediately and call for emergency help.**
- **Contact your doctor immediately if you experience a combination of the following symptoms**
  Nausea, vomiting, anorexia, fatigue, weakness, dizziness and low blood pressure
  Together these symptoms may be a sign of a potentially life-threatening condition called adrenal insufficiency. A condition in which the adrenal glands do not produce enough hormones.

Other side effects

Very common: may affect more than 1 in 10 people
- dizziness, headache
- feeling nauseous, vomiting
- at the site of tablet application: pain, ulcer, irritation, bleeding, numbness, loss of sensation, redness, swelling or spots.

Common: may affect up to 1 in 10 people
- feeling anxious or confused, depression, insomnia
- abnormal taste, weight decreased
- sleepiness, sedation, excessive tiredness, weakness, migraine, numbness, swelling of arms or legs, drug withdrawal syndrome (may manifest by the occurrence of the following side effects nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating), shaking, falls, chills
- constipation, inflammation of the mouth, dry mouth, diarrhoea, heartburn, loss of appetite, stomach pain, uncomfortable stomach, indigestion, toothache, oral thrush
- itching, excessive sweating, rash
- shortness of breath, painful throat
- decrease in white cells in the blood, decrease in red blood cells, decreased or raised blood pressure, unusually fast heart rate
- muscle pain, back pain
- fatigue.

Uncommon: may affect up to 1 in 100 people
- sore throat
- decrease in cells that help the blood to clot,
- feeling elated, nervous, abnormal, jittery or slow; seeing or hearing things that are not really there (hallucinations), reduced consciousness, change in mental state, dependence (reliance on the medicine, addiction), disorientation, lack of concentration, loss of balance, vertigo, problem with speaking, ringing in the ear, ear discomfort
- disturbed or blurred vision, red eye
- unusually low heart rate, feeling very warm (hot flushes),
- severe breathing problems, trouble breathing during sleep,
- one or more of the following problems in the mouth: ulcer, loss of sensation, discomfort, unusual colour, soft tissue disorder, tongue disorder, painful or blistered or ulcerated tongue, gum pain, chapped lips, tooth disorder
- inflammation of the oesophagus, paralysis of the gut, gall bladder disorder
- cold sweat, swollen face, generalised itching, hair loss, muscle twitching, muscular weakness, feeling unwell, chest discomfort, thirst, feeling cold, feeling hot, difficulty passing urine
- malaise
- flushing.

Rare: may affect up to 1 in 1,000 people
- disturbance in thinking, movements disturbance
- blisters in the mouth, dry lips, collection of pus under the skin in the mouth
- lack of testosterone, abnormal sensation in eye, observing flashes of light, brittle nails
- allergic reactions such as rash, redness, swollen lip and face, hives.

Not known: frequency cannot be estimated from the available data
- loss of consciousness, stop in breathing, convulsion (fits)
- lack of sex hormones (androgen deficiency)
- drug tolerance (see section 2)
- drug dependence (addiction) (see section 2)
- drug abuse (see section 2)
- delirium (symptoms may include a combination of agitation, restlessness, disorientation, confusion, fear, seeing or hearing things that are not really there, sleep disturbance, nightmares)
- prolonged treatment with fentanyl during pregnancy may cause withdrawal symptoms in the newborn which can be life-threatening (see section 2).

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Effentora

The pain-relieving medicine in Effentora is very strong and could be life-threatening if taken accidentally by a child. This medicine must be kept out of the sight and reach of children.
- Do not use this medicine after the expiry/use before date which is stated on the blister package label and the carton. The expiry date refers to the last day of that month.
- Store this medicine in a safe and secure place, where other people cannot access it. It can cause serious harm and be fatal to people who may take this medicine by accident, or intentionally when it has not been prescribed for them.
- Store in the original package in order to protect from moisture.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Effentora contains
The active substance is fentanyl.
- Each Effentora 100 micrograms Buccal Tablet contains 100 micrograms fentanyl (as citrate).
- Each Effentora 200 micrograms Buccal Tablet contains 200 micrograms fentanyl (as citrate).
- Each Effentora 400 micrograms Buccal Tablet contains 400 micrograms fentanyl (as citrate).
- Each Effentora 600 micrograms Buccal Tablet contains 600 micrograms fentanyl (as citrate).
- Each Effentora 800 micrograms Buccal Tablet contains 800 micrograms fentanyl (as citrate).

The other ingredients are mannitol, sodium starch glycolate type A, sodium hydrogen carbonate, sodium carbonate, citric acid, magnesium stearate.

What Effentora looks like and contents of the pack
The buccal tablets are flat-faced, round bevelled-edge tablet, embossed one side with a "C" and on the other side with "1" for Effentora 100 micrograms, with "2" for Effentora 200 micrograms, with "4" for Effentora 400 micrograms, with "6" for Effentora 600 micrograms, with "8" for Effentora 800 micrograms.
Each blister contains 4 buccal tablets, supplied in cartons of 4 or 28 buccal tablets.
Not all pack sizes may be marketed.

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Manufacturer:
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