Important risk minimisation information for healthcare professionals Pecfent®(Fentanyl)Nasal Spray

Healthcare Professional Guide

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Version-1-Approved by SFDA on April 2019

Introduction

The PecFent® Healthcare Professional Guide is designed to support healthcare professionals in the diagnosis of breakthrough cancer pain, and in the initiation, administration and dose titration of PecFent®. This document should be referred to in conjunction with important information contained within the PecFent® Summary of Product Characteristics (SmPC) and the PecFent® Prescribing Information at the back of this booklet.

Treatment should be initiated by, and remain under the supervision of, a physician experienced in the management of opioid therapy in cancer patients. Healthcare professionals, i.e. physicians and pharmacists, must be familiar with the risk management material of Pecfent® prior to using it within their organisation.

Healthcare professionals are asked to report any suspected adverse reactions to:
The National Pharmacovigilance Centre (NPC)
Saudi Food and Drug Authority (SFDA)
SFDA call center: 19999
Toll free phone: 8002490000
Fax: +966-11-2057662
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa

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PecFent® Healthcare Professional Guide

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 Treatment

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 a 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

Defining Breakthrough Cancer Pain

- Breakthrough pain is a transient exacerbation of otherwise controlled chronic background pain
- Breakthrough cancer pain is characterised 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
- Engaging with patients is a vital part of supporting them in the management of their breakthrough pain, from assessment through to diagnosis and treatment

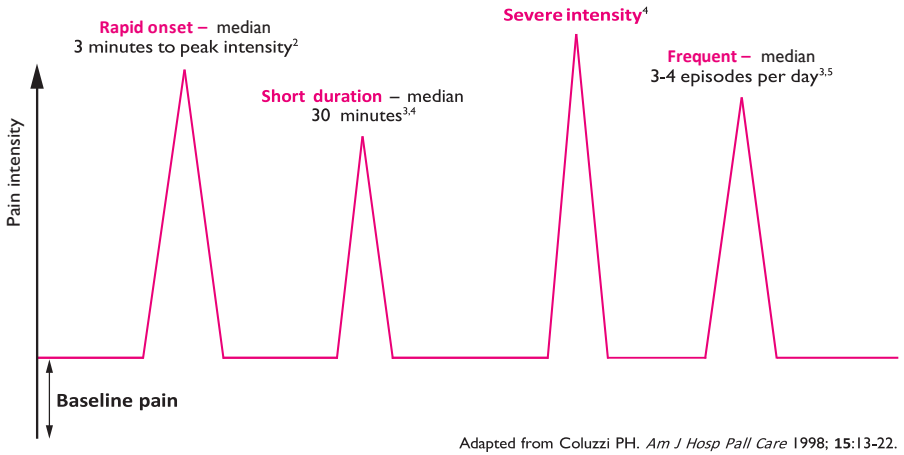
Types and Triggers of Breakthrough Cancer Pain

Predictable: incident breakthrough cancer pain[1]

- **Voluntary**: triggered by movement such as walking
- **Involuntary**: triggered by reflex movements such as coughing
- **Procedural**: related to a therapeutic intervention e.g. wound dressing

Unpredictable: - spontaneous breakthrough cancer pain

- Unrelated to any identifiable action



Adapted from Coluzzi PH. *Am J Hosp Pall Care* 1998; **15**:13-22.

Diagnosing Breakthrough Cancer Pain

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

(i) Assess whether a patient's complaint of pain is due to inadequately controlled background cancer pain, including end of dose failure.

(ii) Optimise 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.

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 episodic 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)[1]
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[1]

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. Advice should also be given to avoid volitional triggers, such as walking, where possible.

3. Introduction to Pecfent®

Product Overview

Pecfent® is indicated for the management of breakthrough pain (BTP) in adults who are already receiving maintenance opioid therapy for chronic cancer pain. Breakthrough pain is a transitory exacerbation of pain that occurs on a background of otherwise controlled persistent pain.[6]

PecFent® should be prescribed and administered in accordance with the licensing information contained within the PecFent® Summary of Product Characteristics (SmPC) and the PecFent® Prescribing Information at the back of this booklet.

Selecting the PecFent® Patient

PecFent® 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 take 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.

It is important that PecFent® is only initiated in patients whose dose of long-acting opioid has been stabilised. Ensure appropriate patient selection:

- The safety and efficacy of Pecfent® in children and adolescents aged below 18 years have not yet been established
- Ensure that the patient has no contra-indications for PecFent®. These include:
  - Hypersensitivity to the active substance or any of the excipients listed in section 6.1 of the SmPC
  - Patients without maintenance opioid therapy as there is an increased risk of respiratory depression
  - Severe respiratory depression or severe obstructive lung conditions
  - Treatment of acute pain other than breakthrough pain

PecFent should be administered with caution to patients with moderate or severe hepatic or renal impairment, and such patients monitored closely during titration. Clearance of intravenous fentanyl products has been shown to be altered in patients with hepatic and renal impairment due to alterations in metabolic clearance and plasma proteins. (Refer to SmPC sections 4.2 and 4.4).

Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as fentanyl.

Inform patients/carers that PecFent® contains an active substance in an amount that can be fatal to a child, therefore remember to always return the PecFent® nasal spray device to the child-resistant container for storage (even when all doses are used) and keep this out of the sight and reach of children.

For further detailed information relating to contra-indications, special warnings and precautions for use, interactions with other medicinal products, and the use of PecFent® in pregnancy and during breastfeeding refer to the SmPC (sections 4.1, 4.2, 4.3, 4.4, 4.5 and 4.6).

Patients should also be advised about the importance of correct use, storage and disposal (see section 6.6 of the SmPC) of the nasal spray device and child-resistant container.

PecFent® must not be used for treatment of acute pain or any other pain status other than breakthrough cancer pain.

Use in patients without opioid maintenance therapy risks potentially serious adverse reactions including respiratory depression. It is therefore important that long acting opioid treatment used to treat patients persistent background cancer pain has been stabilised before PecFent® therapy begins.

4. Titrating to the Correct Dose

Necessity of Titrating

PecFent® must be titrated to an 'effective' dose. An effective dose is the dose that provides adequate analgesia without causing undue (or intolerable) adverse reactions, for two consecutively treated episodes of breakthrough cancer pain (section 4.2 of the SmPC).

PecFent® is available in two strengths:

Yellow carton
100 microgram/spray strength

Violet carton
400 microgram/spray strength

Dose Titration

The initial dose of PecFent® should always be 100 micrograms titrating upwards as necessary until an effective dose is reached. During titration, patients should be instructed to assess pain relief 30 minutes after Pecfent® administration. If an effective dose is not reached, at the next breakthrough cancer pain episode, the patient should proceed to the next higher dose and wait at least 4 hours before administering it.

Patients must wait at least 4 hours before treating another episode of breakthrough cancer pain with Pecfent®. Refer to the Pecfent® SmPC and the figure overleaf that highlights the titration schedule to be followed.

PecFent® Titration Process

Always start dose with 100 micrograms – 1 spray
Always wait 4 hours before next dose

100 micrograms

1 spray

If adequate pain relief is not achieved increase to 200 micrograms for next episode

200 micrograms

2 sprays (one spray into each nostril)

If adequate pain relief is not achieved increase to 400 micrograms for next episode

400 micrograms

1 spray

If adequate pain relief is not achieved increase to 800 micrograms for next episode

800 micrograms

2 sprays (one spray into each nostril)

Progress down titration chart until adequate pain relief achieved

Always assess pain relief at 30 minutes after administration

If pain relief is not adequate, increase to a higher dose for the next breakthrough pain episode. Wait at least 4 hours before the next dose of PecFent®

Once adequate dose has been achieved continue on this dose for future breakthrough pain episodes

Do not exceed 800 micrograms per episode
Do not treat more than 4 episodes per day

For full details on method of titration, please refer to the full Summary of Product Characteristics

PecFent® can deliver 100, 200, 400 and 800 microgram doses as follows:

Dose required (microgram)	Product strength (microgram/spray)	Pack colour	Amount
100	100	Yellow	One spray administered into **one** nostril
200	100	Yellow	Two sprays; one administered into **each** nostril
400	400	Violet	One spray administered into **one** nostril
800	400	Violet	Two sprays; one administered into **each** nostril

- In order to minimise the risk of opioid-related adverse reactions and to identify the appropriate dose, it is imperative that patients be individually titrated and monitored closely by healthcare professionals during the titration process

Maintenance Therapy and Dose Re-adjustment

Once an 'effective' dose has been achieved patients should continue on this dose for future breakthrough cancer pain episodes.

No more than 2 sprays of the same dose strength should be administered for a single episode of breakthrough cancer pain.

The highest available dose of 800 micrograms (2 sprays of 400 micrograms) should not be exceeded per episode.

In order to minimise the risk of addiction/potential overdose, a patient should be prescribed a maximum four (4) doses per day and instructed to wait at least four (4) hours after a dose before treating another breakthrough cancer pain episode.

If the patient continues to experience more than 4 episodes of breakthrough cancer pain per 24 hours, consider reviewing the patient's background opioid therapy.

For further information on titration, ongoing maintenance and dose re-adjustment refer to SmPC, section 4.2.

Switching Medication

- Switching from other fentanyl or other opioid containing products must **not** occur at a 1:1 ratio because of difference in bioavailability profiles and can result in fatal respiratory depression.
- If patients are switched from another fentanyl or opioid containing, a new dose titration with PecFent® is required, starting at 100 micrograms.
- PecFent® should similarly not be substituted for another fentanyl containing product based on the same principle.

- When a patient is switched from PecFent to another fentanyl containing product indicated for the treatment of breakthrough cancer pain, the product's corresponding SmPC must be consulted for further guidance on recommended dose and titration

Stopping PecFent® altogether

- PecFent® should be discontinued immediately if the patient no longer experiences breakthrough pain 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 followed by the doctor in order to avoid the possibility of abrupt withdrawal effects

Referring Patients

If, after titration, patients do not experience relief for their breakthrough cancer pain 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 with an interest in breakthrough cancer pain.

5. Important Considerations

Treatment with opioid-based formulations can be associated with adverse effects. The risk of serious adverse effects is reduced if medications for breakthrough cancer pain are used under the following conditions:

- When prescribed to the right patient (refer to **Selecting the PecFent® Patient** in section 3)
- When titrated within the parameters of the titration schedule (refer to section 4 **Titrating to the Correct Dose**)
- In accordance with the licensed indications and licensing information (refer to the PecFent® SmPC)

Undesirable Effects

Refer to SmPC, section 4.8. This is a tabulated summary of adverse reactions with PecFent® and/or other fentanyl containing compounds. Healthcare professionals are reminded of the potential for abuse of this product.

In order to minimise the risk of opioid–related adverse reactions, including early evidence of respiratory depression, it is imperative that patients be monitored closely by healthcare professionals during the titration process and thereafter. Ensure appropriate instructions are provided to patients regarding monitoring for the signs of respiratory depression. For further information on respiratory depression refer to SmPC sections 4.3, 4.4, 4.5, 4.6, 4.8, 4.9 and 5.1

Undesirable effects typical of opioids are to be expected with PecFent®; they tend to decrease in intensity with continued use. The most serious potential adverse reactions associated with opioid use are respiratory depression (which could lead to respiratory arrest or apnoea), somnolence, confusion, hypotension and shock.

In addition, patients may experience symptoms of opioid withdrawal upon discontinuation, see also section 4.2 of SmPC.

The most frequently observed adverse reactions with PecFent® include disorientation, dysgeusia, dizziness, somnolence, headache, epistaxis, rhinorrhoea, nasal discomfort, vomiting, nausea, constipation and pruritus

Patients should be monitored for circulatory depression, hypotension and shock. PecFent® should be used with caution in patients with previous or pre-existing bradyarrhythmias.

Symptoms of opioid withdrawal, i.e. nausea, vomiting, diarrhoea, anxiety, chills, tremor, and sweating have been observed with transmucosal fentanyl.

Long term use of PecFent® has not been fully established. Patients receiving long term use of PecFent® should be monitored carefully.

Please refer to the SmPC (sections 4.4 and 4.8).

Local Tolerability

Use of PecFent® has been associated with local tolerability adverse events. If a patient experiences recurrent issues of epistaxis or nasal discomfort, an alternative treatment should be considered.

Serotonin Syndrome

As with other fentanyl products, caution is advised when PecFent® is co-administered with drugs that affect the serotonergic neurotransmitter systems.

The development of potentially life-threatening serotonin syndrome may occur with the concomitant use of serotonergic drugs such as Selective Serotonin Re-Uptake Inhibitors (SSRIs) and Serotonin Norepinephrine Re-Uptake Inhibitors (SNRIs), and with drugs that impair metabolism of serotonin (including Monoamine Oxidase Inhibitors (MAOIs)). This may occur within the recommended dose. PecFent® is not recommended in patients who have received MAOIs within 14 days.

Serotonin syndrome may include mental-status changes (e.g. agitation, hallucinations, coma), autonomic instability (e.g. tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g. hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g. nausea, vomiting, diarrhoea).

Advise patients of the symptoms and seriousness of serotonin syndrome and to contact their physician if suspected.

If serotonin syndrome is suspected, treatment with PecFent® should be discontinued. Further details on serotonin syndrome are found in section

4.4 and 4.5 of the SmPC.

Pregnancy and Breastfeeding

PecFent® should not be used during pregnancy unless clearly necessary.

Fentanyl should not be used by breastfeeding women and breastfeeding should not be restarted until at least 5 days after the last administration of fentanyl.

Patients should be advised of the potentially serious side-effects of using PecFent® while breastfeeding.

Further details can be found in section 4.6 and 5.3 of the SmPC and section 2 of the patient information leaflet (PIL).

6. Providing Guidance for Patients & Carers

Patients and carers should be referred to the PecFent® patient information leaflet, ensuring they are aware of and understand the information contained within it. Advise patients about the two strengths and the colour differentiation between strength packs. They should also be given a copy of the PecFent® Patient and Carer Guide. In addition, patients and their carers should be made aware of the information specified below and overleaf:

Correct Treatment Administration & Adherence

- PecFent® must be taken exactly as prescribed and must not be given to anyone else
- The patient should remain on background opioids when taking PecFent®
- There are other restrictions of use, including not taking certain medications and avoiding alcohol (Refer to section 4.5 of the SmPC and section 2 of the PIL)
- The patient should not use more than 4 doses of PecFent® per day
- The patient should wait at least 4 hours after a dose before treating another breakthrough cancer pain episode with PecFent®
- If PecFent® is not used according to instructions, there is an increased risk of side-effects and addiction

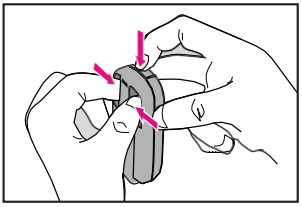
How to take PecFent®

PecFent® is contained in a clear glass bottle, fitted with a pump which delivers an exact dose of medicine with each spray. The pump has a spray counter that clicks so the patient can hear as well as see that the spray has been given (this is important because the spray is very fine, and the patient may not feel it. Patients should rely on the click and counter to check they have correctly administered a spray).

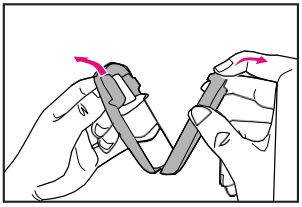
- The click provides an audible signal that the spray has been administered
- The number on the counter moves forward providing a visual signal of how many sprays have been used

After the PecFent® bottle has been primed (prepared for use), it delivers 8 full sprays. The PecFent® bottle must always be stored in the child-resistant container.

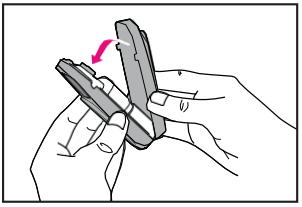
Instructions on how to open and close the child-resistant container:



1. Insert fingers into rear cavities and squeeze while pushing down top button



2. Open



3. Close (listen for confirmation click)

PecFent® is only to be used by spraying into the nostril

Preparing (priming) the PecFent® bottle for use

Before using a new bottle of PecFent® it needs to be prepared for use. This is called 'priming'.

To prime the bottle, please advise the patient to follow the instructions below:

1. A new bottle of PecFent® will show two red lines in the counting window in the white plastic top on the bottle (Figure 1 and Figure 3a)
2. Take off the clear plastic protective cap from the nozzle (Figure 1)
3. Aim the nasal spray away from them (and any other people or animals)
4. Hold the PecFent® nasal spray upright with their thumb on the bottom of the bottle, and their first and middle fingers on the finger grips each side of the nozzle (Figure 2)
5. Firmly press down on the finger grips until a 'click' is heard and then let go of the grips (Figure 2). They will hear a second 'click' and there should be a single large red bar in the counting window (Figure 3b)

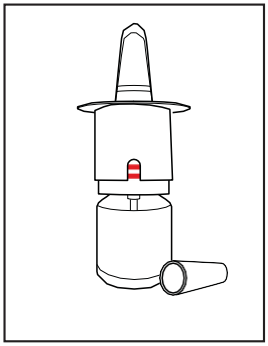


Figure 1

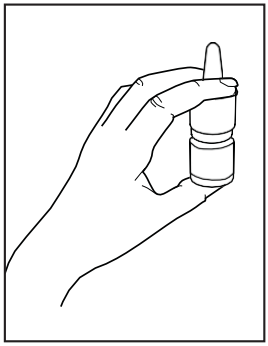


Figure 2

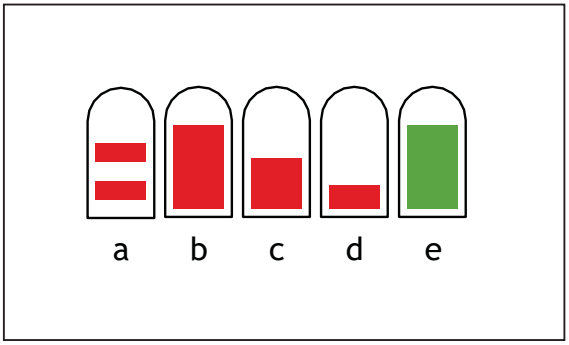


Figure 3

6. Repeat step 5 three times. As the patient repeats step 5, the red bar will become smaller and smaller until they see a green bar in the counting window (Figure 3b-e). The green bar means the PecFent® nasal spray is ready to use
7. Wipe the nozzle with a tissue and flush the tissue down the toilet
8. If the patient is not going to take their medicine straight away, they should put the protective cap back on, then put the PecFent® bottle in the child-resistant storage container. If the bottle has not been used for 5 days, it should be re-primed by spraying once. The bottle should be discarded 60 days after first opening.
9. The date on which the PecFent® bottle was first primed should be written on the space on the child-resistant container label.

Using PecFent® for the first time

Please advise the patient to follow the instructions below:

1. Check that there is green bar showing in the counting window (Figure 4), this confirms that the PecFent® bottle has been primed (see the section called **Preparing the PecFent® bottle for use** on page 19 of this booklet)
2. Blow their nose if they feel they need to
3. Sit down with their head upright
4. Take off the protective cap from the nozzle
5. Hold the PecFent® bottle with their thumb on the bottom of the bottle and their first and middle fingers on the finger grips (Figure 4)
6. Put the nozzle a short distance (about 1 cm) into their nostril. Point it slightly inwards towards the middle wall of their nose. This will tilt the bottle slightly (Figure 5)
7. Close the other nostril with a finger from their other hand (Figure 5)

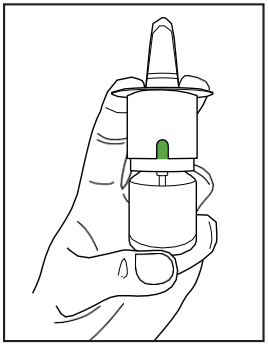


Figure 4

Figure 5

8. Firmly press down on the finger grips so that PecFent® sprays into their nostril. When they hear a click let go of the grips. N.B. Advise the patient that they may not feel anything happen in their nose at all – do not trust this to mean the spray did not operate – rely on the click and number counter. The counting window will show a black “1” confirming the spray has been delivered

9. Breathe in gently through the nose and out through the mouth

10. If they have been prescribed a second spray, repeat steps 5 to 9, using the other nostril

    Do not use more than the dose that has been prescribed to treat any single pain episode. If they have used a second spray, the counting window will show a black “2” confirming the spray has been delivered

11. Put the bottle back in the child-resistant container after each use. Keep out of the sight and reach of children (Figure 6)

12. Stay sitting for at least 1 minute after using the nasal spray

13. Do not blow their nose straight after using the PecFent® nasal spray

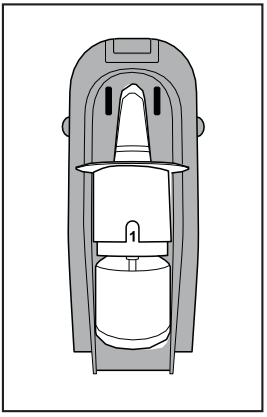


Figure 6

Using a PecFent® bottle the patient has used before

Please advise the patient to follow the instructions below:

1. Check the bottle is within its use-by (expiry) date. Dispose of the bottle and prime a new one if more than 60 days have passed since they primed or used the bottle for the first time (to help them remember, there is a space on the child resistant container label to write the date of first use)
2. Make sure there is a black number in the counting window then follow steps 2-13 in the section of this booklet called **Using PecFent® for the first time** (page 21). If the bottle has not been used for 5 days, re-prime by spraying once
3. If there is a red "8" in the counting window, the bottle is empty and should be disposed of safely and the patient should prime a new bottle

Please see the section called Safe-keeping, Dispensing and Disposal on page 25 of this booklet for a detailed description of how to correctly store and dispose of this medicine.

Monitoring Effectiveness

The patient should continually monitor the effectiveness of PecFent® in providing relief for their breakthrough cancer pain during the titration phase, 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?

Long term use of PecFent® has not been fully established. Patients receiving long term treatment with PecFent® should be monitored carefully.

Action in the Event of an Accidental Overdose

During patient selection it is important to assess whether the patient might be at risk from accidental or intentional overdose. Instruct patients/carers about the seriousness, symptoms of, and what to do in case of overdose.

The symptoms of fentanyl overdose are an extension of its pharmacological actions, the most serious effect being respiratory depression, which may lead to respiratory arrest. Instruct patients/carers about the seriousness of the symptoms of, and what to do in case of, overdose (refer to section 3 of the PIL).

For the symptoms, management and treatment of PecFent® overdose refer to the SmPC (section 4.9).

Abuse/Diversion/Dependence

During patient selection, it is important to assess whether the patient has demonstrated an abuse or may be at risk of abuse of their pain medication.

There is potential for abuse and diversion with this product, so patients should be informed about the risk of abuse, addiction and diversion with opioids, including PecFent®. Please refer also to **Selecting the PecFent® Patient** in section 3 of this booklet.

Patients should be advised that inappropriate use of this medicine may lead to dependence.

Patients should be advised about the importance of correct storage/disposal of this medicine, as inappropriate storage/disposal could put someone else (other than the patient) at risk of accidental opioid-naïve use, or drug diversion.

All unused, partially used, or used bottles should be returned systematically according to the local regulations. See also **Safe-keeping, Dispensing and Disposal** below.

For further details on abuse, diversion and dependence refer to the SmPC (section 4.4).

Misuse

Any situation where PecFent® is intentionally and inappropriately used not in accordance with authorised product information should be reported as an adverse event. This includes situations where incorrect or no titration (including incorrect switching) has been performed.

Safe-keeping, Dispensing &Disposal

Partially used PecFent® bottles may contain enough medicine to be harmful or life-threatening to a child. Even if there is little or no medicine left in the bottle, PecFent® must be disposed of properly, according to the following steps:

- Patients and caregivers must be instructed to dispose of all unused, partially used and used PecFent® bottles properly. If there are any unwanted therapeutic sprays remaining in the bottle, instruct the patient to expel these by aiming the spray away from themselves (and any other people) until the red number “8” appears in the counting window and there are no more full therapeutic sprays obtainable from the bottle
- After the counter has advanced to “8”, the patient should continue to push down on the finger grips (there will be some increased resistance) a total of four times in order to expel any residual medicine from the bottle
- After the 8 therapeutic sprays have been emitted, the patient will not hear a click and the counter will not advance beyond “8”; further sprays emitted will not be full sprays and should not be used therapeutically

As soon as PecFent® is no longer needed, patients and members of their household must be advised to dispose of any bottles remaining from a prescription as soon as possible by emptying them of any residual medicine, as described above, returning them to their child-resistant container and discarding them, according to local requirements or by returning them to the pharmacy.

References

1. Davies A (Ed.) Cancer-related breakthrough pain (2nd edition). Oxford: Oxford University Press. 2012; 1-11
2. Portenoy RK *et al*, *Pain* 1999: **81**: 129-134
3. Portenoy RK. *Pain* 1990: **41**: 273-281
4. Simmonds MA. Oncology 1999: **13**: (8): 1-9
5. Überall MA, Müller-Schwefe GHH. Curr Med Res Opin 2011; 27 (7) 1385-94
6. PecFent® Summary of Product Characteristics

PecFent® (fentanyl citrate) Nasal Spray Prescribing Information

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing

Name: PecFent 100 micrograms/spray nasal spray solution and PecFent 400 micrograms/spray nasal spray solution. **Active Ingredient:** ***PecFent 100***; each ml of solution contains 1,000 mcg fentanyl (as citrate); **PecFent 400**; each ml of solution contains 4,000 mcg fentanyl (as citrate). **Indication:** Management of breakthrough pain (BTP) in adult patients already receiving maintenance opioid therapy for chronic cancer pain. **Dosage and Administration:** Treatment should be initiated by and supervised by a physician experienced in opioid therapy in cancer patients. ***Adults;*** Initially one 100 mcg spray. If the initial dose is unsuccessful the dose may be titrated up to a maximum of two 400 mcg sprays (one in each nostril). No more than 4 doses should be taken per day. During titration and maintenance, patients should wait at least 4 hours before treating another BTP episode. PecFent should be discontinued immediately if the patient no longer experiences breakthrough pain 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 followed by the doctor in order to avoid the possibility of abrupt withdrawal effects. ***Elderly;*** Care should be exercised in use in the elderly. ***Children and adolescents;*** Safety and efficacy of PecFent is not established in patients under 18 years of age. **Adverse Effects:** The most serious adverse reactions include respiratory depression, circulatory depression, hypotension and shock. Common adverse reactions include disorientation, dysgeusia, dizziness, somnolence, headache, epistaxis, rhinorrhoea, nasal discomfort, vomiting, nausea, constipation and pruritus. Opioid withdrawal symptoms have been observed with transmucosal fentanyl. Prescribers should consult the summary of product characteristics for further details of side effects. **Precautions:** Patients and carers must be instructed to keep PecFent out of the sight and reach of children. Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids. A clinically significant risk of respiratory depression exists with fentanyl; chronic opioid use lowers this risk. Fentanyl use may cause more serious adverse reactions in patients with chronic obstructive pulmonary disease. Administer with extreme caution in patients with increased intracranial pressure or impaired consciousness. In head injury use only if clinically warranted. Use with caution in patients with previous or pre-existing bradyarrhythmias. Administer with caution in hepatic or renal impairment. Give careful consideration to patients with hypovolaemia and hypotension. PecFent contains propyl parahydroxybenzoate, which may cause allergy, and bronchospasm. As with other opioids, in absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered. **Interactions:** Inducers of CYP3A4 may reduce fentanyl activity. Concomitant use of strong or moderate CYP3A4 inhibitors may result in increased fentanyl plasma concentrations, and potentially cause serious adverse drug reactions. Possible symptoms of withdrawal on cessation are nausea, vomiting, diarrhoea, anxiety, chills, tremor and sweating. The development of a potentially life-threatening serotonin syndrome may occur with the concomitant use of serotonergic drugs. Serotonin syndrome may include mental-status changes, autonomic instability, neuromuscular abnormalities, and/or gastrointestinal symptoms. Discontinue PecFent if serotonin syndrome is suspected. PecFent is not recommended in patients receiving MAOIs within the previous 14 days. Concomitant use of partial opioid agonists/antagonists is not recommended. Concomitant use of nasal oxymetazoline has shown decreased fentanyl absorption; use of nasal vasoconstrictive decongestive agents during titration is not recommended. Other nasally administered products should be avoided within 15 minutes of PecFent use. **Pregnancy:** Long-term treatment may cause withdrawal symptoms in newborn infant. Do not use during labour and delivery. **Lactation:** Fentanyl passes into breast milk and should not be used by breastfeeding women. Breast-feeding should not be restarted until at least 5 days after the last administration of fentanyl. **Contraindications:** Hypersensitivity to the active substance or excipients. Use in opioid-naïvepatients. Severe respiratory depression or severe obstructive lung conditions. Treatment of acute pain other than BTP.

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Version-1-Approval by SFDA on April 2019