Patient Leaflet According to the Pharmacists' Regulations (Preparations) - 1986

This medicine is sold with a doctor's prescription only

Fenta SL 67, Fenta SL 133, Fenta SL 267
Fenta SL 400, Fenta SL 533, Fenta SL 800
Sublingual tablets

Active ingredient:
Fenta SL 67: each sublingual tablet contains fentanyl citrate equivalent to 67 mcg fentanyl.
Fenta SL 133: each sublingual tablet contains fentanyl citrate equivalent to 133 mcg fentanyl.
Fenta SL 267: each sublingual tablet contains fentanyl citrate equivalent to 267 mcg fentanyl.
Fenta SL 400: each sublingual tablet contains fentanyl citrate equivalent to 400 mcg fentanyl.
Fenta SL 533: each sublingual tablet contains fentanyl citrate equivalent to 533 mcg fentanyl.
Fenta SL 800: each sublingual tablet contains fentanyl citrate equivalent to 800 mcg fentanyl.

For a list of the other ingredients, please see section 6. See also 'Important information about some of the medicine's ingredients' in section 2.

Read this entire leaflet carefully before using this medicine.
This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for treating your condition. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.
This medicine is intended for adults over 18 years old.

Medicines of the opioids group may cause addiction, especially with prolonged use and they have a potential for misuse and overdose. A reaction to an overdose, may be manifested by slow breathing and may even cause death. Make sure you know the name of the medicine, the dosage that you take, how often you take it, the duration of treatment, potential side effects and risks.
Additional information regarding the risk of dependence and addiction can be found at the following link:
https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/risk/DocLib/opioids_en.pdf

Taking this medicine along with medicines from the benzodiazepines group, other medicines which depress the central nervous system (including drugs) or alcohol may cause a feeling of profound drowsiness, breathing difficulties (respiratory depression), coma and death.

1. What is the medicine intended for?

This medicine is used to relieve breakthrough pain in adult patients with cancer who are already receiving opioid therapy for relieving their persistent pain. Breakthrough pain is an additional, sudden pain that occurs even though your usual opioid pain-relieving medicines are taken.

Therapeutic group: opioid analgesics.

2. Before using the medicine

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient or to any of the other ingredients this medicine contains (for a list of the other ingredients, please see section 6).
- You are not treated regularly (every day on a regular schedule, for at least a week) with a prescribed opioid (e.g. codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine), to control your persistent pain. If you are not using any of these medicines, do not use Fenta SL, because it may increase the risk of your breathing becoming dangerously slow and/or shallow, or even stopping.
- You have severe breathing problems (such as severe respiratory depression) or if you suffer from severe obstructive lung disease.
- You are taking medicines of the monoamine oxidase inhibitor group (for the treatment of depression), or if you have taken such a medicine within the last two weeks.
- You suffer from short-term pain (acute), which is not a breakthrough pain.

Special warnings regarding the use of this medicine:

- **Fenta SL contains an active ingredient in an amount that can be life-threatening to a child. Therefore, keep all tablets out of the reach and sight of children and anyone other than the**

patient. Store the tablets in a locked place, and do not transfer the tablets to a different storage place, other than the blister package.

- Using opioids (including fentanyl) may cause dependence (physical and psychological) and also there is a potential for drug abuse. See boxed warning at the top of the leaflet.
- Prolonged use may cause tolerance to the medicine.
- Elderly patients may be more sensitive to the medicine's effects.

Before the treatment with Fenta SL (and during it) tell your doctor if:

- You are not stabilized yet on your other opioid therapy you receive for the relief of the persistent cancer pain.
- You suffer or have suffered in the past from breathing problems (such as asthma, wheezing, shortness of breath).
- You suffer or have suffered in the past from head injury, increased intracranial pressure, altered consciousness (such as clouded consciousness or loss of consciousness).
- You suffer or have suffered in the past from liver or kidney problems.
- You suffer or have suffered in the past from problems with your heart (especially slow or irregular heart rate, low blood volume or low blood pressure).
- You suffer from an inflammation or sores in the mucous membrane in your mouth.
- You take antipsychotics or antidepressants medicines (see section 'Drug Interactions').
- You experience pain, or increased sensitivity to pain (hyperalgesia), which do not respond to a higher dosage of the medicine as prescribed by your doctor.
- You experience a combination of the following symptoms: nausea, vomiting, loss of appetite/ anorexia, fatigue, weakness, dizziness and low blood pressure. These symptoms may be a sign of a potentially life-threatening condition called adrenal insufficiency, in which the adrenal glands do not produce enough hormones.
- You have ever developed adrenal insufficiency or lack of sex hormones (androgens) while using opioids.

Use in children:
This medicine is not intended for children and adolescents under 18 years old.

Tests and follow-up:

- During the dosage adjustment period, it is important to be medically monitored so that your response to this medicine can be checked.
- During the treatment, you should undergo periodic checkups to evaluate the continued need for this medicine.

Drug Interactions:
If you are taking or have recently taken any other medicines, including non-prescription medicines and nutrition supplements, please tell your doctor or pharmacist. Especially inform your doctor or pharmacist if you are taking the following medicines (it should be noted that the following list mentions the active ingredients of the medicines. If you are unsure whether you are using one of these medicines, please consult with your doctor or pharmacist):

- Medicines of the monoamine oxidase inhibitor group (for the treatment of depression): do not use Fenta SL if you are taking medicines from this group or if you have taken such a medicine within the last two weeks.
- Other medicines containing fentanyl that you were previously prescribed with for treating breakthrough pain.
- Medicines that affect the central nervous system, such as: sleeping pills, sedatives, medicines to treat anxiety (such as benzodiazepines), certain antihistamines, other opioids, anesthetics, phenothiazines, certain muscle relaxants, or any medicine which might cause sleepiness (have a sedative effect). See boxed warning at the top of the leaflet.
- Certain antipsychotics or antidepressants medicines (such as SSRIs or SNRIs): your doctor will decide if Fenta SL is suitable for you. The risk of side effects may increase if taken concomitantly with Fenta SL. These reactions are part of serotonin syndrome, and include changes in mental state (agitation, hallucinations, coma); body temperature above 38˚C, increase in heart rate, unstable blood pressure, exaggeration of reflexes, muscular rigidity, lack of coordination, gastrointestinal symptoms (e.g. nausea, vomiting, diarrhea). If you experience these reactions, contact your doctor immediately.
- Medicines that might influence the way your body breaks down the medicine and as a result affect the medicine's activity:
  - Medicines that inhibit the breakdown of Fenta SL, such as: medicines for treating HIV infection/AIDS (such as ritonavir, indinavir, nelfinavir, saquinavir); medicines for treating fungal infections (such as ketoconazole, itraconazole, or fluconazole); medicines for treatment of bacterial infections (such as clarithromycin, erythromycin, telithromycin, which are macrolide antibiotics); medicines for treatment of high blood pressure or heart diseases (such as diltiazem or verapamil from the calcium channel

blockers group); medicines used against severe nausea (such as aprepitant, dronabinol); fluoxetin (an antidepressant); cimetidine (medicine for treating heartburn and indigestion).

- Medicines that induce the breakdown of Fenta SL, such as: rifampicin, rifabutin (to treat tuberculosis); barbiturates (such as phenobarbital); carbamazepine, oxcarbazepine, phenytoin (anticonvulsants); certain anti-viral medicines (such as nevirapine, efavirenz); anti-inflammatory or immunosuppressive medicines such as glucocorticosteroids; medicines for the treatment of diabetes such as pioglitazone; modafinil (used among other things to treat drowsiness); medicines containing hypericum plant (St. John's wort) for treating depression.
- Other types of strong medicines for treating pain (partial agonist/antagonists) e.g. buprenorphine, pentazocine, nalbuphine: you may experience withdrawal symptoms such as nausea, vomiting, diarrhea, anxiety, chills, tremor and sweating while using these medicines.

Use of this medicine and food:

- Fenta SL may be taken before or after, but not during, meals. You may drink some water before taking the medicine to help moisten your mouth, but you should not drink or eat anything while taking the medicine.
- You should not drink grapefruit juice during the treatment with Fenta SL, because it may affect the way your body breaks down the medicine.

Use of this medicine and alcohol consumption:
Do not drink alcohol during the treatment with Fenta SL. It can increase the risk of experiencing dangerous side effects.

Pregnancy and breast-feeding:
If you are pregnant, think you may be pregnant, planning to get pregnant or are breast-feeding, consult your doctor before taking this medicine:

- Do not use Fenta SL during pregnancy without consulting your doctor. Prolonged use during pregnancy may cause withdrawal symptoms in the newborn.
- Do not use Fenta SL during childbirth because fentanyl may cause respiratory depression and withdrawal symptoms in the fetus or in the newborn.
- Do not use Fenta SL if you are breast-feeding. Fentanyl can pass into breast milk and may cause side effects in the breastfed infant (such as sedation, respiratory depression). You should not breast-feed for at least 5 days after the last dose of the medicine.

Driving and use of machinery: You should consult your doctor regarding the safety of driving or operating machinery during the treatment with this medicine, because it may affect your ability to perform these actions. It is important that you know how you react to this medicine before driving or operating machinery. Do not drive or operate machinery if you experience side effects such as: sleepiness or dizziness; vision disorders such as blurred or double vision; concentrating difficulties.

Important information about some of the medicine's ingredients:
Each tablet contains 0.651 mg sodium. To be taken into consideration if you are on a low sodium diet.

3. How to use this medicine?

Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure regarding the dosage and the manner of treatment with the medicine.
The dosage and the manner of treatment will be determined by the doctor only.
The medicine is intended for sublingual use (under the tongue) see 'Instructions for use'.

The standard dosage is usually:
Initial phase: your doctor will set for you, the dose that could treat a breakthrough pain episode. You may need to try different strengths of tablets (over a number of episodes of breakthrough pain) until the doctor will determine the most appropriate dose for you. Sometimes, in order to do so your doctor may instruct you to take two tablets. Do not take two tablets, unless your doctor instructs you to, as this may result in overdose.
Maintenance phase: once the most appropriate dose that controls your breakthrough pain has been found, do not take this dose more than 4 times a day. The dose may consist of more than one tablet.
If you think that the dose you are taking is not controlling your breakthrough pain, refer to your doctor.

Do not exceed the recommended dose. Do not change your dose, unless instructed by your doctor.

If your doctor has switched you to Fenta SL after using another medicine that contains fentanyl, do not use both medicines concurrently to treat breakthrough pain. Nevertheless, you should continue taking the opioids medicines that you take to relieve the persistent cancer pain, while you are taking Fenta SL.

Instructions for use:

The medicine is intended for sublingual use. This means that the tablet is taken by placing it under the tongue, where it dissolves rapidly and allows the active ingredient (fentanyl) to be absorbed through the lining of the mouth.
When you experience a breakthrough pain, take the dose determined by your doctor, as follows:

- If your mouth is dry, take a sip of water to moisten it. Swallow or spit out the water.
- Remove the tablets from the blister pack immediately before use.
- Peel the aluminum foil from the back of the blister and remove the tablet. Do not try to push the tablet through the foil.
- Place the tablet under your tongue as far back as you can and let it dissolve completely.
- The tablet dissolves rapidly under your tongue and is absorbed, thus providing pain relief. Therefore do not suck, chew or swallow the tablet.
- If after 30 minutes, pieces of the tablet remain, they may be swallowed.
- You should not drink or eat until the tablet has completely dissolved under your tongue.

If you have accidentally taken a higher dosage: remove any remaining pieces of tablets from your mouth and tell another person what has happened. Proceed immediately to a doctor or a hospital for consultation and treatment. Bring the package of the medicine with you. Symptoms of overdose include: altered mental status, loss of consciousness, extreme drowsiness, slow and shallow breathing. If you experience these symptoms, seek emergency medical assistance immediately.

Note to caregivers/ accompanying people: while waiting for medical assistance, try to keep the patient awake by talking to or shaking her/him now and then. Make sure the patient's airways are clear and that the patient is breathing.

If a child or a person other than the patient has used the medicine or swallowed it, seek emergency medical assistance immediately. Also see note to caregivers/ accompanying people, above.

If you forgot to take the medicine: do not take a double dose, to compensate for the forgotten dose.

Continue with the treatment as recommended by the doctor. If you think that you are no longer experiencing breakthrough pain episodes, contact your doctor, who will advise you about continued use of this medicine.

Even if your state of health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

If you stop taking the medicine: continue taking your usual medicines for relieving the persistent pain, as instructed by your doctor. You may occasionally experience withdrawal symptoms (see section 'Side effects').

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have any further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of Fenta SL may cause side effects in some users. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

Stop the treatment and refer immediately to the doctor or a hospital emergency room if the following serious side effects occur:

- Severe breathing problems (such as respiratory depression).
- Low or extremely low blood pressure and shock.
- If you become very sleepy.

Additional side effects:

Very common side effects (appear in more than one user out of ten):
Nausea, constipation; sleepiness, sedation, dizziness.
Common side effects (appear in 1-10 users out of 100):
Confusion, anxiety, seeing or hearing things that are not really there (hallucinations), abnormal thoughts; weakness, headache, muscle spasms, dizziness or spinning sensation (vertigo), loss of consciousness, dry mouth, taste alteration, low blood pressure, vomiting, abdominal pain, digestive disturbances or indigestion; sweating, itchy skin; accidental injury (for example, falls).
Uncommon side effects (appear in 1-10 users out of 1,000):
Decreased appetite, flatulence, abdominal bloating, tooth decay, blockage of the gut (ileus); generally feeling unwell; changes in sensation such as numbness, sensory over-sensitivity, or tingling (also around the mouth),

difficulty coordinating movements, convulsion (fits), coma, abnormal dreams, feeling detached, depression, mood swings, euphoria, shortness of breath, vision alteration such as blurred or double vision, skin rash, increased or altered sensitivity to touch; difficulty passing urine (urinary retention).
Side effects of unknown frequency (effects whose frequency has not yet been determined):

Flushing, feeling warm (hot flushes), diarrhea, receding gums, tooth loss, fatigue, swelling of arms and legs (edema), insomnia, fever; withdrawal symptoms such as: nausea, vomiting, diarrhea, anxiety, chills, tremor and sweating; drug dependence (addiction), drug abuse; withdrawal symptoms which can be life-threatening in babies born to mothers who used the medicine for a prolonged period during the pregnancy. See section 'Pregnancy and breast-feeding'.

If a side effect appears, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with your doctor.

Side effects can be reported to the Ministry of Health (MoH) by clicking on the link "Report on side effects following medicinal treatment" on the MoH home page (www.health.gov.il) which refers to the online form for side effects reporting, or by entering the link:

https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

5. How to store the medicine?

- Avoid poisoning! This medicine **especially**, and any other medicine, **must be stored in a safe and locked place out of the reach and sight of children and/or infants to avoid poisoning, that might cause life-threatening harm**. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions: store below 25°C, in the original package, in order to protect from light.
  Do not transfer the tablets to a different storage place, other than the blister package.
- When you no longer need the tablets consult your pharmacist about how to dispose of them.

6. Additional information

In addition to the active ingredient, the medicine also contains the following ingredients:

Calcium hydrogen phosphate anhydrous, microcrystalline cellulose PH200, disodium phosphate anhydrous, hypromellose, macrogol 6000, macrogol 8000, magnesium stearate, maltodextrin, titanium dioxide, triacetin, printing ink (shellac, iron oxide black).

What does the medicine look like and what does the package contain?

Fenta SL 67: white tablet, triangular, convex, printed with '0' in black on one side.

Fenta SL 133: white tablet, triangular, convex, printed with '1' in black on one side.

Fenta SL 267: white tablet, triangular, convex, printed with '2' in black on one side.

Fenta SL 400: white tablet, triangular, convex, printed with '4' in black on one side.

Fenta SL 533: white tablet, triangular, convex, printed with '5' in black on one side.

Fenta SL 800: white tablet, triangular, convex, printed with '8' in black on one side.

The tablets are available in a peelable, child resistant blister. The package contains 30 tablets.

Registration holder: Rafa Laboratories Ltd., P.O.Box 405, Jerusalem 9100301.

Manufacturer: Ethypharm, Saint-Cloud Cedex, France

Medicine registration number in the National Medicines Registry of the Ministry of Health:

Fenta SL 67 Sublingual tablets: 157-04-34567

Fenta SL 133 Sublingual tablets: 157-05-34575

Fenta SL 267 Sublingual tablets: 157-06-34576

Fenta SL 400 Sublingual tablets: 157-07-34577

Fenta SL 533 Sublingual tablets: 157-08-34578

Fenta SL 800 Sublingual tablets: 157-09-34579

This leaflet was checked and approved by the Ministry of Health in September 2016, and was updated according to the guidelines of the Ministry of Health in January 2019.

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