PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
The medicine is dispensed with a doctor's prescription only

Fentora® 100 microgram
Buccal tablets
For oromucosal use
Composition
Each tablet contains:
Fentanyl (as citrate) 100 microgram

Fentora® 200 microgram
Buccal tablets
For oromucosal use
Composition
Each tablet contains:
Fentanyl (as citrate) 200 microgram

Fentora® 400 microgram
Buccal tablets
For oromucosal use
Composition
Each tablet contains:
Fentanyl (as citrate) 400 microgram

Fentora® 600 microgram
Buccal tablets
For oromucosal use
Composition
Each tablet contains:
Fentanyl (as citrate) 600 microgram

Fentora® 800 microgram
Buccal tablets
For oromucosal use
Composition
Each tablet contains:
Fentanyl (as citrate) 800 microgram

For information on the inactive and allergenic ingredients in the medicine, see section 2 – "Important information about some of the ingredients of the medicine" and section 6 – "Further Information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.
This medicine is not intended for use in children and adolescents under 18 years of age.

Taking this medicine with benzodiazepines, other central nervous system depressants (including drugs) or alcohol, may cause a sensation of severe sleepiness, breathing difficulties (respiratory depression), coma and death.

Medicines from the opioid group may cause addiction, especially with prolonged use, and have the potential for misuse and overdose. An overdose reaction can be manifested by slow breathing and can even cause death.
Make sure that you are familiar with the name of the medicine, the dosage you take, the frequency of administration, the duration of treatment, the side effects and the potential risks. Additional information about 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

1. WHAT IS THE MEDICINE INTENDED FOR?
To treat breakthrough pain in adult patients with cancer who are already being regularly treated with other opioid medicines for their persistent (around-the-clock) cancer pain.
Breakthrough pain is additional and sudden pain that occurs despite your routine use of an opioid pain-relieving medicine.

Therapeutic group: Opioid analgesics.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are not taking pain-relieving opioids on a daily basis (e.g., codeine, fentanyl, hydromorphone, morphine, oxycodone, pethidine) for at least one week to control your persistent pain. If you are not taking pain-relieving opioids regularly, you **must not** use Fentora because it may increase the risk that breathing could become dangerously slow and/or shallow, or even stop.
- You are sensitive (allergic) to the active ingredient fentanyl, or to any of the additional ingredients contained in the medicine (see section 6 – "Further Information").
- You are suffering from severe breathing difficulties or severe obstructive pulmonary diseases.
- You are suffering from short-term pain that is not breakthrough pain.

Special warnings regarding use of the medicine
Continue taking the medicine intended to relieve the persistent cancer pain while using Fentora.
During the course of treatment with Fentora, do not use other fentanyl-containing medicines previously prescribed to relieve your breakthrough pain. If you have such medicines in your possession, consult the pharmacist about how to dispose of medicines that are no longer needed.
Repeated use of the medicine may result in the medicine being less effective (you become accustomed to it) or you becoming dependent on it.

Before treatment with Fentora, tell the doctor if:
- The optimal dosage of your opioid medicine intended to relieve your persistent cancer pain has not yet been found.
- You are suffering from any condition which may affect your respiratory system (e.g., asthma, wheezing or shortness of breath).
- You have a head injury.
- You have an abnormally slow heart rate or other heart problems.
- You have a liver or kidney problem, as these organs affect the process through which the medicine is broken down in your body.
- You have a low amount of fluid in the blood circulation or low blood pressure.
- You are over 65 years of age – you may need a lower dosage and each dosage increase will be carefully evaluated by your doctor.
- You are suffering from heart problems, especially from a slow heart rate.
- You are using benzodiazepines (see section 2 under "Drug interactions"). Use of benzodiazepines can increase the chance of onset of serious side effects, including death.
- You are using antidepressants or antipsychotics (selective serotonin reuptake inhibitors [SSRIs], serotonin and norepinephrine reuptake inhibitors [SNRIs], monoamine oxidase [MAO] inhibitors – see section 2 under "Drug interactions"). Use of these medicines together with Fentora can lead to serotonin syndrome, a condition that may be life-threatening (see section 2 under "Drug interactions").
- You have suffered in the past from adrenal gland insufficiency, a condition in which the adrenal glands do not produce enough hormones, or sex hormone deficiency (androgen deficiency) when using opioids (see section 4 under "Severe side effects").
- You have ever abused or been dependent on opioids or any other medicine, alcohol or illegal drugs.
- You drink alcohol (see section 2 under "Use of the medicine and alcohol consumption").

Consult your doctor while using the medicine if:
- You experience pain or increased sensitivity to pain (hyperalgesia) which does not respond to the higher dosage of the medicine as determined by your doctor.
- You experience a combination of the following symptoms: nausea, vomiting, drastic drop in appetite, tiredness, weakness, dizziness and low blood pressure. The combination of these symptoms may indicate a potentially life-threatening condition called adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones.

Refer for immediate medical assistance if:
- You experience symptoms such as difficulty breathing or dizziness, swelling of the tongue, lips or throat while using Fentora. These may be early symptoms of severe allergic reactions (anaphylaxis, hypersensitivity, see section 4 under "Severe side effects").

What to do if someone accidentally took Fentora
If you think that someone accidentally took Fentora, immediately seek medical assistance. Try to keep the person awake until medical assistance arrives.
If someone accidentally took Fentora, the side effects that may appear are identical to those detailed in section 3 under "If you accidentally took a higher dosage".

Children and adolescents
This medicine is not intended for use in children and adolescents under 18 years of age.

Drug interactions
If you are taking, or have recently taken, other medicines including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. In particular, if you are taking:
- Concomitant use of Fentora and sedatives, such as benzodiazepines or similar medicines increase the risk of sleepiness, breathing difficulties (respiratory depression), coma and may be life-threatening. For this reason, concomitant use must only be considered when other treatment options are not possible. However, if your doctor prescribed Fentora together with sedatives, the dosage and duration of the combined treatment will be limited by your doctor.
- Tell the doctor about any sedative you are taking (e.g., sleeping pills, medicines to treat anxiety, certain medicines to treat allergic reactions [antihistamines] or other tranquilizers) and strictly follow your doctor's recommendation. It is recommended that you explain to your friends and relatives how to identify the signs and symptoms described above. Contact your doctor when you experience these symptoms.
- Certain muscle relaxants, e.g., baclofen, diazepam (also see section 2 under "Special warnings regarding use of the medicine").
- Medicines that affect the process by which Fentora is broken down in the body, such as ritonavir, nelfinavir, amprenavir and fosamprenavir (to treat HIV infection), other medicines of the CYP3A4 enzyme inhibitor type, such as ketoconazole, itraconazole or fluconazole (for treatment of fungal infections), troleandomycin, clarithromycin or erythromycin (antibiotics to treat bacterial infections), aprepitant (to treat severe nausea), diltiazem and verapamil (medicines for treatment of high blood pressure or heart diseases).
- Medicines of the monoamine oxidase inhibitor type (MAO inhibitors) (to treat depression) or if you have used these medicines in the last two weeks.
- Certain medicines for treatment of strong pain belonging to the partial opioid agonist/antagonist group such as buprenorphine, nalbuphine, and pentazocine (medicines to treat pain). You may experience withdrawal symptoms (nausea, vomiting, diarrhea, anxiety, chills, tremor, and sweating) while using these medicines.
- The risk of side effects increases if you are taking certain medicines such as antidepressants or antipsychotics. A drug interaction may occur with Fentora, which causes mood changes (e.g., restlessness, hallucinations, coma), and other effects such as a rise in body temperature above 38°C, increase in heart rate, unstable blood pressure, exaggeration of reflexes, muscle rigidity, lack of coordination and/or digestive system effects (e.g., nausea, vomiting, diarrhea). The doctor will consider whether Fentora is suitable for you.

Use of the medicine and food
- Take Fentora before or after, but not during, meals. You may drink some water before taking Fentora to moisten your mouth, but do not drink or eat while taking Fentora.
- Avoid drinking grapefruit juice during the course of treatment with Fentora because it may affect the process through which Fentora is broken down in the body.

Use of the medicine and alcohol consumption
- Do not drink alcohol during the course of treatment with Fentora, since it may increase the chance of severe side effects, including death.

Pregnancy and breastfeeding
If you are pregnant, breastfeeding, think you are pregnant, or are considering becoming pregnant, consult the doctor or pharmacist before using the medicine.
Pregnancy
Do not use Fentora during pregnancy unless you have consulted your doctor.
If Fentora is used for a long time during pregnancy, there is risk of the newborn having withdrawal symptoms, which may be life-threatening if not identified and treated by the doctor.
Do not use Fentora during childbirth since fentanyl (the active ingredient) may cause respiratory system depression in the newborn baby.
Breastfeeding
Fentanyl may be secreted into the breast milk and therefore, may cause side effects in the breastfeeding baby. Do not use Fentora if you are breastfeeding. Do not start to breastfeed for at least 5 days after taking the last dose of Fentora.

Driving and operating machinery
Consult your doctor to determine if you can drive or operate machinery after taking Fentora. Do not drive or operate machinery if you are feeling sleepy or are dizzy, have blurred or double vision, or if you have difficulty in concentrating. It is important that you know how you respond to Fentora before driving or operating machinery.

Important information about some of the ingredients of the medicine
Fentora 100 mcg:
This medicine contains 10 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 0.5% of the recommended maximum daily dietary intake of sodium for an adult.
Fentora 200 mcg, 400 mcg, 600 mcg, 800 mcg:
This medicine contains 20 mg sodium (main component of cooking/table salt) in each tablet. This is equivalent to 1% of the recommended maximum daily dietary intake of sodium for an adult.

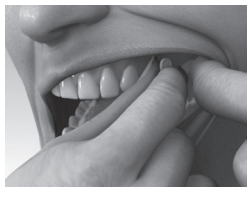
3. HOW SHOULD YOU USE THE MEDICINE?
Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

Dosage and frequency of taking the medicine
When starting treatment with Fentora, the doctor will determine, with your assistance, the appropriate dosage to relieve the breakthrough pain. It is very important to precisely follow the instructions for use of Fentora, as provided by your doctor. The initial dosage is 100 mcg (microgram). When determining the dosage appropriate for you, the doctor may give you more than one tablet in each breakthrough pain episode. If you do not feel relief of the breakthrough pain within 30 minutes, use **only one** more Fentora tablet during the dosage adjustment period.
As a rule of thumb, once the right dosage has been determined for you, take one tablet for each breakthrough pain episode.
During treatment, your need for analgesia may change. Higher dosages may be necessary. If you took one tablet and your breakthrough pain is not relieved within 30 minutes, use **only one** more Fentora tablet.
Consult your doctor if the dosage of Fentora determined for you does not relieve your breakthrough pain. Your doctor will consider whether the dosage should be changed.
Wait at least 4 hours before taking Fentora again to treat breakthrough pain.
Tell your doctor immediately if you are using Fentora more than 4 times per day, as there may be a need to change your dosage regimen. The doctor may change the treatment for persistent pain; when your persistent pain is controlled, the doctor may consider changing your Fentora dosage. If your doctor suspects that you developed Fentora-related increased sensitivity to pain (hyperalgesia), he may consider lowering the Fentora dosage (see section 2 under "Special warnings regarding use of the medicine"). To obtain the most effective relief, tell your doctor about your pain and how Fentora works for you, so that the dosage can be adjusted if needed.
Do not change the dosages of Fentora or of your other pain-relieving medicines on your own. Any change in dosage must be recorded and monitored by your doctor.

Do not exceed the recommended dose.
If you are not sure about the appropriate dosage, or if you have questions related to taking the medicine, you should refer to your doctor.

Mode of administration
Fentora tablets are tablets for oromucosal administration. After placing the tablet in the oral cavity, the tablet dissolves and the medicine is absorbed through the mucosal membrane of the mouth into the blood system. This mode of administration allows for rapid absorption that helps relieve breakthrough pain.

How to take
- Open the blister package only when you are ready to take the tablet. Use the tablet immediately after removing it from the blister.
- Separate one of the blister units from the blister tray by tearing at the perforations.
- Bend the blister unit along the line as marked.
- Peel the blister backing to expose the tablet. Do not attempt to push the tablet through the blister – this may damage the tablet.
- Remove the tablet from the blister unit and **immediately** place the entire tablet near a molar tooth between the gums and the cheek (see the picture). Alternatively, the doctor may recommend that you put the tablet under the tongue.
- Do not attempt to crush or split the tablet.
- Do not bite, suck, chew or swallow the tablet, as this will result in a reduced pain relief effect, in comparison to a tablet taken as directed.
- Leave the tablet between the cheek and gums until dissolved – which usually takes approximately 14-25 minutes.
- You may feel a gentle bubbling sensation between the cheek and gums as the tablet dissolves.
- If you experience irritation, you may change the position of the tablet on the gums.
- If, after 30 minutes, pieces of the tablet remain after dissolving, they can be swallowed with a glass of water.



If you accidentally took a higher dosage
- The most common side effects are feeling sleepy, sick, or dizzy. If you start to feel very dizzy or extremely fatigued before the tablet completely dissolves, you should rinse your mouth with water and immediately spit the remaining pieces of the tablet into the sink or toilet.
- A serious side effect of Fentora is slow and/or shallow breathing. This may occur in cases of a higher dosage of Fentora or when taking a large quantity of Fentora. If this occurs, seek immediate medical assistance.

If you forgot to take the medicine
If the breakthrough pain is still ongoing, take Fentora as prescribed by your doctor. If the breakthrough pain disappeared, do not take Fentora until recurrence of breakthrough pain. Adhere to the treatment regimen as recommended by the doctor.

If you stop taking the medicine
Stop taking the medicine if you do not experience breakthrough pain. However, you should continue taking your usual opioid pain reliever to treat the persistent cancer pain, as recommended by your doctor. When you stop taking Fentora, you may experience withdrawal symptoms similar to the side effects of Fentora (see section 4 "Side Effects", under the description "Withdrawal symptoms of the medicine"). If you experience withdrawal symptoms or if you have any doubt about relieving your pain, consult the doctor, who will consider prescribing a medicine that relieves or stops the withdrawal symptoms.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS
As with any medicine, use of Fentora may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Severe side effects
- **The most severe side effects include shallow breathing, low blood pressure, and shock. Like other fentanyl-containing medicines, Fentora may cause severe breathing problems, which may cause death. If you experience extreme fatigue or are suffering from slow and/or shallow breathing, you or your caretaker must refer immediately to a doctor or receive emergency medical care.**
- **Refer to a doctor immediately if you experience a combination of the following symptoms:**
  Nausea, vomiting, extreme drop in appetite, tiredness, weakness, dizziness and low blood pressure. When these symptoms occur together, they can be indicative of a life-threatening condition called adrenal insufficiency, a condition in which the adrenal glands do not produce enough hormones.

Additional side effects
Very common side effects (affect more than 1 in 10 patients)
- Dizziness, headache.
- Feeling nauseous, vomiting.
- Effects relating to the location of the tablet in the mouth: pain, ulcer, irritation, bleeding, numbness, redness, swelling or spots.

Common side effects (affect up to 1 in 10 patients)
- Feeling anxious or confused, depression, insomnia.
- Abnormal taste, weight loss.
- Sleepiness, sedation, excessive tiredness, weakness, migraine, numbness, swelling of hands or legs, symptoms of withdrawal from the medicine (can manifest by the following side effects: nausea, vomiting, diarrhea, anxiety, chills, tremor, and sweating), tremors, falls, chills.
- Constipation, inflammation in the mouth, dry mouth, diarrhea, heartburn, lack of appetite, abdominal pain, stomach discomfort, indigestion, toothache, oral thrush.
- Itching, excessive sweating, rash.
- Shortness of breath, sore throat.
- Decrease in white blood cells, decrease in red blood cells, decrease or increase in blood pressure, fast and abnormal heart rate.
- Muscle pain, back pain.
- Fatigue.

Uncommon side effects (affect up to 1 in 100 patients)
- Sore throat.
- Decrease in blood cells that help in the blood clotting process.
- Feeling elated, nervous, abnormal feeling, tense feeling or fuzzy thinking, seeing or hearing things that do not exist (hallucinations), reduced awareness, change in mental state, dependence (addiction to the medicine), disorientation, lack of concentration, balance problems, vertigo, speech problems, ringing in the ears, ear discomfort.
- Disturbed or blurred vision, red eyes.
- Unusually slow heart rate, hot flushes.
- Severe breathing difficulties, breathing disturbances during sleep.
- One or more of the following problems in the mouth: ulcer, numbness, discomfort, discoloration, impaired soft tissue function, impaired tongue function, pain or blisters or ulcers on the tongue, gum pain, chapped lips, tooth problems.
- Inflammation of the esophagus, paralysis of the gut, impaired gallbladder function.
- Cold sweat, swollen face, generalized irritation, hair loss, muscle twitching, muscle weakness, feeling unwell, chest discomfort, thirst, feeling cold, feeling hot, difficulty passing urine.
- Malaise.
- Flushing.

Rare side effects (affect up to 1 in 1,000 patients)
- Disturbances in thinking, movement disturbances.
- Blisters in the mouth, dry lips, collection of pus under the skin in the mouth.
- Lack of testosterone, strange sensation in the eye, seeing flashes of light, brittle nails.
- Allergic reactions such as rash, redness, swelling of the lips and face, skin allergy (urticaria).

Side effects occurring at a low frequency, but whose exact frequencies are not known:
- Loss of consciousness, cessation of breathing, seizures.
- Reduced sex hormones (androgen deficiency).
- Drug dependency (addiction).
- Drug abuse.
- 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 use of fentanyl during pregnancy may cause withdrawal symptoms in the newborn, which may be life-threatening (see section 2 under "Pregnancy and breastfeeding").

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

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link:
https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?
- Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Store below 25°C. Keep in original packaging to protect from moisture.**
- Do not discard medicines in the wastewater or household waste bin. Ask the pharmacist how to discard of medicines that are no longer in use. These measures will help protect the environment.

6. FURTHER INFORMATION
In addition to the active ingredient, the medicine also contains:
mannitol, sodium hydrogen carbonate, citric acid, sodium carbonate, sodium starch glycolate (type A), magnesium stearate.

What the medicine looks like and the contents of the package
Fentora 100 mcg: a round, white and flat tablet, with beveled edges, with "C" debossed on one side and the number "1" debossed on the other side.
Fentora 200 mcg: a round, white and flat tablet, with beveled edges, with "C" debossed on one side and the number "2" debossed on the other side.
Fentora 400 mcg: a round, white and flat tablet, with beveled edges, with "C" debossed on one side and the number "4" debossed on the other side.
Fentora 600 mcg: a round, white and flat tablet, with beveled edges, with "C" debossed on one side and the number "6" debossed on the other side.
Fentora 800 mcg: a round, white and flat tablet, with beveled edges, with "C" debossed on one side and the number "8" debossed on the other side.
The tablets are packaged in blisters; each package contains 4 or 28 tablets.
Not all package types may be marketed.

Name of License Holder and its Address
Abic Marketing Ltd. (from the Teva Group), P.O.B. 8077, Netanya.
Name of Manufacturer and its Address
Cephalon Inc., West Chester, Pennsylvania, USA.
Revised in February 2021 according to MOH guidelines.
Registration numbers of the medicine in the National Drug Registry of the Ministry of Health:
Fentora 100 microgram - buccal tablets: 152.90.34050
Fentora 200 microgram - buccal tablets: 152.91.34051
Fentora 400 microgram - buccal tablets: 152.92.34052
Fentora 600 microgram - buccal tablets: 152.93.34053
Fentora 800 microgram - buccal tablets: 152.94.34054

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