Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

JEVTANA

Concentrate and solvent for solution for infusion

Name and concentration of active ingredient:
Each vial of 1.5 mL of concentrate contains 60 mg cabazitaxel

Inactive ingredients and allergens: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine, and every time before you receive another treatment with this medicine.
This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed for you. 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.

Neutropenia (reduced number of white blood cells): may cause severe infections and lead to death. Your doctor will check your white blood cell counts regularly during your treatment with JEVTANA. Do not use JEVTANA if your white blood cell count ≥ 1500 cells/mm^3. Your doctor may prescribe a medicine for you called G-CSF to prevent complications, if your white blood cell count is too low.
Severe hypersensitivity (allergy): Hypersensitivity reactions may occur and may include rash, skin redness, low blood pressure, bronchospasm. Severe hypersensitivity reaction requires immediate discontinuation of the JEVTANA infusion and suitable treatment. Your doctor will give you a medicine before your infusion. Do not use JEVTANA if you have ever had a severe allergic reaction to cabazitaxel or to other medicines containing polysorbate 80.

1. What is this medicine intended for?

JEVTANA is used in combination with prednisone (a steroid medicine) to treat patients with metastatic castration-resistant prostate cancer (resistant to medical or surgical treatments that lower testosterone) who have been treated with another therapy that includes docetaxel.

Therapeutic group:
JEVTANA is an anti-tumor medicine that belongs to a group of medicines called taxanes.

Mechanism of action
JEVTANA works by stopping cells from growing and multiplying.

2. Before using this medicine

Do not use this medicine if:

- your white blood cell count (neutrophils) is too low (a count that is less than or equal to 1,500 cells/mm^3)
- you have or ever had a severe allergic reaction to cabazitaxel or other medicines that contain polysorbate 80, or to any of the other ingredients of this medicine (see section 6). Ask your doctor if you are not sure.
- you have serious liver problems

Special warnings about using this medicine
JEVTANA may cause serious side effects including:

- **Low level of white blood cell count:** Low level of white blood cell count is common during treatment with JEVTANA and can cause serious infections that may lead to death. Men who are 65 years or older may be more likely to have these problems.
  Your doctor
  - will check your white blood cell counts regularly during your treatment with JEVTANA;
  - may lower your dose of JEVTANA, change how often you receive JEVTANA, or stop JEVTANA treatment until your doctor decides that you have enough white blood cells;
  - may prescribe a medicine for you called G-CSF to help prevent complications if your white blood cell count is too low.

  Tell your doctor right away if you have any of the symptoms of infection (see the section 'Side effects').
  Tell your doctor if you have any diarrhea during the time that your white blood cell count is low. Your doctor will prescribe treatment for you as needed.
- **Severe hypersensitivity (allergic) reactions:** Severe hypersensitivity reactions can happen within a few minutes after your infusion of JEVTANA starts, especially during the first and second treatments. Your doctor should prescribe medicines before each infusion to help prevent severe allergic reactions. Tell your doctor or nurse right away if you have any symptom of a severe allergic reaction (see the section 'Side effects') during or soon after an infusion of JEVTANA:
- **Severe stomach and intestine (gastrointestinal) problems:**
  - **JEVTANA can cause severe vomiting and diarrhea, which may lead to death.** Severe vomiting and diarrhea with JEVTANA treatment can lead to loss of too much body fluid (dehydration) or too much of your body salts (electrolytes). There are reports of deaths as a result of this condition. You may need to go to a hospital for treatment. Your doctor will prescribe medicines to prevent or treat vomiting and diarrhea, as needed. **Tell your doctor right away** if you develop vomiting or diarrhea or if your symptoms get worse or do not get better.
  - **JEVTANA can cause a leak in the stomach or intestine, intestinal blockage, infection, and bleeding in the stomach or intestine, which may lead to death.**

  The risk of this may be increased with neutropenia, patient age, steroid use, concomitant use of NSAIDs (nonsteroidal anti-inflammatory drugs), antiplatelet therapy or anticoagulants, and in patients with a prior history of pelvic radiotherapy, adhesions, ulceration and bleeding in the digestive system.
  Tell your doctor if you develop any of the symptoms of stomach or intestine problems (see the section 'Side effects').
- **Kidney failure:** may happen with JEVTANA because of severe infection, loss of too much body fluid (dehydration), and other reasons, which may lead to death. Your doctor will check you for this problem and treat you if needed. Tell your doctor if you develop any signs or symptoms of kidney failure (see the section 'Side effects').
- **Inflammation of the bladder and blood in the urine:** Blood in the urine is common with JEVTANA treatment, but it can be severe in some cases. People who have had pelvic radiation in the past may develop inflammation of the bladder and blood in the urine that are severe enough that they need to be hospitalized for medical treatment or surgery. Your doctor will check you for these problems during treatment with JEVTANA. Your doctor may stop your treatment with JEVTANA for a short time, or permanently, if you develop inflammation of the bladder and bleeding that is severe.
  Tell your doctor if you have blood in your urine, burning or pain during urination, or frequent or urgent need to urinate.
- **Lung or breathing problems:** Lung problems (pneumonia, interstitial lung disease) or breathing problems may happen with JEVTANA and may lead to death. Men who have lung disease before receiving JEVTANA may have a higher risk for developing lung or breathing problems with JEVTANA treatment. Your doctor will check you for this problem and treat you if needed. Tell your doctor right away if you develop any new or worsening symptoms (see the section 'Side effects').

Before treatment with JEVTANA, tell your doctor if:

- you are over the age of 65
- you have had allergic reactions in the past
- you have kidney or liver problems
- you have lung problems
- you are pregnant or plan to become pregnant. JEVTANA can cause harm to your unborn baby (miscarriage).
- you are a male and your female partner is fertile (able to become pregnant). Men should use effective birth control during treatment with JEVTANA and for four months after the last dose of JEVTANA.

Children and adolescents:
It is not known if JEVTANA is safe and effective in children.

Tests and follow-up:
You will be referred for blood tests regularly to check your blood cell counts during your treatment with JEVTANA.

Interactions with other medicines:
If you are taking, have recently taken, or might take other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.
JEVTANA can interact with many other medicines. Do not take any new medicine without asking your doctor first. Your doctor will tell you if it is safe to take the new medicine with JEVTANA.
Particularly, tell your doctor if you are taking:
- ketoconazole, itraconazole, voriconazole (for fungal infection)
- clarithromycin, telithromycin (antibiotics for infections)
- atazanavir, indinavir, nelfinavir, ritonavir, saquinavir (for HIV)
- nefazodone (for depression)

These medicines may increase the concentration of JEVTANA in your plasma.
- rifampicin (for tuberculosis) — may reduce the concentration of JEVTANA in your plasma.

Pregnancy, breastfeeding, and fertility
There is no information regarding the safety and the efficacy of the use of JEVTANA in women.
Pregnancy and breastfeeding
JEVTANA may harm your unborn baby or cause loss of pregnancy. There is no information about using JEVTANA while breastfeeding.

Fertility
- Males with a female partner of reproductive potential should use effective contraception during treatment with JEVTANA and for four months after the last dose of JEVTANA.
- Treatment with JEVTANA can cause fertility problems in men which may affect your ability to father a child. Talk to your doctor if you are concerned about this.

Driving and using machines
You may feel tired or dizzy during JEVTANA treatment. If this happens, do not drive or use any tools or machines until you feel better.

Important information about some of this medicine's ingredients
This medicine contains 573 mg alcohol (ethanol) in each solvent vial (13% w/w). The amount in one dose of this medicine is equivalent to less than 11 mL beer or 5 mL wine. This small amount of alcohol has no noticeable effect.
If you are addicted to alcohol, have liver disease or epilepsy, talk to your doctor or pharmacist before taking this medicine.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

JEVTANA will be given to you by an intravenous infusion (infusion into your vein). Your treatment will take about one hour.

Dosage
Only your doctor will determine your dose and how you should take this medicine. JEVTANA is usually given every 3 weeks. Your doctor will decide how often you will receive JEVTANA.
Your doctor will prescribe another medicine called prednisone for you to take by mouth every day during treatment with JEVTANA. Your doctor will explain how and when to take your prednisone. It is important that you take prednisone exactly as prescribed by your doctor. If you forget to take your prednisone, or do not take it on schedule, tell your doctor or nurse.
Before each infusion of JEVTANA, you may receive other medicines to prevent or treat side effects; these include antihistamine, corticosteroid, H_2 antagonist.

Do not exceed the recommended dose.
Adhere to the treatment as recommended by your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using JEVTANA may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

JEVTANA may cause serious side effects including:

- **Low white blood cell count** (see information at the beginning of this leaflet and under 'Special warnings about using this medicine').
  Contact your doctor right away if you have any of the following symptoms of infection during treatment with JEVTANA:
  - fever—Take your temperature often during treatment with JEVTANA.
  - cough
  - burning on urination
  - muscle pain

  Tell your doctor if you have any diarrhea during the time that your white blood cell count is low. Your doctor will prescribe treatment for you as needed.
- **Severe allergic reaction** (see information at the beginning of this leaflet and under 'Special warnings about using this medicine').
  Contact your doctor or nurse right away if you have any of the following symptoms of severe allergic reaction during or soon after an infusion of JEVTANA:
  - rash or itching
  - feeling dizzy or faint
  - chest or throat tightness
  - skin redness
  - breathing problems
  - swelling of your face
- **Severe stomach and intestine (gastrointestinal) problems** (see 'Special warnings about using this medicine'):
  - severe vomiting and diarrhea, which may lead to death
  - Tell your doctor right away if you develop vomiting or diarrhea or if your symptoms get worse or do not get better.
  - a leak in the stomach or intestine, intestinal blockage, infection, and bleeding in the stomach or intestine, which may lead to death

  Tell your doctor if you develop any of the following symptoms:
  - severe stomach-area pain
  - constipation
  - fever
  - blood in your stool, or changes in the color of your stool
- **Kidney failure** (see 'Special warnings about using this medicine'):
  Tell your doctor if you develop any of the following signs or symptoms:
  - swelling of your face or body
  - decrease in the amount of urine that your body makes each day
  - blood in urine
- **Inflammation of the bladder and blood in the urine** (see 'Special warnings about using this medicine'). Tell your doctor if you have blood in your urine, burning or pain during urination, or frequent or urgent need to urinate.
- **Lung or breathing problems** (see 'Special warnings about using this medicine'):
  Tell your doctor right away if you develop any new or worsening symptom, including:
  - breathing problems
  - shortness of breath
  - chest pain
  - cough
  - fever.

Most common side effects (may affect more than 1 in 10 people):
- low red blood cell count (anemia). This condition is common with JEVTANA, but can sometimes also be serious. Your doctor will regularly check your red blood cell count. Symptoms of anemia include shortness of breath and tiredness.
- low blood platelet count. This condition is common with JEVTANA, but can sometimes also be serious. Tell your doctor if you have any unusual bruising or bleeding.
- diarrhea
- nausea
- tiredness
- weakness
- vomiting
- constipation
- decreased appetite
- back pain
- stomach pain

Common side effects (may affect up to 1 in 10 people):
- arrhythmia (rapid or irregular heartbeat)
- dyspepsia
- peripheral edema
- dehydration
- arthralgia (joint pain)
- muscle spasm
- peripheral neuropathy
- dysgeusia (alternation of taste)
- headache
- alopecia (short-term hair loss)
- hypotension

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il

5. How to store the medicine?

Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions
Store below 30°C. Do not refrigerate.
Information about storage of this medicine once it has been diluted is described in the full prescribing information and in the instructions for healthcare professionals.
Do not throw away the medicine via wastewater or household waste. Ask the pharmacist how to throw away this medicine (medicines you no longer use). This will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:
polysorbate 80
Solvent:
ethanol 96%, water for injection.

What the medicine looks like and contents of the pack:
concentrate for solution for sterile infusion, and a solvent.
The concentrate is a clear yellow to brownish-yellow, sterile, oily, non-pyrogenic solution.
The solvent is a clear, colorless, sterile, non-pyrogenic solution.
Each pack contains a glass vial with 1.5 mL concentrate and a glass vial with 4.5 mL solvent.

Registration holder and importer's name and address: Sanofi Israel Ltd., Greenwork Park, P.O. box 47 Yakum.

Revised in November 2023 according to MOH guidelines.

This leaflet does not contain all the information about your medicine. If you have any question or are not sure about anything, ask your doctor.
Registration number of the medicine in the Ministry of Health's National Drug Registry: 1452333286

הוראות שימוש לצוות הרפואי

تعليمات الاستعمال للطاقم الطبي

Directions for use for healthcare professionals

JEVTANA concentrate and solvent for solution for I.V. infusion

Preparation and Administration
JEVTANA is a cytotoxic anticancer drug. Follow applicable special handling and disposal procedures. If JEVTANA, first diluted solution, or second (final) dilution for intravenous infusion should come into contact with the skin or mucous, immediately and thoroughly wash with soap and water.
Do not use PVC infusion containers or polyurethane infusions sets for preparation and administration of JEVTANA infusion solution.
JEVTANA should not be mixed with any other drugs.

Preparation
Read this entire section carefully before mixing and diluting. JEVTANA requires two dilutions prior to administration. Follow the preparation instructions provided below, as improper preparation may lead to overdose.
Note: Both the JEVTANA injection and the diluent vials contain an overfill to compensate for liquid loss during preparation. This overfill ensures that after dilution with the entire contents of the accompanying diluent, there is an initial diluted solution containing 10 mg/mL JEVTANA.
Inspect the JEVTANA injection and supplied diluent vials. The JEVTANA injection is a clear yellow to brownish-yellow viscous solution.

Step 1 – first dilution
Each vial of JEVTANA (cabazitaxel) 60 mg/1.5 mL must first be mixed with the entire contents of supplied diluent. Once reconstituted, the resultant solution contains 10 mg/mL of JEVTANA.
When transferring the diluent, direct the needle onto the inside wall of JEVTANA vial and inject slowly to limit foaming. Remove the syringe and needle and gently mix the initial diluted solution by repeated inversions for at least 45 seconds to assure full mixing of the drug and diluent. Do not shake.
Let the solution stand for a few minutes to allow any foam to dissipate, and check that the solution is homogeneous and contains no visible particulate matter. It is not required that all foam dissipate prior to continuing the preparation process.
The resulting initial diluted JEVTANA solution (cabazitaxel 10 mg/mL) requires further dilution before administration. The second dilution should be done immediately (within 30 minutes) to obtain the final infusion as detailed in Step 2.

Step 2 – second (final) dilution
Withdraw the recommended dose from the JEVTANA solution containing 10 mg/mL as prepared in Step 1 using a calibrated syringe and further dilute into a sterile 250 mL PVC-free container of either 0.9% sodium chloride solution or 5% dextrose solution for infusion. If a dose greater than 65 mg of JEVTANA is required, use a larger volume of the infusion vehicle so that a concentration of 0.26 mg/mL JEVTANA is not exceeded. The concentration of the JEVTANA final infusion solution should be between 0.10 mg/mL and 0.26 mg/mL.
Remove the syringe and thoroughly mix the final infusion solution by gently inverting the bag or bottle.
As the final infusion solution is supersaturated, it may crystallize over time. Do not use if this occurs and discard.
Fully prepared JEVTANA infusion solution (in either 0.9% sodium chloride solution or 5% dextrose solution) should be used within 8 hours at ambient temperature (including the one-hour infusion), or for a total of 24 hours (including the one-hour infusion) under the refrigerated conditions.
Discard any unused portion.

Administration
Inspect visually for particulate matter, any crystals and discoloration prior to administration. If the JEVTANA first diluted solution or second (final) infusion solution is not clear or appears to have precipitation, it should be discarded.
Use an in-line filter of 0.22 micrometer nominal pore size (also referred to as 0.2 micrometer) during administration.
The final JEVTANA infusion solution should be administered intravenously as a one-hour infusion at room temperature.

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