The following information is intended for healthcare professionals only.

JEVTANA® 60 mg
concentrate and solvent for solution for infusion
cabazitaxel

SANOFI

PRACTICAL INFORMATION FOR MEDICAL OR HEALTHCARE PROFESSIONALS ON PREPARATION, ADMINISTRATION AND HANDLING OF JEVTANA 60 mg CONCENTRATE AND SOLVENT FOR SOLUTION FOR INFUSION

This information supplements sections 3 and 5 for the user.
It is important that you read the entire content of this procedure prior to the preparation of the infusion solution.

Incompatibilities
This medicine must not be mixed with other medicines except those used for the dilutions.

Shelf life and special precautions for storage
For the pack of Jevtana 60 mg concentrate and solvent
Do not store above 30°C. Do not refrigerate.

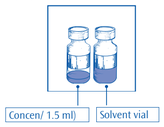
After opening
The concentrate and solvent vials must be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hour at 2°C – 8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Preparation and administration precautions
As for any other antineoplastic agent, caution should be exercised when handling and preparing Jevtana solutions, taking into account the use of containment devices, personal protective equipment (e.g. gloves), and preparation procedures.
If Jevtana, at any step of its handling, should come into contact with the skin, wash immediately and thoroughly with soap and water. If it should come into contact with mucous membranes, wash immediately and thoroughly with water.
Jevtana should only be prepared and administered by personnel trained in handling cytotoxic agents. Pregnant staff should not handle it.
Always dilute the concentrate for solution for infusion with the **entire** supplied solvent before adding to infusion solutions.

Preparation steps
Read this **ENTIRE** section carefully before mixing and diluting.
Jevtana requires **TWO** dilutions prior to administration. Follow the preparation instructions provided below.
Note: Both the Jevtana 60 mg/1.5 ml concentrate vial (fill volume: 73.2 mg of cabazitaxel/1.83 ml) and the solvent vial (fill volume: 5.67 ml) contain an overfill to compensate for liquid loss during preparation. This overfill ensures that after dilution with the **ENTIRE** contents of the accompanying solvent, there is solution containing 10 mg/ml cabazitaxel.
The following two-step dilution process must be carried out in an aseptic manner for preparing the solution for infusion.

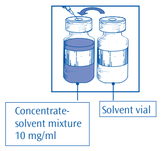
Step 1: Initial dilution of the concentrate for solution for infusion with the supplied solvent.

Step 1.1
Inspect the concentrate vial and the supplied solvent. The concentrate solution and the solvent should be clear.



Step 1.2
Using a syringe fitted with a needle, aseptically withdraw the **entire** contents of the supplied solvent by partially inverting the vial.

Step 1.3
Inject the **entire** contents into the corresponding concentrate vial.
To limit foaming as much as possible when injecting the solvent, direct the needle onto the inside wall of the vial of concentrate solution and inject slowly.
Once reconstituted, the resultant solution contains 10 mg/ml of cabazitaxel.



Step 1.4
Remove the syringe and needle and mix manually and gently by repeated inversions until obtaining a clear and homogeneous solution. It could take approximately
45 seconds.

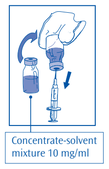
Step 1.5
Let this solution stand for approximately 5 minutes and check then that the solution is homogeneous and clear. It is normal for foam to persist after this time period.

This resulting concentrate-solvent mixture contains 10 mg/ml of cabazitaxel (at least 6 ml deliverable volume). The second dilution should be done immediately (within 1 hour) as detailed in Step 2.

More than one vial of the concentrate-solvent mixture may be necessary to administer the prescribed dose.

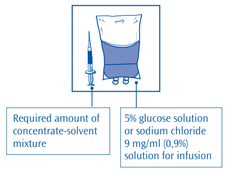
Step 2: Second (final) dilution for infusion

Step 2.1
Aseptically withdraw the required amount of concentrate-solvent mixture (10 mg/ml of cabazitaxel), with a graduated syringe fitted with a needle. As an example, a dose of 45 mg Jevtana would require 4.5 ml of the concentrate solvent mixture prepared following Step 1.



Since foam may persist on the wall of the vial of this solution, following its preparation described in Step 1, it is preferable to place the needle of the syringe in the middle when extracting.

Step 2.2
Inject in a sterile PVC-free container of either 5% glucose solution or sodium chloride 9 mg/ml (0.9%) solution for infusion. The concentration of the infusion solution should be between 0.10 mg/ml and 0.26 mg/ml.



Step 2.3
Remove the syringe and mix the content of the infusion bag or bottle manually using a rocking motion.

Step 2.4
As with all parenteral products, the resulting infusion solution should be visually inspected prior to use. As the infusion solution is supersaturated, it may crystallize over time. In this case, the solution must not be used and should be discarded.

The infusion solution should be used immediately. However, in-use storage time can be longer under specific conditions mentioned in section **Shelf life and special precautions for storage** above.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Method of administration
Jevtana is administered as a 1 hour infusion.
An in-line filter of 0.22 micrometer nominal pore size (also referred to as 0.2 micrometer) is recommended during administration.
PVC infusion containers or polyurethane infusion sets should not be used for the preparation and administration of the infusion solution.

PACKAGE LEAFLET: INFORMATION FOR THE USER

JEVTANA® 60 mg,
concentrate and solvent for solution for infusion
cabazitaxel

SANOFI

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet :

1. WHAT JEVTANA IS AND WHAT IT IS USED FOR
The name of your medicine is Jevtana. Its common name is cabazitaxel. It belongs to a group of medicines called "taxanes" used to treat cancers.
Jevtana is used to treat prostate cancer that has progressed after having had other chemotherapy. It works by stopping cells from growing and multiplying.
As part of your treatment, you will also take a corticosteroid medicine (prednisone or prednisolone) by mouth every day. Ask your doctor to give you information about this other medicine.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN JEVTANA
Contraindications
Do not use Jevtana if:
- you are allergic (hypersensitive) to cabazitaxel, to other taxanes, or polysorbate 80 or any of the other excipients of this medicine (listed in section 6),
- the number of your white blood cells is too low (neutrophil counts less than or equal to 1,500 /mm^3),
- you have severe abnormal liver function,
- you have recently received or are about to receive a vaccine against yellow fever.

You should not be given Jevtana if any of the above apply to you. If you are not sure, talk to your doctor before having Jevtana.

Warnings and precautions
Before each treatment with Jevtana, you will have blood tests to check that you have enough blood cells and sufficient liver and kidney functions to receive Jevtana.
Tell your doctor immediately if:
- you have fever. During treatment with Jevtana, it is more likely that your white blood cell count may be reduced. Your doctor will monitor your blood and general condition for signs of infections. He/she may give you other medicines to maintain the number of your blood cells. People with low blood counts can develop life-threatening infections. The earliest sign of infection may be fever, so if you experience fever, tell your doctor right away.
- you have ever had any allergies. Serious allergic reactions can occur during treatment with Jevtana.
- you have severe or long-lasting diarrhoea, you feel sick (nausea) or you are being sick (vomiting). Any of these events could cause severe dehydration. Your doctor may need to treat you.
- you have feeling of numbness, tingling, burning or decreased sensation in your hands or feet.
- you have any bleeding problems from the gut or have changes in the colour of your stool or stomach pain. If the bleeding or pain is severe, your doctor will stop your treatment with Jevtana. This is because Jevtana may increase the risk of bleeding or developing holes in the gut wall.
- you have kidney problems.
- liver problems occur during the treatment.
- you experience any significant increase or decrease in daily urinary volume.
- you have blood in your urine.

If any of the above applies to you, tell your doctor immediately. Your doctor may reduce the dose of Jevtana or stop the treatment.

Other medicines and Jevtana
Please tell your doctor, pharmacist or nurse if you are taking or have recently taken any other medicines. This includes medicines obtained without a prescription. This is because some medicines can affect the way Jevtana works or Jevtana can affect how other medicines work. These medicines include the following:
- ketoconazole, rifampicin (for infections);
- carbamazepine, phenobarbital or phenytoin (for seizures);
- St John's Wort *(Hypericum perforatum)* (herbal remedy for depression and other conditions);
- statins (such as simvastatin, lovastatin, atorvastatin, rosuvastatin, or pravastatin) (for reducing the cholesterol in your blood);
- valsartan (for hypertension);
- repaglinide (for diabetes).

Talk to your doctor before getting vaccinations while you are receiving Jevtana.

Pregnancy, breast-feeding and fertility
Jevtana should not be used in pregnant women or women of childbearing age not using contraception.
Jevtana should not be used during breast-feeding.
Use a condom during sex if your partner is or could become pregnant. Jevtana could be present in your semen and may affect the foetus. You are advised not to father a child during and up to 6 months after treatment and to seek advice on conservation of sperm prior to treatment because Jevtana may alter male fertility.

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

Jevtana contains ethanol
This medicine contains 15% v/v ethanol equivalent to 14 ml of beer or 6 ml of wine. This medicine may be harmful for those suffering from alcoholism.
To be taken into account if you are in a high-risk group such as patients with liver disease, or epilepsy.

3. HOW TO USE JEVTANA
Instructions for use
Anti-allergic medicines will be given to you before you have Jevtana to reduce the risk of allergic reactions.
- Jevtana will be given to you by a doctor or a nurse.
- Jevtana must be prepared (diluted) before it is given. Practical information for handling and administration of Jevtana for doctors, nurses and pharmacists is provided with this leaflet.
- Jevtana will be given by a drip (infusion) into one of your veins (intravenous use) in hospital for about an hour.
- As part of your treatment, you will also take a corticosteroid medicine (prednisone or prednisolone) by mouth every day.

How much and how often to have
- The usual dose depends on your body surface area. Your doctor will calculate your body surface area in square meters (m^2) and will decide the dose you should have.
- You will usually have an infusion once every 3 weeks.
- If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. POSSIBLE SIDE EFFECTS
Like all medicines, this medicine can cause side effects, although not everybody gets them.

Your doctor will discuss these with you and will explain the potential risks and benefits of your treatment.
See a doctor immediately if you notice any of the following side effects:
- fever (high temperature). This is very common (may affect more than 1 in 10 people).
- severe loss of body fluids (dehydration). This is common (may affect up to 1 in 10 people). This can occur if you have severe or long-lasting diarrhoea, or fever, or if you are being sick (vomiting).
- severe stomach pain or stomach pain that doesn't go away. This can occur if you have a hole in the stomach, food pipe, gut or bowel (gastrointestinal perforation). This can lead to death.
- If any of the above applies to you, tell your doctor immediately.

Other side effects include:
Very common (may affect more than 1 in 10 people):
- decrease in the number of red (anaemia), or white blood cells (which are important in fighting infection)
- decrease in the number of platelets (which results in increased risk of bleeding)
- loss of appetite (anorexia)
- alteration in sense of taste
- shortness of breath
- cough
- stomach upsets including feeling sick (nausea), being sick (vomiting), diarrhoea or constipation
- abdominal pain
- short term hair loss (in most cases normal hair growth should return)
- back pain
- joint pain
- blood in the urine
- feeling tired, weak or lack of energy.

Common (may affect up to 1 in 10 people):
- urinary tract infection
- lack of white blood cells associated with fever and infection
- feeling of numbness, tingling, burning or decreased sensations in hands and feet
- dizziness
- headache
- decrease or increase in blood pressure
- uncomfortable feeling in the stomach, heart burn or belching
- stomach pain
- haemorrhoids
- muscle spasm
- painful or frequent urination
- urinary incontinence
- kidney disease or problems
- sore in the mouth or on lips
- infections or risk of infections
- high blood sugar
- low blood potassium
- mental confusion
- feeling anxious
- abnormal feeling or loss of sensation or pain in hands and feet
- ringing in the ear
- trouble with balance
- rapid or irregular heartbeat
- blood clot in the leg
- skin feeling hot or flushed
- pain in mouth or throat
- rectal bleeding
- redness of the skin
- muscle discomfort, aches or pain
- swelling of the feet or legs
- chills.

Uncommon (may affect up to 1 in 100 people):
- inflammation of the bladder, which can occur when your bladder has been previously exposed to radiation therapy (cystitis due to radiation recall phenomenon).

Frequency not known (cannot be estimated from the available data):
- interstitial lung disease (inflammation of the lungs causing coughing and difficulty breathing).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.
By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE JEVTANA
KEEP THIS MEDICINE OUT OF THE SIGHT AND REACH OF CHILDREN.
Do not use this medicine after the expiry date which is stated on the outer carton and on the label of the vials after EXP. The expiry date refers to the last day of that month.
Do not store above 30°C. Do not refrigerate.
Information about storage and the time to use Jevtana, once it has been diluted and is ready to use, are described in the section "PRACTICAL INFORMATION FOR MEDICAL OR HEALTHCARE PROFESSIONALS ON PREPARATION, ADMINISTRATION AND HANDLING OF JEVTANA".
Any unused product or waste material should be disposed of in accordance with local requirements. These measures will help to protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION
What Jevtana contains
The active substance is cabazitaxel. One ml of concentrate contains 40 mg cabazitaxel. Each vial of concentrate contains 60 mg cabazitaxel.
The other ingredients are polysorbate 80 and citric acid in the concentrate, and ethanol 96% and water for injections in the solvent (see section 2 "Jevtana contains ethanol").
Note: Both the Jevtana 60 mg/1.5 ml concentrate vial (fill volume: 73.2 mg of cabazitaxel/1.83 ml) and the solvent vial (fill volume: 5.67 ml) contain an overfill to compensate for liquid loss during preparation. This overfill ensures that after dilution with the **ENTIRE** contents of the accompanying solvent, there is solution containing
10 mg/ml cabazitaxel.

What Jevtana looks like and contents of the pack
JEVTANA is a concentrate and solvent for solution for infusion (sterile concentrate). The concentrate is a clear yellow to brownish-yellow oily solution.
The solvent is a clear and colourless solution.
One pack of Jevtana contains:
- One single useclear glass vial, closed with a grey chlorobutyl rubber closure sealed by an aluminium cap with a light green plastic flip-off cover, containing 1.5 ml (nominal volume) concentrate.
- One single use clear glass vial, closed with a grey chlorobutyl rubber closure sealed by a gold colour aluminium cap with a colourless plastic flip-off cover, containing 4.5 ml (nominal volume) solvent.

Not all pack size may be marketed in your country.

Marketing Authorization Holder:
sanofi-aventis groupe
54, rue La Boétie
F-75008 Paris
France

Manufacturer
Sanofi-Aventis Deutschland GmbH
Industriepark Höchst
65926 Frankfurt am Main
Germany

This leaflet was last revised in: November 2016.

THIS MEDICAMENT
Is a product, which affects your health, and its consumption contrary to instructions is dangerous for you.
Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of reach of children.

Council of Arab Health Ministers, Union of Arab Pharmacists.