HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use JEVTANA safely and effectively. See full prescribing information for JEVTANA.

JEVTANA® (cabazitaxel) injection, for intravenous use
Initial U.S. Approval: 2010

WARNING: NEUTROPENIA AND HYPERSENSITIVITY
See full prescribing information for complete boxed warning.

- **Neutropenic deaths have been reported. Obtain frequent blood counts to monitor for neutropenia. JEVTANA is contraindicated in patients with neutrophil counts of ≤1,500 cells/mm^3. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. Consider primary prophylaxis with G-CSF in all patients receiving a dose of 25 mg/m^2 (4, 5.1, 5.2)**
- **Severe hypersensitivity can occur and may include generalized rash/erythema, hypotension and bronchospasm. Discontinue JEVTANA immediately if severe reactions occur and administer appropriate therapy. (2.1, 5.2)**
- **Contraindicated if history of severe hypersensitivity reactions to cabazitaxel or to drugs formulated with polysorbate 80. (4)**

----------RECENT MAJOR CHANGES----------

Warnings and Precautions (5.1, 5.2)	12/2020
Dosage and Administration (2.1)	12/2020
Warnings and Precautions (5.9)	02/2020

----------INDICATIONS AND USAGE----------

JEVTANA is a microtubule inhibitor indicated in combination with prednisone for treatment of patients with metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing treatment regimen. (1)

----------DOSAGE AND ADMINISTRATION----------

Recommended Dose: JEVTANA 20 mg/m^2 administered every three weeks as a one-hour intravenous infusion in combination with oral prednisone 10 mg administered daily throughout JEVTANA treatment. (2.1)
A dose of 25 mg/m^2 can be used in select patients at the discretion of the treating healthcare provider. (2.1, 5.1, 5.2, 6.1, 14)

- JEVTANA requires **two** dilutions prior to administration. (2.5)
- Use the **entire contents** of the accompanying diluent to achieve a concentration of 10 mg/mL JEVTANA. (2.5)
- PVC equipment should not be used. (2.5)
- **Premedication Regimen:** Administer intravenously 30 minutes before each dose of JEVTANA:
  - Antihistamine (dexchlorpheniramine 5 mg or diphenhydramine 25 mg or equivalent antihistamine)
  - Corticosteroid (dexamethasone 8 mg or equivalent steroid)
  - H_2 antagonist (ranitidine 50 mg or equivalent H_2 antagonist) (2.1)

  Antiemetic prophylaxis (oral or intravenous) is recommended as needed. (2.1)
- **Dosage Modifications:** See full prescribing information (2.2, 2.3, 2.4)

----------DOSAGE FORMS AND STRENGTHS----------

- Single dose vial 60 mg/1.5 mL, supplied with diluent (5.7 mL) for JEVTANA (3)

----------CONTRAINDICATIONS----------

- Neutrophil counts of ≤1,500/mm^3 (2.2, 4)
- History of severe hypersensitivity to JEVTANA or polysorbate 80 (4)
- Severe hepatic impairment (Total Bilirubin >3 × ULN) (4)

----------WARNINGS AND PRECAUTIONS----------

- Bone marrow suppression (particularly neutropenia) and its clinical consequences (febrile neutropenia, neutropenic infections, and death): Monitor blood counts frequently to determine if dosage modification or initiation of G-CSF is needed. Closely monitor patients with hemoglobin <10 g/dL. (2.2, 4, 5.1)
- Increased toxicities in elderly patients: Patients ≥65 years of age were more likely to experience fatal outcomes and certain adverse reactions, including neutropenia and febrile neutropenia. Monitor closely. (5.2, 8.5)
- Hypersensitivity: Severe hypersensitivity reactions can occur. Premedicate with corticosteroids and H_2 antagonists. Discontinue infusion immediately if hypersensitivity is observed and treat as indicated. (4, 5.3)
- Gastrointestinal disorders: Nausea, vomiting, and diarrhea may occur. Mortality related to diarrhea has been reported. Rehydrate and treat with antiemetics and antidiarrheals as needed. If experiencing Grade ≥3 diarrhea, dosage should be modified. (2.2) Deaths have occurred due to gastrointestinal hemorrhage, perforation and neutropenic enterocolitis. Delay or discontinue JEVTANA and treat as indicated. (5.4)
- Renal failure, including cases with fatal outcomes, has been reported. Identify cause and manage aggressively. (5.5)
- Urinary disorders including cystitis: Cystitis, radiation cystitis, and hematuria may occur. Monitor patients who previously received pelvic radiation for signs and symptoms of cystitis. Interrupt or discontinue JEVTANA and provide medical or surgical supportive care, as needed, in patients experiencing severe hemorrhagic cystitis.
- Respiratory disorders: Interstitial pneumonia/pneumonitis, interstitial lung disease and acute respiratory distress syndrome, including fatal outcomes, have been reported. Delay or discontinue JEVTANA and treat as indicated. (5.7)
- Hepatic impairment: Administer JEVTANA at a dose of 20 mg/m^2 in patients with mild hepatic impairment. Administer JEVTANA at a dose of 15 mg/m^2 in patients with moderate hepatic impairment. (2.3, 5.8)
- Embryo-fetal toxicity: JEVTANA can cause fetal harm and loss of pregnancy. Advise males with female partners of reproductive potential to use effective contraception. (5.9, 8.1, 8.3)

----------ADVERSE REACTIONS----------

Most common all grades adverse reactions and laboratory abnormalities (≥10%) with JEVTANA 20 mg/m^2 or 25 mg/m^2 are neutropenia, anemia, diarrhea, nausea, fatigue, asthenia, vomiting, hematuria, constipation, decreased appetite, back pain, and abdominal pain. (6)

To report SUSPECTED ADVERSE REACTIONS, contact sanofi-aventis U.S. LLC at 1-800-633-1610 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

Avoid coadministration of JEVTANA with strong CYP3A inhibitors. If patients require coadministration of a strong CYP3A inhibitor, consider a 25% JEVTANA dose reduction. (2.4, 7.1, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: NEUTROPENIA AND HYPERSENSITIVITY

Neutropenia: Neutropenic deaths have been reported. Monitor for neutropenia with frequent blood cell counts. JEVTANA is contraindicated in patients with neutrophil counts of ≤1,500 cells/mm^3. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. Consider primary prophylaxis with G-CSF in all patients receiving a dose of 25 mg/m^2 *[see Contraindications (4) and Warnings and Precautions (5.1, 5.2)]*.

Severe hypersensitivity: Severe hypersensitivity reactions can occur and may include generalized rash/erythema, hypotension and bronchospasm. Severe hypersensitivity reactions require immediate discontinuation of the JEVTANA infusion and administration of appropriate therapy. Patients should receive premedication. JEVTANA is contraindicated in patients who have a history of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80 *[see Dosage and Administration (2.1), Contraindications (4), and Warnings and Precautions (5.3)]*.

1 INDICATIONS AND USAGE

JEVTANA® is indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing treatment regimen.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The recommended dose of JEVTANA is based on calculation of the Body Surface Area (BSA), and is 20 mg/m^2 administered as a one-hour intravenous infusion every three weeks in combination with oral prednisone 10 mg administered daily throughout JEVTANA treatment.

A dose of 25 mg/m^2 can be used in select patients at the discretion of the treating healthcare provider *[see Warnings and Precautions (5.1, 5.2), Adverse Reactions (6.1), and Clinical Studies (14)]*.

Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features**.** Consider primary prophylaxis with G-CSF in all patients receiving a dose of 25 mg/m^2 *[see Contraindications (4) and Warnings and Precautions (5.1, 5.2)]*.

Premedicate at least 30 minutes prior to each dose of JEVTANA with the following intravenous medications to reduce the risk and/or severity of hypersensitivity *[see Warnings and Precautions (5.3)]*:

- antihistamine (dexchlorpheniramine 5 mg, or diphenhydramine 25 mg or equivalent antihistamine),
- corticosteroid (dexamethasone 8 mg or equivalent steroid),
- H_2 antagonist (ranitidine 50 mg or equivalent H_2 antagonist).

Antiemetic prophylaxis is recommended and can be given orally or intravenously as needed *[see Warnings and Precautions (5.3)]*.

JEVTANA injection single-dose vial requires **two** dilutions prior to administration *[see Dosage and Administration (2.5)]*.

2.2 Dose Modifications for Adverse Reactions

Reduce or discontinue JEVTANA dosing for adverse reactions as described in Table 1.

Table 1: Recommended Dosage Modifications for Adverse Reactions in Patients Treated with JEVTANA

Toxicity	Dosage Modification
Prolonged grade ≥3 neutropenia (greater than 1 week) despite appropriate medication including granulocyte-colony stimulating factor (G-CSF)	Delay treatment until neutrophil count is >1,500 cells/mm^3, then reduce dosage of JEVTANA by one dose level. Use G-CSF for secondary prophylaxis.
Febrile neutropenia or neutropenic infection	Delay treatment until improvement or resolution, and until neutrophil count is >1,500 cells/mm^3, then reduce dosage of JEVTANA by one dose level. Use G-CSF for secondary prophylaxis.
Grade ≥3 diarrhea or persisting diarrhea despite appropriate medication, fluid and electrolytes replacement	Delay treatment until improvement or resolution, then reduce dosage of JEVTANA by one dose level.
Grade 2 peripheral neuropathy	Delay treatment until improvement or resolution, then reduce dosage of JEVTANA by one dose level.
Grade ≥3 peripheral neuropathy	Discontinue JEVTANA.

Patients at a 20 mg/m^2 dose who require dose reduction should decrease dosage of JEVTANA to 15 mg/m^2 *[see Adverse Reactions (6.1)]*.

Patients at a 25 mg/m^2 dose who require dose reduction should decrease dosage of JEVTANA to 20 mg/m^2. One additional dose reduction to 15 mg/m^2 may be considered *[see Adverse Reactions (6.1)]*.

2.3 Dose Modifications for Hepatic Impairment

- Mild hepatic impairment (total bilirubin >1 to ≤1.5 × Upper Limit of Normal (ULN) or AST >1.5 × ULN): Administer JEVTANA at a dose of 20 mg/m^2.
- Moderate hepatic impairment (total bilirubin >1.5 to ≤3 × ULN and AST = any): Administer JEVTANA at a dose of 15 mg/m^2 based on tolerability data in these patients; however, the efficacy of this dose is unknown.
- Severe hepatic impairment (total bilirubin >3 × ULN): JEVTANA is contraindicated in patients with severe hepatic impairment *[see Warning and Precautions (5.8) and Clinical Pharmacology (12.3)]*.

2.4 Dose Modifications for Use with Strong CYP3A Inhibitors

Concomitant drugs that are strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole) may increase plasma concentrations of cabazitaxel. Avoid the coadministration of JEVTANA with these drugs. If patients require coadministration of a strong CYP3A inhibitor, consider a 25% JEVTANA dose reduction *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3)]*.

2.5 Preparation and Administration

JEVTANA is a cytotoxic anticancer drug. Follow applicable special handling and disposal procedures *[see References (15)]*. 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 *[see Overdosage (10)]*.

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.

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