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. Do not give JEVTANA if neutrophil counts are ≤1,500 cells/mm^3. (2.2)(4)**
- **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 JEVTANA or to drugs formulated with polysorbate 80. (4)**

----------RECENT MAJOR CHANGES----------
Warnings and Precautions (5.5) 09/2016

----------INDICATIONS AND USAGE----------
JEVTANA is a microtubule inhibitor indicated in combination with prednisone for treatment of patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing treatment regimen. (1)

----------DOSAGE AND ADMINISTRATION----------
Recommended dose: JEVTANA 25 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)

- 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 (dexchloropheniramine 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 x ULN) (4)

----------WARNINGS AND PRECAUTIONS----------
- Bone marrow suppression (particularly neutropenia) and its clinical consequences (febrile neutropenia, neutropenic infections): Monitor blood counts frequently to determine if dosage modification or initiation of G-CSF is needed. Primary prophylaxis with G-CSF should be considered in patients with high-risk clinical features. Use caution in patients with hemoglobin < 10 g/dL. (2.2)(4)(5.1)
- Hypersensitivity: Severe hypersensitivity reactions can occur. Premedicate with corticosteroids and H2 antagonists. Discontinue infusion immediately if hypersensitivity is observed and treat as indicated. (4)(5.2)
- Gastrointestinal disorders: Nausea, vomiting, and diarrhea may occur. Mortality related to diarrhea has been reported. Rehydrate and treat with anti-emetics and anti-diarrheals 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. (5.3)
- Renal failure, including cases with fatal outcomes, has been reported. Identify cause and manage aggressively. (5.4)
- 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. (5.5)
- Elderly patients: Patients ≥ 65 years of age were more likely to experience fatal outcomes not related to disease progression and certain adverse reactions, including neutropenia and febrile neutropenia. Monitor closely. (5.6)(6)(8.5)
- Hepatic impairment: Reduce the JEVTANA dose to 20 mg/m^2 in patients with mild hepatic impairment and to 15 mg/m^2 in patients with moderate hepatic impairment. (2.3)
- JEVTANA can cause fetal harm when administered to a pregnant woman. (5.8)(8.1)

----------ADVERSE REACTIONS----------
Most common all grades adverse reactions (≥10%) are neutropenia, anemia, leukopenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, asthenia, abdominal pain, hematuria, back pain, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysgeusia, cough, arthralgia, and alopecia. (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 co-administration 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: 09/2016

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. In order to monitor the occurrence of neutropenia, frequent blood cell counts should be performed on all patients receiving JEVTANA. JEVTANA is contraindicated in patients with neutrophil counts of ≤1,500 cells/mm^3 *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

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 (5.2)]*.

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

The individual dosage of JEVTANA is based on calculation of the Body Surface Area (BSA) and is 25 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.

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 (5.2)]:*

- 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-use 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 to 20 mg/m^2. 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 to 20 mg/m^2. 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 to 20 mg/m^2.
Grade 2 peripheral neuropathy	Delay treatment until improvement or resolution, then reduce dosage of JEVTANA to 20 mg/m^2.
Grade ≥3 peripheral neuropathy	Discontinue JEVTANA

Discontinue JEVTANA treatment if a patient continues to experience any of these reactions at the 20 mg/m^2 dosage.

2.3 Dose Modifications for Hepatic Impairment

- Mild hepatic impairment (total bilirubin > 1 to ≤ 1.5 x Upper Limit of Normal (ULN) or AST >1.5 x ULN): Reduce JEVTANA starting dose to 20 mg/m^2.
- Moderate hepatic impairment (total bilirubin > 1.5 to ≤ 3 x ULN and AST = any): Reduce JEVTANA starting dose to 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 X ULN): JEVTANA is contraindicated in patients with severe hepatic impairment *[see Warning and Precautions (5.6) 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 co-administration 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)]*.[1] 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.

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