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/mm³. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. (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 (5.9) 01/2020

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/m² 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/m² 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 (doxchlorpheniramine 5 mg or diphenhydramine 25 mg or equivalent antihistamine)
  - Corticosteroid (dexamethasone 8 mg or equivalent steroid)
  - H₂ antagonist (ranitidine 50 mg or equivalent H₂ 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)

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

CONTRAINDICATIONS

- Neutrophil counts of ≤1,500/mm³ (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, and death); Monitor blood counts frequently to determine if dosage modification or initiation of G-CSF is needed. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. 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 H₂ 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. (5.6)
- 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/m² in patients with mild hepatic impairment. Administer JEVTANA at a dose of 15 mg/m² 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/m² or 25 mg/m² are neutropenia, anemia, leukopenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, anemia, 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 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: 03/2020
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 the calculation of the Body Surface Area (BSA), and is 20 mg/m² administered as a one-hour intravenous infusion every three weeks in combination with oral prednisone 10 mg administered daily throughout the JEVTANA treatment.

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

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Dosage Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged grade ≥3 neutropenia (greater than 1 week) despite appropriate medication including granulocyte-colony stimulating factor (G-CSF)</td>
<td>Delay treatment until neutrophil count is &gt;1,500 cells/mm³; then reduce dosage of JEVTANA by one dose level. Use G-CSF for secondary prophylaxis.</td>
</tr>
<tr>
<td>Febrile neutropenia or neutropenic infection</td>
<td>Delay treatment until improvement or resolution, and until neutrophil count is &gt;1,500 cells/mm³; then reduce dosage of JEVTANA by one dose level. Use G-CSF for secondary prophylaxis.</td>
</tr>
<tr>
<td>Grade ≥3 diarrhea or persisting diarrhea despite appropriate medication, fluid and electrolytes replacement</td>
<td>Delay treatment until improvement or resolution, then reduce dosage of JEVTANA by one dose level.</td>
</tr>
<tr>
<td>Grade 2 peripheral neuropathy</td>
<td>Delay treatment until improvement or resolution, then reduce dosage of JEVTANA by one dose level.</td>
</tr>
<tr>
<td>Grade ≥3 peripheral neuropathy</td>
<td>Discontinue JEVTANA.</td>
</tr>
</tbody>
</table>

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/m².
- Moderate hepatic impairment: Total bilirubin >1.5 to ≤3 × ULN and AST > any: Administer JEVTANA at a dose of 15 mg/m² 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 CYP3A4 Inhibitors
Concomitant drugs that are strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, azithromycin, simvastatin, lovastatin, diltiazem, verapamil, and anti-retroviral medications) may increase plasma concentrations of cabazitaxel. Avoid the coadministration of JEVTANA with these drugs. If patients require coadministration of a strong CYP3A4 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 the 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 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 bottle or bottle.

As the final infusion solution is supersaturated, it may crystalize 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.

3 DOSAGE FORMS AND STRENGTHS
JEVTANA (cabazitaxel) injection is supplied as a kit consisting of the following:
- Cabazitaxel injection: 60 mg/1.5 mL; a clear yellow to brownish-yellow viscous solution
- Diluent: 5.7 mL of 13% (w/v) ethanol in water; a clear colorless solution
4 CONTRAINDICTIONS

JEVTANA is contraindicated in patients with:
• neutrophil counts of <1,500/mm³ [see Warnings and Precautions (5.1)]
• history of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80 [see Warnings and Precautions (5.3)]
• severe hepatic impairment (total bilirubin >3 × ULN) [see Warnings and Precautions (5.8)]

5 WARNINGS AND PRECAUTIONS

5.1 Bone Marrow Suppression

JEVTANA is contraindicated in patients with neutrophils <1,500/mm³ [see Contraindications (4)]. Closely monitor patients with hemoglobin <10 g/dL.

Bone marrow suppression manifested as neutropenia, anemia, thrombocytopenia and/or pancytopenia may occur. Neutropenic deaths have been reported.

In a randomized trial (TROPIC) in patients with metastatic castration-resistant prostate cancer, five patients (1.3%) died from infection (sepsis or septic shock). All had grade 4 neutropenia and one had febrile neutropenia. One additional patient’s death was attributed to neutropenia without a documented infection. Twenty-two (8%) patients discontinued JEVTANA treatment due to neutropenia, febrile neutropenia, infection, or sepsis. The most common adverse reaction leading to treatment discontinuation in the JEVTANA group was neutropenia (2%). Grade 3–4 neutropenia has been observed in 82% of patients treated with JEVTANA in the randomized trial. In a randomized trial (PROSELICA) comparing two doses of JEVTANA in previously treated metastatic castration-resistant prostate cancer, 8 patients (1%) on the 20 mg/m² arm and 15 patients (3%) on the 25 mg/m² arm died from infection; of these, 4 deaths on the 20 mg/m² arm and 8 deaths on the 25 mg/m² arm occurred within the first 30 days of treatment.

Fewer patients receiving JEVTANA 20 mg² were reported to have infectious adverse reactions. Grade 1–4 infections were experienced by 160 patients (28%) on the 20 mg/m² arm and 227 patients (38%) on the 25 mg/m² arm. Grade 5–6 infections were experienced by 57 patients on the 20 mg/m² arm (8%) and 60 patients (9%) on the 25 mg/m² arm. Noninferiority for overall survival was demonstrated between these two arms [see Clinical Studies (14)].

Based on guidelines for the use of G-CSF and the adverse reactions profile of JEVTANA primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features (older patients, poor performance status, previous episodes of febrile neutropenia, extensive prior radiation ports, poor nutritional status, or other serious comorbidities) that predispose them to increased complications from prolonged neutropenia. The effectiveness of prophylaxis with G-CSF in patients receiving JEVTANA has not been studied. Therapeutic use of G-CSF and secondary prophylaxis should be considered in at least increased risk for neutropenia complications.

Monitoring of complete blood counts is essential on a weekly basis during cycle 1 and before each treatment cycle thereafter so that the dose can be adjusted, if needed [see Dosage and Administration (2.2)].

5.2 Increased Toxicities in Elderly Patients

In a randomized trial (TROPIC) the 20% of patients (3/131) <65 years of age and 6% (15/240) ≥65 years of age died of causes other than disease progression within 30 days of the last JEVTANA dose. Patients ≥65 years of age are more likely to experience certain adverse reactions, including neutropenia and febrile neutropenia. The incidence of the following grade 3–4 adverse reactions were higher in patients ≥65 years of age compared to younger patients: neutropenia (87% vs 74%), and febrile neutropenia (8% vs 6%).

In a randomized clinical trial (PROSELICA) comparing two doses of JEVTANA, deaths due to infection within 30 days of starting JEVTANA occurred in 0.7% (4/580) patients on the 20 mg/m² arm and 1.3% (8/595) patients on the 25 mg/m² arm; all of these patients were ≥60 years of age.

In PROSELICA, on the 20 mg/m² arm, 3% (5/178) of patients <65 years of age and 2% (9/402) ≥65 years of age died of causes other than disease progression within 30 days of the last JEVTANA dose. The 25 mg/m² arm, 2% (3/158) of patients <65 years of age and 5% (20/420) ≥65 years of age died of causes other than disease progression within 30 days of the last JEVTANA dose [see Adverse Reactions (6) and Use in Specific Populations (8.5)]

5.3 Hypersensitivity Reactions

Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of JEVTANA, thus facilities and equipment for the treatment of hypotension and bronchospermia should be available. Severe hypersensitivity reactions can occur and may include generalized rash/erythema, hypotension and bronchospermia.

Premedicate all patients prior to the initiation of the infusion of JEVTANA [see Dosage and Administration (2.1)]. Observe patients closely for hypersensitivity reactions, especially during the first and second infusions. Severe hypersensitivity reactions require immediate discontinuation of the infusion and appropriate therapy. JEVTANA is contraindicated in patients with a history of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80 [see Contraindications (4)].

5.4 Gastrointestinal Adverse Reactions

Nausea, vomiting, diarrhea, and anes, may occur. Deaths related to diarrhea and electrolyte imbalance occurred in the randomized clinical trials. Intensive measures may be required for severe diarrhea and electrolyte imbalance. Antimetic prophylaxis is recommended. Treat patients with rehydration, antiarrhythmic or antiemetic medications as needed. Treatment delay or dosage reduction may be necessary if patients experience Grade ≥3 diarrhea [see Dosage and Administration (2.2)].

Gastrointestinal (GI) hemorrhage and perforation, ileus, enterocolitis, neutropenic enterocolitis, including fatal outcome, have been reported in patients treated with JEVTANA [see Adverse Reactions (6)]. These events may be irreversible in patients with underlying lung disease may be at higher risk for these events. Adult respiratory distress syndrome may occur in the setting of infection. Interrupt JEVTANA if new or worsening pulmonary symptoms develop. Closely monitor, promptly investigate, and appropriately treat patients receiving JEVTANA. Consider discontinuation. The benefit of resuming JEVTANA treatment must be carefully evaluated.

5.5 Use in Patients with Renal Impairment

Cabazitaxel is extensively metabolized in the liver.

JEVTANA is contraindicated in patients with severe hepatic impairment (total bilirubin >3 × ULN) [see Contraindications (4)]. Dose should be reduced for patients with mild (total bilirubin >1 to ≤1.5 × ULN or AST >1.5 × ULN and moderate (total bilirubin 1.5 to ≤3.0 × ULN) hepatic impairment based on tolerability data in these patients [see Dosage and Administration (2.3) and Use in Specific Populations (8.7)]. Administration of JEVTANA to patients with mild and moderate hepatic impairment should be undertaken with close clinical monitoring of safety.

5.6 Embryo-Fetal Toxicity

Based on findings in animal reproduction studies and its mechanism of action, JEVTANA can cause fetal harm when administered to a pregnant woman [see Clinical Pharmacology (12.1)]. There are no available data in pregnant women to inform the drug-associated risk. In 84 pregnant women enrolled in combination chemotherapy for breast cancer, the incidence of congenital anomalies in the offspring of pregnant women during organogenesis caused embryonic and fetal death at doses lower than the maximum recommended human dose (approximately 0.06 times the Cmax in patients at the recommended human dose). Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of JEVTANA [see Use in Specific Populations (8.1), (8.3)].

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in another section of this label.

• Bone Marrow Suppression [see Warnings and Precautions (5.1)]
• Increased Toxicities in Elderly Patients [see Warnings and Precautions (5.2)]
• Hypersensitivity Reactions [see Warnings and Precautions (5.3)]
• Gastrointestinal Adverse Reactions [see Warnings and Precautions (5.4)]
• Respiratory Adverse Reactions [see Warnings and Precautions (5.5)]
• Urinary Disorders Including Cystitis [see Warnings and Precautions (5.6)]
• Respiratory Disorders [see Warnings and Precautions (5.7)]
• Use in Patients with Hepatic Impairment [see Warnings and Precautions (5.8)]

6.1 ClinicalTrialsExperience

Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed in clinical practice. TROPIC Trial (JEVTANA + prednisone compared to mitoxantrone)

The safety of JEVTANA in combination with prednisone was evaluated in 371 patients with metastatic castration-resistant prostate cancer treated in the randomized TROPIC trial, a placebo-controlled study comparing JEVTANA 20 mg/m² with mitoxantrone plus prednisone.

Deaths due to causes other than disease progression within 30 days of last study drug dose were reported in 18% (5%) JEVTANA-treated patients and 3 (1%) mitoxantrone-treated patients. The most common fatal adverse reactions in JEVTANA-treated patients were infection (n=5) and renal failure (n=4). The majority (4 of 5 patients) of fatal infection-related adverse reactions occurred after a single dose of JEVTANA. Other fatal adverse reactions in JEVTANA-treated patients included venous fibrillation, cerebral hemorrhage, and dyspnea.

The most common (≥10%) grade 1–4 adverse reactions were anemia, leukopenia, neutropenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, asthe- nia, abdominal pain, hematia, back pain, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysgeusia, cough, arthralgia, and alopecia.

The most common (≥10%) grade 3–4 adverse reactions in patients who received JEVTANA were neutropenia, leukopenia, anemia, febrile neutropenia, diarrhea, fatigue, and asthe- nia.

Treatment discontinuations due to adverse drug reactions occurred in 18% of patients who received JEVTANA and 8% of patients who received mitoxantrone. The most common adverse drug reaction leading to treatment discontinuation in the JEVTANA group was neutropenia and renal failure. Dose reductions were reported in 12% of JEVTANA-treated patients and 4% of mitoxantrone-treated patients. Dose delays were reported in 28% of JEVTANA-treated patients and 15% of mitoxantrone-treated patients.
Table 2: Incidence of Adverse Reactions* and Hematologic Abnormalities in ≥5% of Patients Receiving JEVTAÑA in Combination with Prednisone or Mitoxantrone in Combination with Prednisone in TROPIC

<table>
<thead>
<tr>
<th>Organ Class</th>
<th>Preferred Term</th>
<th>Grade 1–4 n (%)</th>
<th>Grade 3–4 n (%)</th>
<th>Grade 1–4 n (%)</th>
<th>Grade 3–4 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Neutropenia¹</td>
<td>347 (94%)</td>
<td>303 (82%)</td>
<td>325 (87%)</td>
<td>215 (58%)</td>
</tr>
<tr>
<td></td>
<td>Febrile Neutropenia</td>
<td>27 (7%)</td>
<td>27 (7%)</td>
<td>5 (1%)</td>
<td>5 (1%)</td>
</tr>
<tr>
<td></td>
<td>Anemia¹</td>
<td>361 (96%)</td>
<td>39 (11%)</td>
<td>302 (82%)</td>
<td>18 (5%)</td>
</tr>
<tr>
<td></td>
<td>Leukopenia¹</td>
<td>355 (96%)</td>
<td>253 (69%)</td>
<td>343 (93%)</td>
<td>157 (42%)</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia¹</td>
<td>176 (48%)</td>
<td>15 (4%)</td>
<td>160 (43%)</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>Cardiac Disorders</td>
<td>Arhythmia²</td>
<td>18 (5%)</td>
<td>4 (1%)</td>
<td>6 (2%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Diarrhea</td>
<td>173 (47%)</td>
<td>23 (6%)</td>
<td>39 (11%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>127 (34%)</td>
<td>7 (2%)</td>
<td>85 (23%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>83 (22%)</td>
<td>6 (2%)</td>
<td>38 (10%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Constipation</td>
<td>76 (20%)</td>
<td>4 (1%)</td>
<td>57 (15%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Abdominal Pain³</td>
<td>64 (17%)</td>
<td>7 (2%)</td>
<td>23 (6%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Dyspepsia³</td>
<td>36 (10%)</td>
<td>0</td>
<td>9 (2%)</td>
<td>0</td>
</tr>
<tr>
<td>General Disorders and Administration Site Conditions</td>
<td>Fatigue</td>
<td>136 (37%)</td>
<td>18 (5%)</td>
<td>102 (27%)</td>
<td>11 (3%)</td>
</tr>
<tr>
<td></td>
<td>Asthenia</td>
<td>76 (20%)</td>
<td>17 (5%)</td>
<td>46 (12%)</td>
<td>9 (2%)</td>
</tr>
<tr>
<td></td>
<td>Pyrexia</td>
<td>45 (12%)</td>
<td>4 (1%)</td>
<td>23 (6%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Peripheral Edema</td>
<td>34 (9%)</td>
<td>2 (&lt;1%)</td>
<td>34 (9%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Mucosal Inflammation</td>
<td>22 (6%)</td>
<td>1 (&lt;1%)</td>
<td>10 (3%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>20 (5%)</td>
<td>4 (1%)</td>
<td>18 (5%)</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td>Urinary Tract Infection⁴</td>
<td>29 (8%)</td>
<td>6 (2%)</td>
<td>12 (3%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td>Investigations</td>
<td>Weight Decreased</td>
<td>32 (9%)</td>
<td>0</td>
<td>28 (8%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td>Anorexia</td>
<td>59 (16%)</td>
<td>3 (&lt;1%)</td>
<td>39 (11%)</td>
<td>3 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Dehydration</td>
<td>18 (5%)</td>
<td>8 (2%)</td>
<td>10 (3%)</td>
<td>3 (&lt;1%)</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td>Back Pain</td>
<td>60 (16%)</td>
<td>14 (4%)</td>
<td>45 (12%)</td>
<td>11 (3%)</td>
</tr>
<tr>
<td></td>
<td>Arthralgia</td>
<td>39 (11%)</td>
<td>4 (1%)</td>
<td>31 (8%)</td>
<td>4 (1%)</td>
</tr>
<tr>
<td></td>
<td>Muscle Spasms</td>
<td>27 (7%)</td>
<td>0</td>
<td>10 (3%)</td>
<td>0</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>Peripheral Neuropathy⁵</td>
<td>50 (13%)</td>
<td>3 (&lt;1%)</td>
<td>12 (3%)</td>
<td>3 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Dysgeusia</td>
<td>41 (11%)</td>
<td>0</td>
<td>15 (4%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>30 (8%)</td>
<td>0</td>
<td>21 (6%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>28 (8%)</td>
<td>0</td>
<td>19 (5%)</td>
<td>0</td>
</tr>
<tr>
<td>Renal and Urinary Tract Disorders</td>
<td>Hematuria</td>
<td>62 (17%)</td>
<td>7 (2%)</td>
<td>13 (4%)</td>
<td>1 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Dysuria</td>
<td>25 (7%)</td>
<td>0</td>
<td>5 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory, Thoracic and Mediastinal Disorders</td>
<td>Dyspnea</td>
<td>43 (12%)</td>
<td>4 (1%)</td>
<td>16 (4%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Cough</td>
<td>40 (11%)</td>
<td>0</td>
<td>22 (6%)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Graded using NCI CTCAE version 3.
†Based on laboratory values, JEVTAÑA: n=369, mitoxantrone: n=370.
‡Includes atrial fibrillation, atrial flutter, atrial tachycardia, atrioventricular block complete, bradycardia, palpitations, supraventricular tachycardia, tachyarrhythmia, and tachycardia.
§Includes abdominal discomfort, abdominal pain lower, abdominal tenderness, and GI pain.
¶Includes gastroesophageal reflux disease and reflux gastritis.
†‡Includes urinary tract infection enterococcal and urinary tract infection fungal.
**Includes peripheral motor neuropathy and peripheral sensory neuropathy.

PROSELICA Trial (comparison of two doses of JEVTAÑA) In a noninferiority, multicenter, randomized, open-label study (PROSELICA), 1175 patients with metastatic castration-resistant prostate cancer, previously treated with a docetaxel-containing regimen, were treated with either JEVTAÑA 25 mg/m² (n=595) or the 20 mg/m² (n=580) dose. Deaths within 30 days of last study drug dose were reported in 22 (3.8%) patients in the 20 mg/m² and 32 (5.4%) patients in the 25 mg/m² arm. The most common fatal adverse reactions in JEVTAÑA-treated patients were related to infections, and these occurred more frequently in the 25 mg/m² arm (n=15) than in the 20 mg/m² arm (n=8). Other fatal adverse reactions in JEVTAÑA-treated patients included cerebral hemorrhage, respiratory failure, paralytic ileus, diarrhea, acute pulmonary edema, disseminated intravascular coagulation, renal failure, sudden death, cardiac arrest, ischemic stroke, diverticular perforation, and cardiorenal syndrome. Grade 1–4 adverse reactions occurring ≥5% more commonly in patients on the 25 mg/m² versus 20 mg/m² arms were leukopenia, neutropenia, thrombocytopenia, febrile neutropenia, decreased appetite, nausea, diarrhea, asthenia, and hematuria. Grade 3–4 adverse reactions occurring ≥5% more commonly in patients on the 25 mg/m² versus 20 mg/m² arms were leukopenia, neutropenia, and febrile neutropenia. Treatment discontinuations due to adverse drug reactions occurred in 17% of patients in the 20 mg/m² group and 20% of patients in the 25 mg/m² group. The most common adverse reactions leading to treatment discontinuation were fatigue and hematuria. The patients in the 20 mg/m² group received a median of 6 cycles (median duration of 18 weeks), while patients in the 25 mg/m² group received a median of 7 cycles (median duration of 21 weeks). In the 25 mg/m² group, 158 patients (22%) had a dose reduced from ≥25 to 20 mg/m², 19 patients (3%) had a dose reduced from 20 to 15 mg/m² and 1 patient (0.2%) had a dose reduced from 15 to 12 mg/m². In the 20 mg/m² group, 58 patients (10%) had a dose reduced from 20 to 15 mg/m², and 9 patients (2%) had a dose reduced from 15 to 12 mg/m².

Table 3: Incidence of Adverse Reactions* in ≥5% of Patients Receiving JEVTAÑA 20 mg/m² or 25 mg/m² in Combination with Prednisone in PROSELICA

<table>
<thead>
<tr>
<th>Organ Class</th>
<th>Preferred Term</th>
<th>Grade 1–4 n (%)</th>
<th>Grade 3–4 n (%)</th>
<th>Grade 1–4 n (%)</th>
<th>Grade 3–4 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary System Organ Class</td>
<td>Peripheral Neuropathy⁵</td>
<td>50 (13%)</td>
<td>3 (&lt;1%)</td>
<td>12 (3%)</td>
<td>3 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Dysgeusia</td>
<td>41 (11%)</td>
<td>0</td>
<td>15 (4%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Dizziness</td>
<td>30 (8%)</td>
<td>0</td>
<td>21 (6%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>28 (8%)</td>
<td>0</td>
<td>19 (5%)</td>
<td>0</td>
</tr>
<tr>
<td>Blood and Lymphatic System Disorders</td>
<td>Febrile Neutropenia</td>
<td>12 (2%)</td>
<td>12 (2%)</td>
<td>55 (9%)</td>
<td>55 (9%)</td>
</tr>
<tr>
<td></td>
<td>Neutropenia²</td>
<td>18 (3%)</td>
<td>14 (2%)</td>
<td>65 (11%)</td>
<td>57 (10%)</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td>Urinary tract infection⁴</td>
<td>43 (7%)</td>
<td>12 (2%)</td>
<td>66 (11%)</td>
<td>14 (2%)</td>
</tr>
<tr>
<td></td>
<td>Neutropenic infection⁵</td>
<td>15 (3%)</td>
<td>13 (2%)</td>
<td>42 (7%)</td>
<td>36 (6%)</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td>Decreased appetite</td>
<td>76 (13%)</td>
<td>4 (0.7%)</td>
<td>110 (19%)</td>
<td>7 (1%)</td>
</tr>
</tbody>
</table>
### Table 3: Incidence of Adverse Reactions* in ≥5% of Patients Receiving JEVTANA 20 mg/m² or 25 mg/m² in Combination with Prednisone in PROSELICA (continued)

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>JEVTANA 20 mg/m² every 3 weeks with prednisone 10 mg daily n=580</th>
<th>JEVTANA 25 mg/m² every 3 weeks with prednisone 10 mg daily n=595</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>41 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>Peripheral sensory neuropathy</td>
<td>38 (7%)</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>24 (4%)</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>29 (5%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td><strong>Respiratory, Thoracic and Mediastinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>30 (5%)</td>
<td>5 (0.9%)</td>
</tr>
<tr>
<td>Cough</td>
<td>34 (6%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>178 (31%)</td>
<td>8 (1%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>142 (25%)</td>
<td>4 (0.7%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>84 (15%)</td>
<td>7 (1.2%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>102 (18%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>34 (6%)</td>
<td>3 (0.5%)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>27 (5%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Skin and Subcutaneous Tissue Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>15 (3%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Musculoskeletal and Connective Tissue Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>64 (11%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Bone pain</td>
<td>46 (8%)</td>
<td>10 (2%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>49 (8%)</td>
<td>3 (0.5%)</td>
</tr>
<tr>
<td>Pain in extremity</td>
<td>30 (5%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td><strong>Renal and Urinary Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>82 (14%)</td>
<td>11 (2%)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>31 (5%)</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td><strong>General Disorders and Administration Site Conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>143 (25%)</td>
<td>15 (3%)</td>
</tr>
<tr>
<td>Asthenia</td>
<td>89 (15%)</td>
<td>11 (2%)</td>
</tr>
<tr>
<td>Edema peripheral</td>
<td>39 (7%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>27 (5%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight decreased</td>
<td>24 (4%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrong technique in drug usage process</td>
<td>2 (0.3%)</td>
<td>0</td>
</tr>
</tbody>
</table>

*Grade from NCI CTCAE version 4.03.
†Based on adverse event reporting.
§Includes neutropenic sepsis.

### Table 4: Incidence of Hematologic Laboratory Abnormalities in Patients Receiving JEVTANA 20 mg/m² or 25 mg/m² in Combination with Prednisone in Study PROSELICA

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>JEVTANA 20 mg/m² every 3 weeks with prednisone 10 mg daily n=577</th>
<th>JEVTANA 25 mg/m² every 3 weeks with prednisone 10 mg daily n=590</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1–4 n (%)</td>
<td>Grade 3–4 n (%)</td>
<td>Grade 1–4 n (%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>384 (67%)</td>
<td>241 (42%)</td>
</tr>
</tbody>
</table>

**Hematuria**

In study TROPIC, adverse reactions of hematuria, including those requiring medical intervention, were more common in JEVTANA-treated patients. The incidence of grade ≥3 hematuria was 6% in JEVTANA-treated patients and 2% in mitoxantrone-treated patients. Other factors associated with hematuria were well-balanced between arms and do not account for the increased rate of hematuria on the JEVTANA arm.

In study PROSELICA, hematuria of all grades was observed in 18% of patients overall. Hepatic Laboratory Abnormalities

The incidences of grade 3–4 increased AST, increased ALT, and increased bilirubin were each ≤1%.

### 6.2 Postmarketing Experience

The following adverse reactions have been identified from clinical trials and/or postmarketing surveillance. Because they are reported from a population of unknown size, precise estimates of frequency cannot be made.

Gastrointestinal: Gastritis, intestinal obstruction.

Respiratory: Interstitial pneumonia/pneumonitis, interstitial lung disease and acute respiratory distress syndrome.

Renal and urinary disorders: Radiation recall hemorrhagic cystitis.

### 7. DRUG INTERACTIONS

#### 7.1 CYP3A Inhibitors

Cabazitaxel is primarily metabolized through CYP3A [see Clinical Pharmacology (12.3)]. Strong CYP3A inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, ritonavir, saquinavir, telithromycin, voriconazole) may increase plasma concentrations of cabazitaxel. Avoid the coadministration of JEVTANA with strong CYP3A inhibitors. If patients require coadministration of a strong CYP3A inhibitor, consider a 25% JEVTANA dose reduction [see Dosage and Administration (2.4) and Clinical Pharmacology (12.3)].

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

**Risk Summary**

The safety and efficacy of JEVTANA have not been established in females. There are no human data on the use of JEVTANA in pregnant women to inform the drug-associated risk.

In animal reproduction studies, intravenous administration of cabazitaxel in pregnant rats during organogenesis caused embryonic and fetal death at doses lower than the maximum recommended human dose [see Data].

**Data**

Animal data

In an early embryonic developmental toxicity study in rats, cabazitaxel was administered intravenously for 15 days prior to mating through Day 6 of pregnancy, which resulted in an increase in pre-implantation loss at 0.2 mg/kg/day and an increase in early resorptions at ≥0.1 mg/kg/day (approximately 0.06 and 0.02 times the C_{max} in patients at the recommended human dose, respectively).

In an embryo-fetal developmental toxicity study in rats, cabazitaxel caused maternal and embryo-fetal toxicity consisting of increased postimplantation loss, embryolethality, and fetal deaths when administered intravenously at a dose of 0.16 mg/kg/day (approximately 0.06 times the C_{max} in patients at the recommended human dose). Decreased mean fetal birthweight associated with delays in skeletal ossification was observed at doses ≥0.08 mg/kg. Cabazitaxel crossed the placenta barrier within 24 hours of a single intravenous administration of 0.08 mg/kg to pregnant rats at gestational day 17. A dose of 0.08 mg/kg resulted in a C_{max} approximately 0.02 times that observed in patients at the recommended human dose. Administration of cabazitaxel did not result in fetal abnormalities in rats or rabbits at exposure levels significantly lower than the expected human exposures.

#### 8.2 Lactation

**Risk Summary**

The safety and efficacy of JEVTANA have not been established in females. There is no information available on the presence of cabazitaxel in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production. Cabazitaxel or cabazitaxel metabolites are excreted in maternal milk of lactating rats

In a milk excretion study, radioactivity related to cabazitaxel was detected in the stomachs and intestines of nursing pups within 2 hours of a single intravenous administration of 0.08 mg/kg to pregnant rats at gestational day 17. A dose of 0.08 mg/kg resulted in a C_{max} approximately 0.02 times the C_{max} in patients at the recommended human dose. This was detectable 24 hours post dose. Approximately 0.1 mg/kg/day (approximately 0.06 and 0.02 times the C_{max} in patients at the recommended human dose). Decreased fetal body weight was observed in rats at exposure levels significantly lower than the expected human exposures.
8.3 Females and Males of Reproductive Potential

Contraception

Males

Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the final dose of JEVTANA [see Use in Specific Populations (8.1)].

Infertility

Males

Based on animal toxicity studies, JEVTANA may impair human fertility in males of reproductive potential [see Nonclinical Toxicology (13.1)].

8.4 Pediatric Use

The safety and effectiveness of JEVTANA in pediatric patients have not been established.

JEVTANA was evaluated in 39 pediatric patients (ages 3 to 18 years) receiving prophylactic G-CSF. The maximum tolerated dose (MTD) was 30 mg/m² intravenously over 1 hour on Day 1 of a 21 day cycle in pediatric patients with solid tumors based on the dose-limiting toxicity (DLT) of febrile neutropenia. No objective responses were observed in 11 patients with refractory high grade glioma (HGG) or diffuse intrinsic pontine glioma (DIPG). One patient had a partial response among the 9 patients with ependymoma.

Infusion related/hypersensitivity reactions were seen in 10 patients (26%). Three patients experienced serious adverse events of anaphylactic reaction. The incidence of infusion related/hypersensitivity reactions decreased with steroid pre-medication. The most frequent treatment-emergent adverse events were similar to those reported in adults.

Based on the population pharmacokinetics analysis conducted with data from 31 pediatric patients with cancer (ages 3 to 18 years), the clearances by body surface area were comparable to those in adults.

8.5 Geriatric Use

In the TROPIC study, of the 371 patients with prostate cancer treated with JEVTANA every three weeks plus prednisone, 240 patients (64.7%) were 65 years of age and over, while 70 patients (18.9%) were 75 years of age and over. No overall differences in effectiveness were observed between patients ≥65 years of age and younger patients. Elderly patients (≥65 years of age) may be more likely to experience certain adverse reactions. The incidence of death due to causes other than disease progression within 30 days of the last cabazitaxel dose were higher in patients who were 65 years of age or greater compared to younger patients [see Warnings and Precautions (5.2)]. The incidence of grade 3–4 neutropenia and febrile neutropenia were higher in patients who were 65 years of age or greater compared to younger patients. The following grade 1–4 adverse reactions were reported at rates ≥5% higher in patients 65 years of age or older compared to younger patients: fatigue (40% vs 30%), neutropenia (75% vs 89%), anemia (24% vs 15%), pyrexia (15% vs 8%), dizziness (10% vs 5%), urinary tract infection (10% vs 3%), and dehydration (7% vs 2%), respectively.

In the PROSELICA study, the grade 1–4 adverse reactions reported at rates of at least 5% higher in patients 65 years of age or older compared to younger patients were diarrhea (43% vs 33%), fatigue (30% vs 19%), anemia (22% vs 13%), constipation (20% vs 13%), clinical neutropenia (13% vs 6%), febrile neutropenia (11% vs 5%), and dyspnea (10% vs 3%).

Based on a population pharmacokinetic analysis, no significant difference was observed in pharmacokinetics of cabazitaxel between patients <65 years (n=100) and older (n=70).

8.6 Renal Impairment

No dose adjustment is necessary in patients with renal impairment not requiring hemodialysis. Patients presenting with end-stage renal disease (creatinine clearance ClCR <15 mL/min/1.73 m²), should be monitored carefully during treatment [see Clinical Pharmacology (12.3)].

8.7 Hepatic Impairment

Cabazitaxel is extensively metabolized in the liver. Patients with mild hepatic impairment (total bilirubin ≥1 to ≤1.5 × ULN or AST >1.5 × ULN) should have JEVTANA dose of 20 mg/m². Administration of cabazitaxel to patients with mild hepatic impairment should be undertaken with caution and close monitoring of safety [see Clinical Pharmacology (12.3)].

The maximum tolerated dose in patients with moderate hepatic impairment (total bilirubin >1.5 to ≤3.0 × ULN or AST ≥15) was 15 mg/m², however, the efficacy at this dose level was unknown. JEVTANA was contraindicated in patients with severe hepatic impairment (total bilirubin >3 × ULN) [see Contraindications (4)].

10 OVERDOSE

There is no known antidote for JEVTANA overdose. Overdose has resulted from improper preparation [see Dosage and Administration (2.5)]. Read the entire section Dosage and Administration (2) carefully before mixing or diluting. Complications of overdose include exacerbation of adverse reactions such as bone marrow suppression and gastrointestinal disorders. Overdose has led to fatal outcome.

In case of overdose, the patient should be kept in a specialized unit where vital signs, chemistry and particular functions can be closely monitored. Patients should receive therapeutic G-CSF as soon as possible after discovery of overdose. Other appropriate symptomatic measures should be taken, as needed.

11 DESCRIPTION

JEVTANA (cabazitaxel) injection is an antineoplastic agent belonging to the taxane class that is for parenteral use. It is prepared by semi-synthesis with a precursor extracted from yew needles.

The chemical name of cabazitaxel is (2R,4R,5S,9S,10S,13R)-4-acetoxy-1-acetoxy-21-acetoxy-3,5-dimethoxo-9,10-epoxytax-11-en-2'-yl benzoate – propan-2-one (1:1).

Cabazitaxel has the following structural formula:

![Cabazitaxel Structural Formula]

Cabazitaxel is a white to almost-white powder with a molecular formula of C_{25}H_{30}NO_4·H_2O and a molecular weight of 584.01 (for the acetone solvate) / 395.93 (for the solvent free). It is lipophilic, practically insoluble in water and soluble in alcohol.

JEVTANA (cabazitaxel) injection 60 mg/1.5 mL is a sterile, non-pyrogenic, clear yellow to brownish-yellow viscous solution and is available in single-dose vials containing 60 mg cabazitaxel (anhydrous and solvent free) and 1.56 g polysorbate 80. Each mL contains 40 mg cabazitaxel (anhydrous) and 1.04 g polysorbate 80.

DILUENT for JEVTANA is a clear, colorless, sterile, and non-pyrogenic solution containing 13% (w/v) ethanol in water for injection, approximately 5.7 mL. JEVTANA requires two dilutions prior to intravenous infusion. JEVTANA injection should be diluted only with the supplied DILUENT for JEVTANA, followed by dilution in either 0.9% sodium chloride solution or 5% dextrose solution.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Cabazitaxel is a microtubule inhibitor. Cabazitaxel binds to tubulin and promotes its stabilization of microtubules, which results in the inhibition of mitotic and interphase cellular functions.

12.2 Pharmacokinetics

Cardiac Electrophysiology

The effect of cabazitaxel following a single dose of 25 mg/m² administered by intravenous infusion for 2 hours was evaluated in 94 patients with solid tumors. No large changes in the mean QT interval (i.e., >20 ms) from baseline based on Fridericia correction method were detected. However, a small increase in the mean QTc interval (i.e., <10 ms) cannot be excluded due to study design limitations.

12.3 Pharmacokinetics

A population pharmacokinetic analysis was conducted in 170 patients with solid tumors at doses ranging from 10 to 30 mg/m² weekly or every three weeks.

Absorption

Based on the population pharmacokinetic analysis, after an intravenous dose of cabazitaxel 25 mg/m² every three weeks, the mean C_{max} in patients with metastatic prostate cancer was 228 ng/mL (CV 107%) and was reached at the end of the one-hour infusion (t_{max}). The mean AUC in patients with metastatic prostate cancer was 991 ng·h/mL (CV 14%).

No major deviation from the dose proportionality was observed from 10 to 30 mg/m² in patients with advanced solid tumors.

Distribution

The volume of distribution (V_{d2}) was 4,864 L (2,643 L/m² for a patient with a median BSA of 1.84 m²) at steady state.

In vitro, the binding of cabazitaxel to human serum proteins was 89% to 92% and was not saturable up to 50,000 ng/mL, which covers the maximum concentration observed in clinical trials. Cabazitaxel is mainly bound to human serum albumin (82%) and lipoproteins (88% for HDL, 70% for LDL, and 56% for VLDL). The in vitro blood-to-plasma concentration ratio in human blood ranged from 0.90 to 0.99, indicating that cabazitaxel was equally distributed between blood and plasma.

Metabolism

Cabazitaxel is extensively metabolized in the liver (>95%), mainly by the CYP3A4/5 isoenzyme (80% to 90%), and to a lesser extent by CYP2C8. Cabazitaxel is the main circulating moiety in human plasma. Seven metabolites were detected in plasma (including the 3 active metabolites issued from O-demethylation), with the main one accounting for 5% of cabazitaxel exposure. Around 20 metabolites of cabazitaxel are excreted into human urine and feces.

Elimination

Based on a one-hour intravenous infusion [14C]-cabazitaxel 25 mg/m², approximately 80% of the administered dose was eliminated within 2 weeks. Cabazitaxel is mainly excreted in the feces as numerous metabolites (76% of the dose); while renal excretion of cabazitaxel and metabolites account for 3.7% of the dose (2.3% as unchanged drug in urine). Based on the population pharmacokinetic analysis, cabazitaxel has a plasma clearance of 48.5 L/h (CV 39%, 29.4 L/h/m² for a patient with a median BSA of 1.84 m²) in patients with metastatic prostate cancer. Following a one-hour intravenous infusion, plasma concentrations of cabazitaxel can be described by a three-compartment pharmacokinetic model with α-, β-, and γ- half-lives of 4 minutes, 2 hours, and 95 hours, respectively.

Metabolism

Cabazitaxel is minimally excreted via the kidney. A population pharmacokinetic analysis carried out in 170 patients including 14 patients with moderate renal impairment (30 mL/min <ClCR ≤50 mL/min) and 59 patients with mild renal impairment (50 mL/min <ClCR ≤80 mL/min) showed that mild to moderate renal impairment did not have meaningful effects on the pharmacokinetics of cabazitaxel. This was confirmed by a dedicated comparative pharmacokinetic study in patients with solid tumors with normal renal function (n=8, ClCR >80 mL/min/1.73 m²), or moderate (n=8, 30 mL/min <ClCR ≤80 mL/min/1.73 m²) and severe (n=2, ClCR <30 mL/min/1.73 m²) renal impairment, who received several cycles of cabazitaxel in single IV infusion up to 25 mg/m². Limited pharmacokinetic data were available in patients with end-stage renal disease (n=2, ClCR <15 mL/min/1.73 m²).
CABAZITAXEL \textregistered\ is extensively metabolized in the liver. A dedicated study in 43 cancer patients with hepatic impairment showed no influence of mild (total bilirubin $>1$ to $\leq 1.5 \times$ ULN or AST $>1.5$ to $<3.0 \times$ ULN) hepatic impairment on cabazitaxel pharmacokinetics. The maximum tolerated dose (MTD) of cabazitaxel was 20 and $15 \text{mg/m}^2$, respectively. In 3 patients with severe hepatic impairment (total bilirubin $>3 \times$ ULN), a $39\%$ decrease in clearance was observed. In a repeat-dose study in patients with mild hepatic impairment (ratio $=0.61$, $90\%$ CI: 0.36–1.05), indicating some effect of severe hepatic impairment on cabazitaxel pharmacokinetics. The MTD of cabazitaxel in patients with severe hepatic impairment was not established. Based on safety and tolerability data, cabazitaxel dose should be maintained at $20 \text{mg/m}^2$ in patients with mild hepatic impairment and reduced to $15 \text{mg/m}^2$ in patients with moderate hepatic impairment (see Warnings and Precautions (5.8) and Use in Specific Populations (8.7)). Cabazitaxel is contraindicated in patients with severe hepatic impairment (see Contraindications (4) and Use in Specific Populations (8.7)).

### Drug Interactions

A drug interaction study of JEVTANA in 23 patients with advanced cancers has shown that repeated administration of ketoconazole (400 mg orally once daily), a strong CYP3A inhibitor, increased the exposure to cabazitaxel (5 mg/m$^2$ intravenous) by $25\%$. A drug interaction study of JEVTANA in 13 patients with advanced cancers has shown that repeated administration of aprepitant (125 or $80 \text{mg}$ once daily), a moderate CYP3A inhibitor, did not modify the exposure to cabazitaxel (15 mg/m$^2$ intravenous).

A drug interaction study of JEVTANA in 21 patients with advanced cancers has shown that repeated administration of rifampin (600 mg once daily), a strong CYP3A inducer, decreased the exposure to cabazitaxel (15 mg/m$^2$ intravenous) by $17\%$. A drug interaction study of JEVTANA in 11 patients with advanced cancers has shown that cabazitaxel (25 mg/m$^2$ administered as a single 1-hour infusion) did not modify the exposure to midazolam, a probe substrate of CYP3A.

### 13 NONCLINICAL TOXICOLOGY

#### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential of cabazitaxel. Cabazitaxel was positive for clastogenesis in the in vivo micronucleus test, inducing an increase of micronuclei in rat rats at doses $\geq 0.5 \text{mg/kg}$. Cabazitaxel increased numerical aberrations with or without metabolic activation in an in vitro test in human lymphocytes though no induction of structural aberrations was observed. Cabazitaxel did not induce mutations in the bacterial reverse mutation (Ames) test. The positive in vivo genotoxicity findings are consistent with the pharmacological activity of the compound (inhibition of tubulin depolymerization).

In a fertility study performed in female rats at cabazitaxel doses of 0.05, 0.1, or $0.2 \text{mg/kg/day}$ there was no effect of administration of the drug on mating behavior or the ability to become pregnant. In repeat-dose toxicity studies in rats with cabazitaxel administration once every three weeks for up to 6 months, atrophy of the uterus was observed at the $5 \text{mg/kg}$ dose level (approximately the AUC in patients with cancer at the recommended human dose) along with necrosis of the corpora lutea at doses $\geq 1 \text{mg/kg}$ (approximately 0.2 times the AUC at the clinically recommended human dose).

In a fertility study in male rats, cabazitaxel did not affect mating performances or fertility at doses of 0.05, 0.1, or 0.2 mg/kg/day. In repeat-dose toxicity studies with intravenous cabazitaxel administration once every three weeks for up to 9 months, degeneration of spermatids was observed in dogs treated at a dose of $0.5 \text{mg/kg}$ (approximately 0.1 times the AUC in patients at the recommended human dose).

### 14 CLINICAL STUDIES

#### 14.1 TROPIC Trial (JEVTANA + prednisone compared to mitoxantrone)

The efficacy and safety of JEVTANA in combination with prednisone were evaluated in a randomized, open-label, international, multi-center study in patients with metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing treatment regimen (TROPIC, NCT00417079).

A total of 755 patients were randomized to receive either JEVTANA 25 mg/m$^2$ intravenously every 3 weeks for a maximum of 10 cycles with prednisone 10 mg orally daily (n=378), or to receive mitoxantrone 12 mg/m$^2$ intravenously every 3 weeks for 10 cycles with prednisone 10 mg orally daily (n=377) for a maximum of 10 cycles. This study included patients over 18 years of age with hormone-refractory metastatic prostate cancer either measurable by RECIST criteria or non-measurable disease with rising PSA or appearance of new lesions, and ECOG (Eastern Cooperative Oncology Group) performance status 0–2. Patients had to have neutrophils $>1,500$ cells/mm$^3$, platelets $>100,000$ cells/mm$^3$, hemoglobin $>10 \text{g/dL}$, creatinine $<1.5 \times$ upper limit of normal (ULN), total bilirubin $<1 \times$ ULN, AST $<1.5 \times$ ULN, and ALT $<1.5 \times$ ULN.

Patients with a history of congestive heart failure, or myocardial infarction within the last 6 months, or patients with uncontrolled cardiac arrhythmias, angina pectoris, and/or hypertension were not included in the study.

Demographics, including age, race, and ECOG performance status (0–2) were balanced between the treatment arms. The median age was 68 years (range 46–92) and the racial distribution for all groups was $83.9\%$ Caucasian, $6.9\%$ Asian, $5.3\%$ Black, and $4\%$ Others in the JEVTANA group.

Efficacy results for the JEVTANA arm versus the control arm are summarized in Table 5 and Figure 1.

#### Table 5: Efficacy of JEVTANA in TROPIC in the Treatment of Patients with Metastatic Castration-Resistant Prostate Cancer (intent-to-treat analysis)

<table>
<thead>
<tr>
<th>Overall Survival</th>
<th>Median survival (month) (95% CI)</th>
<th>Hazard Ratio $^*$ (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of deaths (%)</td>
<td>234 (61.9 %)</td>
<td>279 (74.0%)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>378</td>
<td>377</td>
<td></td>
</tr>
<tr>
<td>Hazard Ratio</td>
<td>0.70 (0.59–0.83)</td>
<td></td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Figure 1: Kaplan-Meier Overall Survival Curves (TROPIC)

Investigator-assessed tumor response of 14.4% ($95\%$ CI: 9.6–19.3) was higher for patients in the JEVTANA arm compared to 4.4% ($95\%$ CI: 1.6–7.2) for patients in the mitoxantrone arm, p=0.0006.

#### 14.2 PROSELICA Trial (comparison of two doses of JEVTANA)

In a noninferiority, multicenter, randomized, open-label study (PROSELICA, NCT01385880), 1200 patients with metastatic castration-resistant prostate cancer, previously treated with a docetaxel-containing regimen, were randomized to receive either JEVTANA 25 mg/m$^2$ ($n=602$) or 20 mg/m$^2$ ($n=598$) dose. Overall survival (OS) was the major efficacy outcome.

Demographics, including age, race, and ECOG performance status (0–2) were balanced between the treatment arms. The median age was 68 years (range 45–89) and the racial distribution for all groups was $87\%$ Caucasian, $6.9\%$ Asian, $2.3\%$ Black, and $3.8\%$ Others in the JEVTANA 25 mg/m$^2$ group. The median age was 69 years (range 45–88) and the racial distribution for all groups was $88.7\%$ Caucasian, $6.6\%$ Asian, $1.8\%$ Black, and $2.8\%$ Others in the JEVTANA 25 mg/m$^2$ group.

The study demonstrated noninferiority in overall survival (OS) of JEVTANA 20 mg/m$^2$ in comparison with JEVTANA 25 mg/m$^2$ in an intent-to-treat population (see Table 5 and Figure 2). Based on the per-protocol population, the estimated median OS was 15.1 months on JEVTANA 20 mg/m$^2$ and 15.9 months on JEVTANA 25 mg/m$^2$, the observed hazard ratio (HR) of OS was 1.042 (97.78% CI: 0.886, 1.224). Among the subgroup analyses intended for assessing the heterogeneity, no notable difference in OS was observed in the JEVTANA 25 mg/m$^2$ arm compared to the JEVTANA 20 mg/m$^2$ arm in subgroups based on the stratification factors of ECOG performance status score, measurability of disease, or region.
Table 6: Overall Survival in PROSELICA for JEVTANA 20 mg/m² versus JEVTANA 25 mg/m² (intent-to-treat analysis)

<table>
<thead>
<tr>
<th></th>
<th>CBZ20+PRED</th>
<th>CBZ25+PRED</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>598</td>
<td>602</td>
</tr>
<tr>
<td>Overall Survival</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of deaths</td>
<td>497 (83.1%)</td>
<td>501 (83.2%)</td>
</tr>
<tr>
<td>Median survival</td>
<td>13.4 (12.2 to 14.9)</td>
<td>14.5 (13.5 to 15.3)</td>
</tr>
<tr>
<td>(months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hazard Ratio*</td>
<td>0.9778 CI</td>
<td>1.024 (0.886, 1.184)</td>
</tr>
</tbody>
</table>

*Adjusted for interim OS analyses. The noninferiority margin is 1.214.

Figure 2: Kaplan-Meier Overall Survival Curves (intent-to-treat population) (PROSELICA)

15 REFERENCES

16 HOW SUPPLIED/STORAGE AND HANDLING
16.1 How Supplied
JEVTANA is supplied as a kit consisting of the following:
- One single-dose vial of JEVTANA (cabazitaxel) injection: a clear yellow or brownish-
  yellow viscous solution of 60 mg/1.5 mL in a clear glass vial with a grey rubber
  closure, aluminum cap, and light green plastic flip-off cap
- One single-dose vial of Diluent for JEVTANA: a clear colorless solution of 13% (w/w)
  ethanol in water for injection in a clear glass vial with a grey rubber
  closure, gold-color aluminum cap, and light green plastic flip-off cap
- Both items are in a blister pack in one carton.
NDC 0024-5824-11

16.2 Storage
JEVTANA injection and Diluent for JEVTANA:
Store at 25°C (77°F); excursions permitted between 15°C–30°C (59°F–86°F).
Do not refrigerate.

16.3 Handling and Disposal
JEVTANA is a cytotoxic anticancer drug. Follow applicable special handling and dispos-
able procedures [see References (15)].

17 PATIENT COUNSELING INFORMATION
Advise the patient to read the FDA-approved patient labeling (Patient Information).

Hypersensitivity Reactions
Educate patients about the risk of potential hypersensitivity associated with JEVTANA.
Confirm patients do not have a history of severe hypersensitivity reactions to cabazitaxel.
- or to other drugs formulated with polysorbate 80. Instruct patients to immediately report
  signs of a hypersensitivity reaction [see Contraindications (4) and Warnings and Precaution-
s (5.3)].

Bone Marrow Suppression
Inform patients that JEVTANA decreases blood count such as white blood cells, platelets
and red blood cells. Thus, it is important that periodic assessment of their blood count be
performed to detect the development of neutropenia, thrombocytopenia, anemia, and/or
pancytopenia [see Contraindications (4) and Warnings and Precautions (5.1)]. Instruct
patients to monitor their temperature frequently and immediately report any occurrence of
fever to their healthcare provider.

Increased Toxicities in Elderly Patients
Inform elderly patients that certain side effects may be more frequent or severe [see Warnings and Precautions (5.2) and Use in Specific Populations (8.3)].

Importance of Prednisone
Explain that it is important to take the oral prednisone as prescribed. Instruct patients to
report if they were not compliant with oral corticosteroid regimen [see Dosage and Admin-
istration (2.1)].

Infec
tions, Dehydration, Renal Failure
Explain to patients that severe and fatal infections, dehydration, and renal failure have
been associated with cabazitaxel exposure. Patients should immediately report fever,
significant vomiting or diarrhea, decreased urinary output, and hematuria to their health-
care provider [see Warnings and Precautions (5.1, 5.4, 5.5)].

Urinary Disorders Including Cystitis
Inform patients that hematuria may occur during treatment with JEVTANA. Inform patients
that previously received pelvic radiation that cystitis and radiation cystitis may occur during
 treatment with JEVTANA. Advise patients to report any occurrence of hematuria, or any
signs and symptoms of cystitis or radiation cystitis, to their healthcare provider [see Warnings and Precautions (5.6)].

Respiratory Disorders
Explain to patients that severe and fatal interstitial pneumonia/pneumonitis, interstitial lung
disease and acute respiratory distress syndrome have occurred with JEVTANA. Instruct
patients to immediately report new or worsening pulmonary symptoms to their healthcare
provider [see Warnings and Precautions (5.7)].

Drug Interactions
Inform patients about the risk of drug interactions and the importance of providing a list
of prescription and non-prescription drugs to their healthcare provider [see Drug Interac-
tions (7.1)].

Embryo-Fetal Toxicity
Advise female patients with female partners of reproductive potential to use effective
contraception during treatment and for 3 months after the last dose of JEVTANA [see Use in
Specific Populations (8.3)].

Infertility
Advise male patients that JEVTANA may impair fertility [see Use in Specific Populations
(8.3)].

Manufactured by:
sanofi-aventis U.S. LLC
Bridgewater, NJ 08807
A SANOFI COMPANY

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What is the most important information I should know about JEVTANA?
JEVTANA may cause serious side effects including:
- Low white blood cells. Low white blood cells can cause you
to get serious infections, and may lead to death. Men who are
65 years or older may be more likely to have these problems.
Your healthcare provider:
  - will do blood tests regularly to check your white blood cell
counts during your treatment with JEVTANA.
  - may lower your dose of JEVTANA, change how often you
    receive it, or stop JEVTANA until your healthcare provider
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 healthcare provider right away if you have any of
these symptoms of infection during treatment with
JEVTANA:
  - fever. Take your temperature often during treatment with
    JEVTANA.
  - cough
  - burning on urination
  - muscle aches

Also, tell your healthcare provider if you have any diarrhea
during the time that your white blood cell count is low. Your
healthcare provider may prescribe treatment for you as
needed.
- Severe allergic reactions. Severe allergic reactions can
  happen within a few minutes after your infusion of JEVTANA
  starts, especially during the first and second infusions. Your
  healthcare provider should prescribe medicines before each
  infusion to help prevent severe allergic reactions.
Tell your healthcare provider or nurse right away if you
have any of these symptoms of a severe allergic reaction
during or soon after an infusion of JEVTANA:
- Rash or itching
- Feeling dizzy or faint
- Chest or throat tightness
- Severe stomach and intestine (gastrointestinal) problems.
  - JEVTAHA can cause severe vomiting and diarrhea, which may lead to death. Severe vomiting and diarrhea with JEVTAHA can lead to loss of too much body fluid (dehydration), or too much of your body salts (electrolytes). Death has happened from having severe diarrhea and losing too much body fluid or body salts with JEVTAHA. **You may need to go to a hospital for treatment.** Your healthcare provider will prescribe medicines to prevent or treat vomiting and diarrhea, as needed, with JEVTAHA. Tell your healthcare provider right away if you develop vomiting or diarrhea or if your symptoms get worse or do not get better.
- JEVTAHA can cause a leak in the stomach or intestine, intestinal blockage, infection, and bleeding in the stomach or intestine, which may lead to death. Tell your healthcare provider if you develop any of these symptoms:
  - Severe stomach-area (abdomen) pain
  - Constipation
  - Fever
  - Blood in your stool, or changes in the color of your stool
- Kidney failure. Kidney failure may happen with JEVTAHA, because of severe infection, loss of too much body fluid (dehydration), and other reasons, which may lead to death. Your healthcare provider will check you for this problem and treat you if needed. **Tell your healthcare provider if you develop these signs or symptoms:**
  - Swelling of your face or body
  - Decrease in the amount of urine that your body makes each day
  - Blood in your urine
- Lung or breathing problems. Lung or breathing problems may happen with JEVTAHA and may lead to death. Men who have lung disease before receiving JEVTAHA may have a higher risk for developing lung or breathing problems with JEVTAHA treatment. Your healthcare provider will check you for this problem and treat you if needed. Tell your healthcare provider right away if you develop any new or worsening symptoms, including trouble breathing, shortness of breath, chest pain, cough, or fever.

**What is JEVTAHA?**
JEVTANA is a prescription medicine used with the steroid medicine prednisone. JEVTAHA is used to treat men with castration-resistant prostate cancer (prostate cancer that is resistant to medical or surgical treatments that lower testosterone) that has spread to other parts of the body, and that has worsened (progressed) after treatment with other medicines that included docetaxel.
It is not known if JEVTAHA is safe and effective in children.

**Who should not receive JEVTAHA?**
Do not receive JEVTAHA if:
- Your white blood cell (neutrophil count) is too low
- You have had a severe allergic reaction to cabazitaxel or other medicines that contain polysorbate 80. Ask your healthcare provider if you are not sure.
- You have severe liver problems

**Before receiving JEVTAHA, tell your healthcare provider about all your medical conditions, including if you:**
- Are over the age of 65
- Have allergic reactions in the past
- Have kidney or liver problems
- Have lung problems
- Are pregnant or plan to become pregnant. JEVTAHA can cause harm to your unborn baby and loss of pregnancy (miscarriage).
- Are a male with a female partner who is able to become pregnant. Males should use effective birth control (contraception) during treatment with JEVTAHA and for 3 months after the last dose of JEVTAHA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.
JEVTANA can interact with many other medicines. Do not take any new medicines without asking your healthcare provider first. Your healthcare provider will tell you if it is safe to take the new medicine with JEVTAHA.

**How will I receive JEVTAHA?**
- JEVTAHA will be given to you by an intravenous (IV) infusion into your vein.
- Your treatment will take about 1 hour.
- JEVTAHA is usually given every 3 weeks. Your healthcare provider will decide how often you will receive JEVTAHA.
- Your healthcare provider will also prescribe another medicine called prednisone for you to take by mouth every day during treatment with JEVTAHA.
- Your healthcare provider will tell you how and when to take your prednisone.
- It is important that you take prednisone exactly as prescribed by your healthcare provider. If you forget to take your prednisone, or do not take it on schedule, make sure to tell your healthcare provider or nurse.
- Before each infusion of JEVTAHA, you may receive other medicines to prevent or treat side effects.

**What are the possible side effects of JEVTAHA?**
JEVTANA may cause serious side effects including:
- See “What is the most important information I should know about JEVTAHA?”
- Inflammation of the bladder and blood in the urine. Blood in the urine is common with JEVTAHA, but it can also sometimes be severe. Some people who have had pelvic radiation in the past may develop inflammation of the bladder and blood in the urine that is severe enough that they need to be hospitalized for medical treatment or surgery. Your healthcare provider will check you for these problems during treatment with JEVTAHA. Your healthcare provider may stop your treatment with JEVTAHA for a short time, or permanently, if you develop inflammation of the bladder and bleeding that is severe.

The most common side effects of JEVTAHA include:
- Low red blood cell count (anemia). Low red blood cell count is common with JEVTAHA, but can sometimes also be serious. Your healthcare provider will regularly check your red blood cell count. Symptoms of anemia include shortness of breath and tiredness.
- Low blood platelet count. Low platelet count is common with JEVTAHA, but can sometimes also be serious. Tell your healthcare provider if you have any unusual bruising or bleeding.
- diarrhea
- tiredness
- nausea
- vomiting
- constipation
- weakness
- stomach (abdominal) pain
- back pain
- decreased appetite
- shortness of breath
- hair loss
- cough

JEVTANA may cause fertility problems in males. This may affect your ability to father a child. Talk to your healthcare provider if you have concerns about fertility.

**Tell your healthcare provider if you have any side effect that bothers you or that does not go away.**

These are not all the possible side effects of JEVTANA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

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**General information about the safe and effective use of JEVTANA**

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. You can ask your pharmacist or healthcare provider for information about JEVTANA that is written for health professionals.

**What are the ingredients in JEVTANA?**

**Active ingredient:** cabazitaxel

**Inactive ingredient:** polysorbate 80

Manufactured by: sanofi-aventis U.S. LLC, Bridgewater, NJ 08807, A SANOFI COMPANY

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