SANOFI ONCOLOGY

For U.S. Healthcare Professionals Only

JEVTANA® (cabazitaxel) injection

WARNING: NEUTROPENIA AND HYPERSENSITIVITY
• 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/mm³. [...]
View Full Important Safety Information

For Patients | Full Prescribing Information including Boxed **WARNING**

Dosing

Dosing and Administration

Dosing schedule[1]

For patients with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen:

JEVTANA® 25 mg/m² as a 1-hour IV infusion every 3 weeks + oral predisone 10 mg daily throughout treatment

Dose modifications[1]

Toxicity	Dose modification
Prolonged grade ≥3 neutropenia[a] (>1 week) despite appropriate medication including granulocyte-colony stimulating factor (G-CSF)	Delay treatment until neutrophil count is >1,500 cells/mm³, then reduce dosage of JEVTANA® to 20 mg/m². Use granulocyte-colony stimulating factor (G-CSF) for secondary prophylaxis.
Febrile neutropenia or neutropenic infection	Delay treatment until improvement or resolution, and until neutrophil count is >1,500 cells/mm³, then reduce dosage of JEVTANA to 20 mg/m². Use granulocyte-colony stimulating factor (G-CSF) for secondary prophylaxis.
Grade ≥3 diarrhea or persisting diarrhea despite appropriate medication, fluid and electrolyte replacement	Delay treatment until improvement or resolution, then reduce dosage of JEVTANA® to 20 mg/m².
Grade 2 peripheral neuropathy	Delay treatment until improvement or resolution, then reduce

Important Safety Information for JEVTANA® (cabazitaxel) injection

WARNING: NEUTROPENIA AND HYPERSENSITIVITY

- 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/mm³.
- 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.

Continue

JEVTANA® is a microtubule inhibitor indicated in combination with prednisone for the treatment of

	dosage of JEVTANA to 20 mg/m .
Grade ≥3 peripheral neuropathy	Discontinue JEVTANA.

[a] Absolute neutrophil count <1.0 x 10 [9]/L.

- Discontinue JEVTANA ® treatment if a patient continues to experience any of these reactions at the 20 mg/m [2] dosage
- 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

patients with hormone-refractory metastatic prostate cancer (mHRPC) previously treated with a docetaxel-containing treatment regimen.

Important Safety Information for JEVTANA®[1]

- Observe patients closely for hypersensitivity reactions, especially during the first and second infusions.
- Severe hypersensitivity can occur and may include generalized rash/erythema, hypotension and bronchospasm. Discontinue JEVTANA ® immediately if severe reactions occur and administer appropriate therapy.
- Contraindicated if history of severe hypersensitivity reactions to cabazitaxel or to drugs formulated with polysorbate 80.
- Nausea, vomiting and severe diarrhea, at times, may occur. Death related to diarrhea and electrolyte imbalance occurred in the randomized clinical trial. Intensive measures may be required for severe diarrhea and electrolyte imbalance.
- Females of childbearing potential should be advised to avoid becoming pregnant during treatment with JEVTANA. ®

Important Safety Information for JEVTANA® (cabazitaxel) injection

WARNING: NEUTROPENIA AND HYPERSENSITIVITY

- 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.
- 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.

CONTRAINDICATIONS

- JEVTANA® is contraindicated in patients with:
  - neutrophil counts of ≤1,500/mm^3
  - history of severe hypersensitivity reactions to cabazitaxel or to other drugs formulated with polysorbate 80
  - severe hepatic impairment (total bilirubin > 3 x upper limit of normal (ULN))

WARNINGS AND PRECAUTIONS

- Bone marrow suppression manifested as neutropenia, anemia, thrombocytopenia and/or pancytopenia may occur. Neutropenic deaths have been reported.
  - 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
  - Monitor blood counts frequently to determine if initiation of G-CSF and/or dosage modification is needed
  - Primary prophylaxis with G-CSF should be considered in patients with high-risk clinical features
  - Caution is recommended in patients with hemoglobin < 10 g/dl
- Severe hypersensitivity reactions can occur.
  - Premedicate all patients with antihistamines, corticosteroids and H_2 antagonists prior to the initiation of the JEVTANA® infusion
  - Observe patients closely for hypersensitivity reactions, especially during the first and second infusions
  - Discontinue infusion immediately if severe hypersensitivity is observed and treat as indicated
- 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
- Nausea, vomiting and severe diarrhea, at times, may occur. Death related to diarrhea and electrolyte imbalance occurred in the randomized clinical trial. Intensive measures may be required for severe diarrhea and electrolyte imbalance.
- Gastrointestinal (GI) hemorrhage and perforation, ileus, enterocolitis, neutropenic enterocolitis, including fatal outcome, have been reported.
  - Risk may be increased with neutropenia, age, steroid use, concomitant use of NSAIDs, anti-platelet therapy or anti-coagulants, and prior history of pelvic radiotherapy, adhesions, ulceration and GI bleeding
  - Abdominal pain and tenderness, fever, persistent constipation, diarrhea, with or without neutropenia, may be early manifestations of serious GI toxicity and should be evaluated and treated promptly
  - JEVTANA® treatment delay or discontinuation may be necessary
- Renal failure, including cases with fatal outcomes, has been reported. Identify cause and manage aggressively.
- 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.
- Patients with impaired hepatic function:
  - JEVTANA® is contraindicated in patients with severe hepatic impairment (total bilirubin > 3 x ULN)
  - Dose should be reduced for patients with mild (total bilirubin > 1 to ≤ 1.5 x ULN or AST > 1.5 x ULN) and moderate (total bilirubin > 1.5 to ≤ 3.0 x ULN and any AST) hepatic impairment, based on tolerability data in these patients
  - Administer JEVTANA® with caution in patients with mild and moderate hepatic impairment and closely monitor for safety
- JEVTANA® can cause fetal harm when administered to a pregnant woman.
  - JEVTANA is not indicated for use in female patients
  - There are no adequate and well-controlled studies in pregnant women using JEVTANA®
  - Females of childbearing potential should be advised to avoid becoming pregnant during treatment with JEVTANA®

ADVERSE REACTIONS

- Deaths due to causes other than disease progression within 30 days of last study drug dose were reported in 18 (5%) JEVTANA ®-treated patients. The most common fatal adverse reactions in JEVTANA ®-treated patients were infections (n=5) and renal failure (n=4).
- The most common (≥10%) grade 1-4 adverse reactions were anemia, leukopenia, neutropenia, thrombocytopenia, diarrhea, fatigue, nausea, vomiting, constipation, asthenia, abdominal pain, hematuria, back pain, anorexia, peripheral neuropathy, pyrexia, dyspnea, dysgeusia, cough, arthralgia, and alopecia.
- The most common (≥5%) grade 3-4 adverse reactions in patients who received JEVTANA® were neutropenia, leukopenia, anemia, febrile neutropenia, diarrhea, fatigue, and asthenia.

Please see full prescribing information including boxed **WARNING**.

Reference

1. JEVTANA® Prescribing Information. Bridgewater, NJ: sanofi-aventis U.S. LLC; June 2015.