

HIGHLIGHTS OF PRESCRIBING INFORMATION

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

JEV TANA (cabazitaxel) Injection, 60 mg/1.5 mL,
for intravenous infusion only
Initial U.S. Approval: 2010

WARNING

See full prescribing information for complete boxed warning.

- Neutropenic deaths have been reported. Obtain frequent blood counts to monitor for neutropenia. Do not give JEV TANA if neutrophil counts are $\leq 1,500$ cells/mm³. (2.2)(4)
- Severe hypersensitivity can occur and may include generalized rash/erythema, hypotension and bronchospasm. Discontinue JEV TANA immediately if severe reactions occur and administer appropriate therapy. (2.3)(5.2)
- Contraindicated if history of severe hypersensitivity reactions to JEV TANA or to drugs formulated with polysorbate 80. (4)

INDICATIONS AND USAGE

JEV TANA 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: JEV TANA 25 mg/m² administered every three weeks as a one-hour intravenous infusion in combination with oral prednisone 10 mg administered daily throughout JEV TANA treatment. (2.1)

- JEV TANA requires two dilutions prior to administration (2.5)
 - Use the entire contents of the accompanying diluent to achieve a concentration of 10 mg/mL JEV TANA. (2.5)
 - PVC equipment should not be used (2.5)
 - **Premedication Regimen:** Administer intravenously 30 minutes before each dose of JEV TANA:
 - Antihistamine (dexchlorpheniramine 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) (2.3)
- Antiemetic prophylaxis (oral or intravenous) is recommended as needed. (2.3)
- **Dosage Modifications:** See full prescribing information (2.2)

DOSAGE FORMS AND STRENGTHS

- Single use vial 60 mg/1.5 mL, supplied with diluent (5.7 mL) for JEV TANA (3)

CONTRAINDICATIONS

- Neutrophil counts of $\leq 1,500$ /mm³ (2.2)(4)
- History of severe hypersensitivity to JEV TANA or polysorbate 80 (4)

WARNINGS AND PRECAUTIONS

- Neutropenia, febrile neutropenia: Neutropenic deaths have been reported. 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. (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 symptoms (nausea, vomiting, diarrhea): 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)(5.3)
- Renal failure, including cases with fatal outcomes, has been reported. Identify cause and manage aggressively. (5.4)
- 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 (5.5)(6)(8.5).
- Hepatic impairment: Patients with impaired hepatic function were excluded from the randomized clinical trial. Hepatic impairment is likely to increase the cabazitaxel concentrations. JEV TANA should not be given to patients with hepatic impairment. (5.6)(8.7)
- JEV TANA can cause fetal harm when administered to a pregnant woman. (5.7)(8.1)

ADVERSE REACTIONS

Most common all grades adverse reactions ($\geq 10\%$) 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

- Use with caution in patients taking concomitant medicines that induce or inhibit CYP3A. (7)

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

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FULL PRESCRIBING INFORMATION

WARNING

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 should not be given to patients with neutrophil counts of $\leq 1,500$ 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 [see Warnings and Precautions (5.2)]. Patients should receive premedication [see Dosage and Administrations (2.3)]. JEVTANA must not be given to patients who have a history of severe hypersensitivity reactions to JEVTANA or to other drugs formulated with polysorbate 80 [see Contraindications (4)].

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 General Dosing Information

- The individual dosage of JEVTANA is based on calculation of the Body Surface Area (BSA) and is 25 mg/m² administered as a one-hour intravenous infusion every three weeks in combination with oral prednisone 10 mg administered daily throughout JEVTANA treatment.
- Premedication is recommended prior to treatment [see Dosage and Administration (2.3)].
- JEVTANA should be administered under the supervision of a qualified physician experienced in the use of antineoplastic medicinal products. Appropriate management of complications is possible only when the adequate diagnostic and treatment facilities are readily available.
- JEVTANA Injection single-use vial requires two dilutions prior to administration [see Dosage and Administration (2.5)].
- Do not use PVC infusion containers and polyurethane infusions sets for preparation and administration of JEVTANA infusion solution [see Dosage and Administration (2.5)].
- Both the JEVTANA Injection and the diluent vials contain an overfill to compensate for liquid loss during preparation.

2.2 Dose Modifications

The JEV TANA dose should be reduced to 20 mg/m² if patients experience the following adverse reactions.

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

Toxicity	Dosage Modification
Prolonged grade ≥ 3 neutropenia (greater than 1 week) despite appropriate medication including G-CSF	Delay treatment until neutrophil count is $> 1,500$ cells/mm ³ , then reduce dosage of JEV TANA to 20 mg/m ² . Use G-CSF for secondary prophylaxis.
Febrile neutropenia	Delay treatment until improvement or resolution, and until neutrophil count is $> 1,500$ cells/mm ³ , then reduce dosage of JEV TANA 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 JEV TANA to 20 mg/m ² .

Discontinue JEV TANA treatment if a patient continues to experience any of these reactions at 20 mg/m².

2.3 Premedication

Premedicate at least 30 minutes prior to each dose of JEV TANA with the following intravenous medications to reduce the risk and/or severity of hypersensitivity:

- antihistamine (dexchlorpheniramine 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).

Antiemetic prophylaxis is recommended and can be given orally or intravenously as needed.

2.4 Administration Precautions

JEV TANA is a cytotoxic anticancer drug and caution should be exercised when handling and preparing JEV TANA solutions, taking into account the use of containment devices, personal protective equipment (e.g., gloves), and preparation procedures. Please refer to *Handling and Disposal* (16.3).

If JEV TANA Injection, first diluted solution, or second (final) dilution for intravenous infusion should come into contact with the skin, immediately and thoroughly wash with soap and water.

If JEV TANA Injection, first diluted solution, or second (final) dilution for intravenous infusion should come into contact with mucosa, immediately and thoroughly wash with water.

2.5 Instructions for Preparation

Do not use PVC infusion containers or polyurethane infusions sets for preparation and administration of JEV TANA infusion solution.

Read this entire section carefully before mixing and diluting. JEV TANA requires **two** dilutions prior to administration. Please follow the preparation instructions provided below. **Note:** Both the JEV TANA 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 JEV TANA.

The following two-step dilution process must be carried out under aseptic conditions to prepare the second (final) infusion solution.

Set aside the JEV TANA Injection and supplied diluent vials. The JEV TANA Injection is a clear yellow to brownish-yellow viscous solution, if appropriately stored.

Step 1 – First Dilution

Each vial of JEV TANA (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 JEV TANA.

When transferring the diluent, direct the needle onto the inside wall of JEV TANA 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 JEV TANA 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 JEV TANA 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 JEV TANA is required, use a larger volume of the infusion vehicle so that a concentration of 0.26 mg/mL JEV TANA is not exceeded. The concentration of the JEV TANA final infusion solution should be between 0.10 mg/mL and 0.26 mg/mL.

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