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HIGHLIGHTS OF PRESCRIBING INFORMATION

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

CABAZITAXEL injection, for intravenous use
Initial U.S. Approval: 2010

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

- **Neutropenic deaths have been reported. Obtain frequent blood counts to monitor for neutropenia. Cabazitaxel Injection is contraindicated in patients with neutrophil counts of ≤1,500 cells/mm^3. Primary prophylaxis with G-CSF is recommended in patients with high- risk clinical features. (4, 5.1, 5.2)**
- **Severe hypersensitivity can occur and may include generalized rash/erythema, hypotension and bronchospasm. Discontinue Cabazitaxel Injection 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)**

INDICATIONS AND USAGE

Cabazitaxel Injection 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: Cabazitaxel Injection 20 mg/m^2 administered every three weeks as a one-hour intravenous infusion in combination with oral prednisone 10 mg administered daily throughout Cabazitaxel Injection treatment. (2.1)

- Cabazitaxel Injection requires dilution prior to administration (2.5)
- PVC equipment should not be used (2.5)
- **Premedication Regimen**: Administer intravenously 30 minutes before each dose of Cabazitaxel Injection:
  - Antihistamine (dexchlorpheniramine 5 mg or diphenhydramine 25 mg or equivalent antihistamine)
  - Corticosteroid (dexamethasone 8 mg or equivalent steroid)
  - H_2 antagonist (2.1)

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

DOSAGE FORMS AND STRENGTHS

- Injection: 45 mg/4.5 mL (10 mg/mL) and 60 mg/6 mL (10 mg/mL) in multiple-dose vial (3)

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- Bone marrow suppression (particularly neutropenia) and its clinical consequences (febrile neutropenia, neutropenic infections, and death): Monitor blood counts frequently to determine if dosage modification or initiation of G-CSF is needed. Closely monitor patients with hemoglobin < 10 g/dL. (2.2, 4, 5.1)
- Increased toxicities in elderly patients: Patients ≥65 years of age were more likely to experience fatal outcomes and certain adverse reactions, including neutropenia and febrile neutropenia. Monitor closely. (5.2, 8.5)
- Hypersensitivity: Severe hypersensitivity reactions can occur. Premedicate with corticosteroids and 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 Cabazitaxel Injection 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 Cabazitaxel Injection and provide medical or surgical supportive care, as needed, in patients experiencing severe hemorrhagic cystitis.
- Respiratory disorders: Interstitial pneumonia/pneumonitis, interstitial lung disease and acute respiratory distress syndrome, including fatal outcomes, have been reported. Delay or discontinue Cabazitaxel Injection and treat as indicated. (5.7)
- Hepatic impairment: Administer Cabazitaxel Injection at a dose of 20 mg/m^2 in patients with mild hepatic impairment. Administer Cabazitaxel Injection at a dose of 15 mg/m^2 in patients with moderate hepatic impairment. (2.3, 5.8)
- Embryo-fetal toxicity: Cabazitaxel Injection 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 Cabazitaxel Injection 20 mg/m^2 are anemia, leukopenia, neutropenia, thrombocytopenia, diarrhea, nausea, fatigue, constipation, asthenia, vomiting, hematuria, decreased appetite, and back pain. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Sandoz Inc., at 1-800-525-8747 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Avoid co-administration of Cabazitaxel Injection with strong CYP3A inhibitors. If patients require co-administration of a strong CYP3A inhibitor, consider a 25% Cabazitaxel Injection dose reduction. (2.4, 7.1, 12.3)

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

Revised: 01/2023

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FULL PRESCRIBING INFORMATION

WARNING: NEUTROPENIA AND HYPERSENSITIVITY

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

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

1 INDICATIONS AND USAGE

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

Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features *[see Contraindications (4) and Warnings and Precautions (5.1, 5.2)]*.

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

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

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

Cabazitaxel Injection multiple-dose vial requires dilution prior to administration *[see Dosage and Administration (2.5)]*.

2.2 Dose Modifications for Adverse Reactions

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

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

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

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

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

2.4 Dose Modifications for Use with Strong CYP3A Inhibitors

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

2.5 Preparation and Administration

Cabazitaxel Injection is a hazardous drug. Follow applicable special handling and disposal procedures.[1] If Cabazitaxel Injection, or 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 Cabazitaxel Injection infusion solution.

Cabazitaxel Injection should not be mixed with any other drugs including two vial formulations of cabazitaxel injection.

<u>Preparation</u>

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Read this **entire** section carefully before mixing and diluting. Cabazitaxel Injection requires dilution prior to administration. Follow the preparation instructions provided below, as improper preparation may lead to overdose *[see Overdosage (10)]*.

Note: Cabazitaxel Injection contains an overfill to compensate for liquid loss during preparation.

Inspect the Cabazitaxel Injection vial. The Cabazitaxel Injection is a clear colorless to pale yellow viscous solution.

Dilution

Withdraw the recommended dose from the Cabazitaxel Injection solution containing 10 mg/mL using a calibrated syringe and needle to 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 Cabazitaxel Injection is required, use a larger volume of the infusion vehicle so that a concentration of 0.26 mg/mL cabazitaxel is not exceeded. The concentration of the Cabazitaxel Injection final infusion solution should be between 0.10 mg/mL and 0.26 mg/mL.

Remove the syringe and thoroughly mix the final infusion solution by gently inverting the bag or bottle.

As the final infusion solution is supersaturated, it may crystallize over time. Do not use if this occurs and discard.

Fully prepared Cabazitaxel Injection 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) 20°C to 25°C, or within a total of 24 hours (including the one-hour infusion) under the refrigerated conditions 2°C to 8°C .

After initial withdrawal with a needle, store the remaining portion at room temperature in the vial for no more than 28 days.

Discard any unused portion immediately if a chemospike has been used for withdrawal..

Administration

Inspect visually for particulate matter, any crystals and discoloration prior to administration. If the Cabazitaxel Injection infusion solution is not clear or appears to have precipitation, it should be discarded.

Use a 0.2 or 0.22 micrometer in-line filter during administration.

The final Cabazitaxel Injection infusion solution should be administered intravenously as a one-hour infusion at room temperature.

3 DOSAGE FORMS AND STRENGTHS

Cabazitaxel Injection is a clear colorless to pale yellow viscous solution supplied in a sterile multiple-dose vial as follows:

- Injection: 45 mg/4.5 mL (10 mg/mL)
- Injection: 60 mg/6 mL (10 mg/mL)

4 CONTRAINDICATIONS

Cabazitaxel Injection is contraindicated in patients with:

- neutrophil counts of ≤ 1,500/mm^3 *[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)]*

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- severe hepatic impairment (total bilirubin > 3 × ULN) *[see Warnings and Precautions (5.8)]*

5 WARNINGS AND PRECAUTIONS

5.1 Bone Marrow Suppression

Cabazitaxel Injection is contraindicated in patients with neutrophils ≤1,500/mm^3 *[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.

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)]*.

PROSELICA Trial

In the PROSELICA trial comparing two doses of cabazitaxel, primary prophylaxis with G-CSF was not allowed, but could be administered after development of neutropenia at investigators discretion. Eight patients (1%) on the 20 mg/m^2 died from infection; of these, 4 deaths on the 20 mg/m^2 arm occurred within the first 30 days of treatment. Clinically important neutropenia-related events occurred and included febrile neutropenia (2.1% on 20 mg/m^2 arm), neutropenic infection/sepsis (2.1% on 20 mg/m^2 arm), and neutropenic deaths (0.3% on 20 mg/m^2 arm).

Patients receiving cabazitaxel 20 mg/m^2 were reported to have infectious adverse reactions. Grade 1-4 infections were experienced by 160 patients (28%) on the 20 mg/m^2 arm. Grade 3-4 infections were experienced by 57 patients (10%) on the 20 mg/m^2 arm.

5.2 Increased Toxicities in Elderly Patients

In a randomized clinical trial (PROSELICA) comparing two doses of cabazitaxel, deaths due to infection within 30 days of starting cabazitaxel occurred in 0.7% (4/580) patients on the 20 mg/m^2 arm; all of these patients were >60 years of age.

In PROSELICA, on the 20 mg/m^2 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 cabazitaxel dose.

5.3 Hypersensitivity Reactions

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

Premedicate all patients prior to the initiation of the infusion of Cabazitaxel Injection *[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 cabazitaxel infusion and appropriate therapy. Cabazitaxel Injection 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 and severe diarrhea, at times, 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. Antiemetic prophylaxis is recommended. Treat patients with rehydration, anti-diarrheal or anti-emetic medications as

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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 cabazitaxel *[see Adverse Reactions (6.2)]*. Risk may be increased with neutropenia, age, steroid use, concomitant use of NSAIDs, anti-platelet therapy or anti-coagulants, and patients with a 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 gastrointestinal toxicity and should be evaluated and treated promptly. Cabazitaxel Injection treatment delay or discontinuation may be necessary.

The incidence of gastrointestinal adverse reactions is greater in the patients who have received prior radiation. In PROSELICA, diarrhea was reported in 41% (297/732) of patients who had received prior radiation and in 27% (118/443) of patients without prior radiation.

5.5 Renal Failure

Renal failure, including with fatal outcome, occurred in patients being treated with cabazitaxel at a higher dose. Most cases occurred in association with sepsis, dehydration, or obstructive uropathy *[see Adverse Reactions (6.1)]*. Some deaths due to renal failure did not have a clear etiology. Appropriate measures should be taken to identify causes of renal failure and treat aggressively.

5.6 Urinary Disorders Including Cystitis

Cystitis, radiation cystitis, and hematuria, including that requiring hospitalization, has been reported with cabazitaxel in patients who previously received pelvic radiation *[see Adverse Reactions (6.2)]*. In PROSELICA, cystitis and radiation cystitis were reported in 1.2% and 1.5% of patients who received prior radiation, respectively. Hematuria was reported in 19.4% of patients who received prior radiation and in 14.4% of patients who did not receive prior radiation. Cystitis from radiation recall may occur late in treatment with cabazitaxel. Monitor patients who previously received pelvic radiation for signs and symptoms of cystitis while on Cabazitaxel Injection. Interrupt or discontinue Cabazitaxel Injection in patients experiencing severe hemorrhagic cystitis. Medical and/or surgical supportive treatment may be required to treat severe hemorrhagic cystitis.

5.7 Respiratory Disorders

Interstitial pneumonia/pneumonitis, interstitial lung disease and acute respiratory distress syndrome have been reported and may be associated with fatal outcome *[see Adverse Reactions (6.2)]*. Patients with underlying lung disease may be at higher risk for these events. Acute respiratory distress syndrome may occur in the setting of infection.

Interrupt Cabazitaxel Injection if new or worsening pulmonary symptoms develop. Closely monitor, promptly investigate, and appropriately treat patients receiving Cabazitaxel Injection. Consider discontinuation. The benefit of resuming Cabazitaxel Injection treatment must be carefully evaluated.

5.8 Use in Patients with Hepatic Impairment

Cabazitaxel is extensively metabolized in the liver.

Cabazitaxel Injection 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 and any AST) hepatic impairment, based on tolerability data in these patients *[see Dosage and Administration (2.3) and Use in Specific Populations (8.7)]*. Administration of

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Cabazitaxel Injection to patients with mild and moderate hepatic impairment should be undertaken with caution and close monitoring of safety.

5.9 Embryo-Fetal Toxicity

Based on findings in animal reproduction studies and its mechanism of action, Cabazitaxel Injection 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 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. Advise males with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Cabazitaxel Injection *[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 the 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)]*
- Renal Failure *[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 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed cannot be directly compared to rates in other trials and may not reflect the rates observed in clinical practice.

PROSELICA Trial

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 cabazitaxel 25 mg/m^2 (n=595) or the 20 mg/m^2 (n=580) dose.

Deaths within 30 days of last study drug dose were reported in 22 (3.8%) patients in the 20 mg/m^2 arm. The most common fatal adverse reactions in cabazitaxel-treated patients were related to infections, occuring in 8 patients (1.4%) treated with the 20 mg/m^2 dosage of cabazitaxel. In the PROSELICA study, other fatal adverse reactions in cabazitaxel-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.

Treatment discontinuations due to adverse reactions occurred in 17% of patients in the 20 mg/m^2 group. The most common adverse reactions leading to treatment discontinuation were fatigue and hematuria. The patients in the 20 mg/m^2 group received a median of 6 cycles (median duration of 18 weeks). In the 20 mg/m^2 group, 58 patients (10%) had a dose reduced from 20 to 15 mg/m^2, and 9 patients (2%) had a dose reduced from 15 to 12 mg/m^2.

Table 2: Adverse Reactions* and Hematologic Abnormalities in ≥ 5% of Patients in PROSELICA

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Adverse Reactions	Cabazitaxel 20 mg/m² every 3 weeks with prednisone 10 mg daily n=580		Cabazitaxel 25 mg/m² every 3 weeks with prednisone 10 mg daily n=595	
	Grade 1 to 4 %	Grade 3 to 4 %	Grade 1 to 4 %	Grade 3 to 4 %
Blood and Lymphatic System Disorders				
Anemia†	99.8	10	99.7	14
Leukopenia†	80	29	95	60
Neutropenia†	67	42	89	73
Thrombocytopenia†	35	3	43	4
Febrile Neutropenia	2	2	9	9
Gastrointestinal Disorders				
Diarrhea	31	1	40	4
Nausea	25	0.7	32	1
Constipation	18	0.3	18	0.7
Vomiting	15	1.2	18	1
Abdominal pain	6	0.5	9	1
Stomatitis	5	0	5	0.3
General Disorders and Administration Site Conditions				
Fatigue	25	3	27	4
Asthenia	15	2	20	2
Edema peripheral	7	0.2	9	0.2
Pyrexia	5	0.2	6	0.2
Renal and Urinary Disorders				
Hematuria	14	2	21	4
Dysuria	5	0.3	4	0
Metabolism and Nutrition Disorders				
Decreased appetite	13	0.7	19	1
Musculoskeletal and Connective Tissue Disorders				
Back pain	11	0.9	14	1
Bone pain	8	2	8	2
Arthralgia	8	0.5	7	0.8
Pain in extremity	5	0.2	7	0.5
Nervous System Disorders				
Dysgeusia	7	0	11	0
Peripheral sensory neuropathy	7	0	11	0.7
Dizziness	4	0	5	0
Headache	5	0.2	4	0.2
Infections and Infestations				
Urinary tract infection‡	7	2	11	2
Neutropenic infection§	3	2	7	6
Respiratory, Thoracic and Mediastinal Disorders				
Dyspnea	5	0.9	8	0.7
Cough	6	0	6	0
Investigations				
Weight decreased	4	0.2	7	0
Skin and Subcutaneous Tissue Disorders				
Alopecia	3	0	6.1	0
Injury, Poisoning and Procedural Complications				
Wrong technique in drug usage process	0.3	0	5	0

* Grade from NCI CTCAE version 4.03.

† Based on laboratory values, cabazitaxel 20 mg/m²: n =577, cabazitaxel 25 mg/m²: n =590.

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‡ Includes urinary tract infection staphylococcal, urinary tract infection bacterial, urinary tract infection fungal, and urosepsis.
§ Includes neutropenic sepsis.

6.2 Postmarketing Experience

The following adverse reactions have been identified from clinical trials and/or post-marketing 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, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole) may increase plasma concentrations of cabazitaxel. Avoid the co-administration of Cabazitaxel Injection with strong CYP3A inhibitors. If patients require co-administration of a strong CYP3A inhibitor, consider a 25% Cabazitaxel Injection 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 Cabazitaxel Injection have not been established in females. There are no human data on the use of Cabazitaxel Injection 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 0.03 times the recommended human dose, respectively, based on Body Surface Area [BSA]).

In an embryo-fetal developmental toxicity study in rats, cabazitaxel caused maternal and embryo-fetal toxicity consisting of increased post-implantation loss, embryolethality, and fetal deaths when administered intravenously at a dose of 0.16 mg/kg/day (approximately 0.05 times the recommended human dose based on BSA). 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 in rats is approximately 0.02 times the recommended human dose based on BSA. Administration of cabazitaxel did not result in fetal abnormalities in rats or rabbits at exposure levels significantly lower than the expected human exposures.

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8.2 Lactation

Risk Summary

The safety and efficacy of Cabazitaxel Injection 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 *[see Data]*.

Data

Animal Data

In a milk excretion study, radioactivity related to cabazitaxel was detected in the stomachs of nursing pups within 2 hours of a single intravenous administration of cabazitaxel to lactating rats at a dose of 0.08 mg/kg (approximately 0.02 times the recommended human dose based on BSA). This was detectable 24 hours post dose. Approximately 1.5% of the dose delivered to the mother was calculated to be delivered in the maternal milk.

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 last dose of Cabazitaxel Injection *[see Use in Specific Populations (8.1)]*.

Infertility

Males

Based on animal toxicology studies, Cabazitaxel Injection may impair human fertility in males of reproductive potential *[see Nonclinical Toxicology (13.1)]*.

8.4 Pediatric Use

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

Cabazitaxel was evaluated in 39 pediatric patients (ages 3 to 18 years) receiving prophylactic G- CSF. The maximum tolerated dose (MTD) was 30 mg/m^2 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 premedication. 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.

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8.5 Geriatric Use

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%), asthenia (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 the 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 CL_{CR} < 15mL/min/1.73m^2), 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 use a Cabazitaxel Injection dose of 20 mg/m^2. Administration of Cabazitaxel Injection 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 and AST = any) was 15 mg/m^2, however, the efficacy at this dose level was unknown. Cabazitaxel Injection is contraindicated in patients with severe hepatic impairment (total bilirubin > 3× ULN) *[see Contraindications (4)].*

10 OVERDOSAGE

There is no known antidote for Cabazitaxel Injection overdose. Cabazitaxel 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

Cabazitaxel Injection is an antineoplastic agent belonging to the taxane class that is for intravenous use. It is prepared by semi-synthesis with a precursor extracted from yew needles.

The chemical name of cabazitaxel is (2aR,4S,4aS,6R,9S,11S,12S,12aR,12bS)-12b-(acetyloxy)-12-(benzoyloxy)-2a,3,4,4a,5,6,9,10,11,12,12a,12b-dodecahydro-11-hydroxy-4,6-dimethoxy-4a,8,13,13-tetramethyl-5-oxo-7,11-methano-1Hcyclodeca[3,4]benz[1,2-b]oxet-9-ylester, (αR,βS).

Cabazitaxel has the following structural formula:

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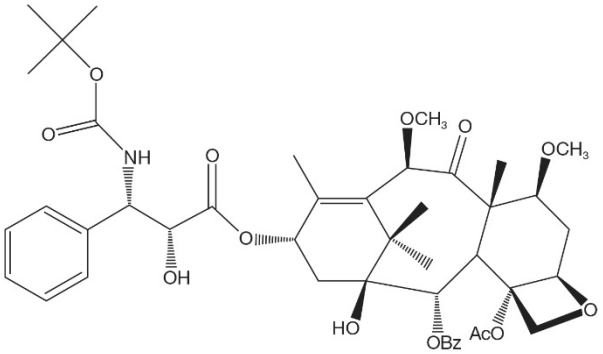

Cabazitaxel is a white to almost-white powder with a molecular formula of $C_{45}H_{57}NO_{14}$ and a molecular weight of 835.93. It is practically insoluble in water, soluble in methanol, soluble in ethanol and freely soluble in methylene chloride.

Cabazitaxel Injection is a sterile, non-pyrogenic, clear colorless to pale yellow viscous solution and is available in multiple-dose vials in two strengths: 45 mg/4.5 mL and 60 mg/6.0 mL. Each mL contains 10 mg cabazitaxel (anhydrous), 4.5 mg anhydrous citric acid, 198 mg dehydrated alcohol, 560 mg polyethylene glycol 300, and 260 mg polysorbate 80.

Cabazitaxel Injection requires dilution prior to intravenous infusion. Cabazitaxel injection should be diluted 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 assembly into microtubules while simultaneously inhibiting disassembly. This leads to the stabilization of microtubules, which results in the inhibition of mitotic and interphase cellular functions.

12.2 Pharmacodynamics

Cardiac Electrophysiology

The effect of cabazitaxel following a single dose of 25 mg/m^2 (1.25 times the recommended dosage) administered by intravenous infusion on QTc interval 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/m^2 weekly or every three weeks.

Absorption

Based on the population pharmacokinetic analysis, after an intravenous dose of cabazitaxel 25 mg/m^2 every three weeks (1.25 times the recommended dosage), the mean C_{max} in patients with metastatic prostate cancer was 226 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 34%).

No major deviation from the dose proportionality was observed from 10 to 30 mg/m^2 in patients with advanced solid tumors.

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Distribution

The volume of distribution (V_{ss}) was 4,864 L (2,643 L/m^2 for a patient with a median BSA of 1.84 m^2) 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

After a one-hour intravenous infusion [^{14}C]-cabazitaxel 25 mg/m^2 (1.25 times the recommended dosage), 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%; 26.4 L/h/m^2 for a patient with a median BSA of 1.84 m^2) 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.

Renal Impairment

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 ≤ CL_{CR} < 50 mL/min) and 59 patients with mild renal impairment (50 mL/min ≤ CL_{CR} < 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, CL_{CR} > 80 mL/min/1.73m^2), or moderate (n=8, 30 mL/min/1.73m^2 ≤ CL_{CR} < 50 mL/min/1.73m^2) and severe (n=9, CL_{CR} < 30 mL/min/1.73m^2) renal impairment, who received several cycles of cabazitaxel in single IV infusion up to 25 mg/m^2. Limited pharmacokinetic data were available in patients with end-stage renal disease (n=2, CL_{CR} < 15 mL/min/1.73m^2).

Hepatic Impairment

Cabazitaxel 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 ≤1.5 × ULN or AST >1.5 × ULN) or moderate (total bilirubin >1.5 to ≤3.0 × ULN) hepatic impairment on cabazitaxel pharmacokinetics. The maximum tolerated dose (MTD) of cabazitaxel was 20 and 15 mg/m^2, respectively.

In 3 patients with severe hepatic impairment (total bilirubin > 3 × ULN), a 39% decrease in clearance was observed when compared to 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

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was not established. Based on safety and tolerability data, cabazitaxel dose should be maintained at 20 mg/m^2 in patients with mild hepatic impairment and reduced to 15 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 cabazitaxel 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 cabazitaxel in 13 patients with advanced cancers has shown that repeated administration of aprepitant (125 or 80 mg once daily), a moderate CYP3A inhibitor, did not modify the exposure to cabazitaxel (15 mg/m^2 intravenous).

A drug interaction study of cabazitaxel 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 cabazitaxel 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.

Prednisone or prednisolone administered at 10 mg daily did not affect the pharmacokinetics of cabazitaxel.

Based on *in vitro* studies, the potential for cabazitaxel to inhibit drugs that are substrates of other CYP isoenzymes (1A2,-2B6,-2C9, -2C8, -2C19, -2E1, -2D6, and CYP3A4/5) is low.

In addition, cabazitaxel did not induce CYP isozymes (-1A, -2C9 and -3A) *in vitro*.

In vitro, cabazitaxel did not inhibit the multidrug-resistance protein 1 (MRP1), 2 (MRP2) or organic cation transporter (OCT1). *In vitro,* cabazitaxel inhibited P-gp, BRCP, and organic anion transporting polypeptides (OATP1B1, OATP1B3). However, the *in vivo* risk of cabazitaxel inhibiting MRPs, OCT1, P-gp, BCRP, OATP1B1 or OATP1B3 is low at the dose of 25 mg/m^2.

In vitro, cabazitaxel is a substrate of P-gp, but not a substrate of MRP1, MRP2, BCRP, OCT1, OATP1B1 or OATP1B3.

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 rats at doses ≥ 0.5 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 mg/kg/day, there was no effect of administration of the drug on mating behavior or the ability to become pregnant. In repeat-dose toxicology studies in rats with intravenous cabazitaxel administration once every three weeks for up to 6 months, atrophy of the uterus was

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observed at the 5 mg/kg dose level (approximately 1.5 times the recommended human dose based on BSA) along with necrosis of the corpora lutea at doses ≥ 1 mg/kg (approximately 0.3 times the recommended human dose based on BSA).

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 toxicology studies with intravenous cabazitaxel administration once every three weeks for up to 9 months, degeneration of seminal vesicle and seminiferous tubule atrophy in the testis were observed in rats at a dose of 1 mg/kg (approximately 0.3 times the recommended human dose based on BSA), and minimal testicular degeneration (minimal epithelial single cell necrosis in epididymis) was observed in dogs treated at a dose of 0.5 mg/kg (approximately 0.5 times the recommended human dose based on BSA).

14 CLINICAL STUDIES

14.1 PROSELICA Trial

The efficacy and safety of cabazitaxel were evaluated in a noninferiority, multicenter, randomized, open-label study (PROSELICA, NCT01308580). A total of 1200 patients with metastatic castration-resistant prostate cancer, previously treated with a docetaxel-containing regimen were randomized to receive either cabazitaxel 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 cabazitaxel 20 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 cabazitaxel 25 mg/m^2 group.

The study demonstrated noninferiority in overall survival (OS) of cabazitaxel 20 mg/m^2 in comparison with cabazitaxel 25 mg/m^2 in an intent-to-treat population (see Table 3 and Figure 1). Based on the per-protocol population, the estimated median OS was 15.1 months on cabazitaxel 20 mg/m^2 and 15.9 months on cabazitaxel 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 on the cabazitaxel 25 mg/m^2 arm compared to the cabazitaxel 20 mg/m^2 arm in subgroups based on the stratification factors of ECOG performance status score, measurability of disease, or region.

Table 3: Overall Survival in PROSELICA for Cabazitaxel 20 mg/m^2 versus Cabazitaxel 25 mg/m^2 (intent-to-treat analysis)

	CBZ20+PRED n=598	**CBZ25+PRED n=602**
Overall Survival		
Number of deaths, n (%)	497 (83.1 %)	501 (83.2%)
Median survival (95% CI) (months)	13.4 (12.2 to 14.9)	14.5 (13.5 to 15.3)
Hazard Ratio* (97.78% CI†)	1.024 (0.886, 1.184)	

* Hazard ratio is estimated using a Cox Proportional Hazards regression model. A hazard ratio <1 indicates a lower risk of death for Cabazitaxel 20 mg/m^2 with respect to 25 mg/m^2.
† Adjusted for interim OS analyses. The noninferiority margin is 1.214.
CBZ20=Cabazitaxel 20 mg/m^2, CBZ25=Cabazitaxel 25 mg/m^2, PRED=Prednisone/Prednisolone.
CI=confidence interval.

Figure 1: Kaplan-Meier Overall Survival Curves (intent-to-treat population) (PROSELICA)

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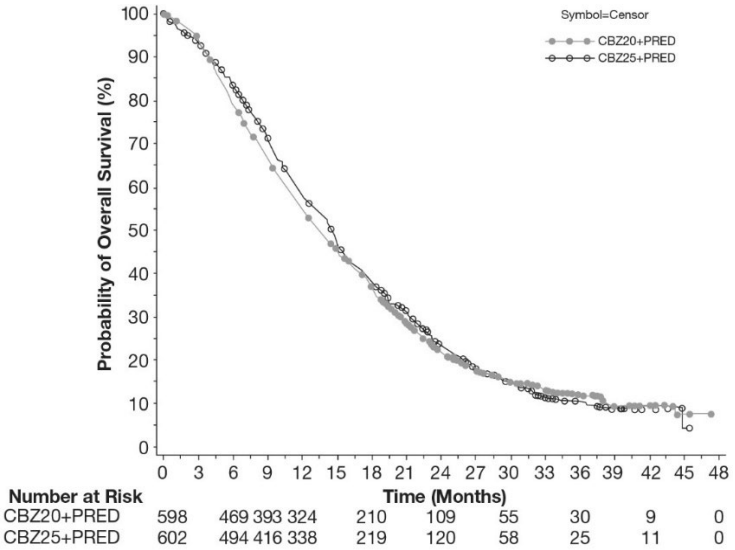

15 REFERENCES

1. OSHA Hazardous Drugs. OSHA. http://www.osha.gov/SLTC/hazardousdrugs/index.html

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 How Supplied

Cabazitaxel Injection is supplied as a sterile multiple-dose vial containing clear colorless to pale yellow viscous solution in a clear glass vial with a grey rubber closure, aluminum cap, and green plastic flip-off cap

NDC 0781- 3186-75 - 45 mg/4.5 mL (10 mg/mL) multiple-dose vial in a carton
NDC 0781- 3193-60 - 60 mg/6 mL (10 mg/mL) multiple-dose vial in a carton

16.2 Storage

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). [*See USP Controlled Room Temperature]*

Do not refrigerate.

16.3 Handling and Disposal

Cabazitaxel Injection is a hazardous drug. Follow applicable special handling and disposable procedures.[1]

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 Cabazitaxel Injection. 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 Precautions (5.3)]*.

Bone Marrow Suppression

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Inform patients that Cabazitaxel Injection 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 (8.5)]*.

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 Administration (2.1)]*.

Infections, 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 healthcare provider *[see Warnings and Precautions (5.1, 5.4, 5.5)]*.

Urinary Disorders Including Cystitis

Inform patients that hematuria may occur during treatment with Cabazitaxel Injection. Inform patients that previously received pelvic radiation that cystitis and radiation cystitis may occur during treatment with Cabazitaxel Injection. 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 Cabazitaxel Injection. 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 Interactions (7.1)]*.

Embryo-Fetal Toxicity

Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Cabazitaxel Injection *[see Use in Specific Populations (8.3)]*.

Infertility

Advise male patients that Cabazitaxel Injection may impair fertility *[see Use in Specific Populations (8.3)]*.

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Patient Information
Cabazitaxel (ka-BAZ-i-TAX-el)
Injection

What is the most important information I should know about Cabazitaxel Injection?

Cabazitaxel Injection 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 Cabazitaxel Injection.
  - may lower your dose of Cabazitaxel Injection, change how often you receive it, or stop Cabazitaxel Injection 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 Cabazitaxel Injection:
  - fever. Take your temperature often during treatment with Cabazitaxel Injection.
  - 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 Cabazitaxel Injection 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 Cabazitaxel Injection:
  - rash or itching
  - feeling dizzy or faint
  - chest or throat tightness
  - skin redness
  - breathing problems
  - swelling of your face
- **Severe stomach and intestine (gastrointestinal) problems.**
  - **Cabazitaxel Injection can cause severe vomiting and diarrhea, which may lead to death.** Severe vomiting and diarrhea with Cabazitaxel Injection 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 Cabazitaxel Injection. **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 Cabazitaxel Injection.
    Tell your healthcare provider right away if you develop vomiting or diarrhea or if your symptoms get worse or do not get better.
  - **Cabazitaxel Injection 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 Cabazitaxel Injection, 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 Cabazitaxel Injection and may lead to death. Men who have lung disease before receiving Cabazitaxel Injection may have a higher risk for developing lung or breathing problems with Cabazitaxel Injection 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 Cabazitaxel Injection?

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Cabazitaxel Injection is a prescription medicine used with the steroid medicine prednisone. Cabazitaxel Injection 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 Cabazitaxel Injection is safe and effective in children.

Who should not receive Cabazitaxel Injection?

Do not receive Cabazitaxel Injection 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 Cabazitaxel Injection, tell your healthcare provider about all of your medical conditions, including if you:

- are over the age of 65
- had allergic reactions in the past
- have kidney or liver problems
- have lung problems
- are pregnant or plan to become pregnant. Cabazitaxel Injection 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 Cabazitaxel Injection and for 3 months after the last dose of Cabazitaxel Injection.

Tell your healthcare provider about all the medicines you take, including prescription and over-the -counter medicines, vitamins, and herbal supplements.

Cabazitaxel Injection 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 Cabazitaxel Injection.

How will I receive Cabazitaxel Injection?

- Cabazitaxel Injection will be given to you by an intravenous (IV) infusion into your vein.
- Your treatment will take about 1 hour.
- Cabazitaxel Injection is usually given every 3 weeks. Your healthcare provider will decide how often you will receive Cabazitaxel Injection.
- Your healthcare provider will also prescribe another medicine called prednisone for you to take by mouth every day during treatment with Cabazitaxel Injection.
- 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 Cabazitaxel Injection, you may receive other medicines to prevent or treat side effects.

What are the possible side effects of Cabazitaxel Injection?

Cabazitaxel Injection may cause serious side effects including:

- **See "What is the most important information I should know about Cabazitaxel Injection?"**
- **Inflammation of the bladder and blood in the urine.** Blood in the urine is common with Cabazitaxel Injection, 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 Cabazitaxel Injection. Your healthcare provider may stop your treatment with Cabazitaxel Injection for a short time, or permanently, if you develop inflammation of the bladder and bleeding that is severe.

The most common side effects of Cabazitaxel Injection include:

- **Low red blood cell counts (anemia).** Low red blood cell counts are common with Cabazitaxel Injection, 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 counts.** Low platelet counts are common with Cabazitaxel Injection, but can sometimes also be serious. Tell your healthcare provider if you have any unusual bruising or bleeding.
- diarrhea
- nausea
- tiredness
- constipation
- weakness
- vomiting
- blood in urine
- decreased appetite
- back pain

This label may not be the latest approved by FDA.
For current labeling information, please visit https://www.fda.gov/drugsatfda

Cabazitaxel Injection 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 of the possible side effects of Cabazitaxel Injection. 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.

General information about the safe and effective use of Cabazitaxel Injection.

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 Cabazitaxel Injection that is written for health professionals.

What are the ingredients in Cabazitaxel Injection?

Active ingredient: cabazitaxel

Inactive ingredients: anhydrous critic acid, dehydrated alcohol, polyethylene glycol 300, and polysorbate 80.

Manufactured by FAREVA Unterach GmbH for Sandoz Inc., Princeton, NJ 08540

For more information, call 1-800-525-8747.

This Patient Information has been approved by the U.S. Food and Drug Administration. Issued: January 2023