09-J1000-77

Original Effective Date: 12/15/12

Reviewed: 03/08/23

Revised: 06/01/26

Subject: Cabazitaxel Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Cabazitaxel (Jevtana) was first approved by the U.S. Food and Drug Administration (FDA) in June 2010 for the treatment of individuals with hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen. Cabazitaxel is a novel semi-synthetic taxane demonstrating *in vitro* activity in docetaxel-sensitive and docetaxel-resistant cell lines and tumor models. Similar to other taxanes (e.g., paclitaxel [Taxol], docetaxel [(Taxotere]), cabazitaxel impairs microtubule assembly ultimately resulting in mitotic arrest and apoptosis. Although cabazitaxel is mechanistically similar to paclitaxel and docetaxel, it has poor affinity for P-glycoprotein (P-gp); consequently, cabazitaxel's penetration of the blood-brain barrier is superior to that of paclitaxel and docetaxel. In January 2023 the FDA approved, via the 505(b)(2) pathway, Cabazitaxel Injection (from Sandoz), based on the reference product Jevtana. Both products share the same FDA-approved indication; however, there are minor difference in the labeling. For example, Jevtana includes reference to a higher 25 mg/m^2 dosage in select patients, while Cabazitaxel Injection does not. In addition, Jevtana comes as a kit with a diluent and require two dilutions prior to administration, while Cabazitaxel Injection comes in a multi-dose vial and requires only a single dilution prior to administration.

For most men with metastatic prostate cancer, androgen-deprivation therapy, usually with a luteinizing hormone-releasing hormone (LHRH) agonist, improves symptoms, but tumors invariably become castration resistant and progressive disease ensues. The NCCN Guidelines for Prostate Cancer list cabazitaxel as the sole category 1 "Preferred regimen" for the treatment of metastatic castration-recurrent prostate cancer (CRPC) in patients who have been previously treated with both docetaxel and a prior novel hormone therapy (i.e., abiraterone, enzalutamide, darolutamide, or apalutamide). For patients with prior docetaxel treatment but no prior novel hormone therapy, cabazitaxel is listed as a category 2A "Preferred regimen"; however, abiraterone and enzalutamide are listed as category 1 preferred regimens. For patient with prior novel hormone therapy, docetaxel treatment, or both, the NCCN lists cabazitaxel in combination with carboplatin as a category 2A recommendation under "Useful in certain circumstances". This regimen includes a footnote stating, "Cabazitaxel 20 mg/m^2 plus carboplatin AUC 4 mg/mL per min with growth factor support can be considered for fit patients with aggressive variant prostate cancer (visceral metastases, low PSA and bulky disease, high LDH, high CEA, lytic bone metastases, NEPC histology) or unfavorable genomics (defects in at least two of *PTEN*, *TP53*, and *RB1*). The NCCN states that all patients with metastatic CRPC should maintain castrate levels of serum testosterone (<50 ng/dL) and received best supportive care. The NCCN guidelines mention that metastatic CRPC patients who are not candidates for docetaxel, who are intolerant of docetaxel, or who have pre-existing mild peripheral

neuropathy should be considered for treatment with cabazitaxel. NCCN recommends that cabazitaxel treatment should be stopped upon clinical disease progression or intolerance.

POSITION STATEMENT:

Drug Waste Reduction: Additional medical necessity criteria for dose optimization may apply depending on the requested dose and member's benefit. Refer to Medical Coverage Guideline Drug Waste Reduction, 09-J5000-54.

The initiation of cabazitaxel (Jevtana) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "7"):

1. Member is diagnosed with metastatic, castration-recurrent prostate cancer (CRPC, a.k.a., castration-resistant or hormone-refractory prostate cancer) - *lab documentation of a recent (past 90 days) serum testosterone level at castrate level (<50 ng/dL) must be submitted for members receiving medical castration. A chart note documenting a bilateral orchiectomy must be submitted for members who have received surgical castration.*
2. **ANY** of the following ("a", "b", "c", or "d"):
    a. Member has previously received a docetaxel-containing regimen for treatment of their prostate cancer and had progressive or relapsed disease
    b. Member has previously received a docetaxel-containing regimen and had intolerable adverse effects that are expected to be less likely with cabazitaxel (e.g., peripheral neuropathy, fluid retention) – *the specific adverse effect must be provided*
    c. Member is not a suitable candidate for docetaxel treatment due to pre-existing peripheral neuropathy – *documentation from the medical record must be submitted*
    d. **BOTH** of the following ("i" and "ii"):
        i. Member has previously received a novel hormone therapy (i.e., abiraterone, enzalutamide, darolutamide, or apalutamide) for treatment of their prostate cancer and had progressive or relapsed disease
        ii. Member has aggressive variant prostate cancer [i.e., **ANY** of the following - visceral metastases, low PSA (<10 ng/mL) with bulky disease, high serum lactate dehydrogenase (LDH) (≥2x ULN), high serum carcinoembryonic antigen (CEA) (≥2x ULN), lytic bone metastases, or neuroendocrine prostate cancer (NEPC) histology]; **OR** unfavorable genomics (i.e., defects in at least two of following three tumor suppressor genes - PTEN, TP53, and RB1)
3. Cabazitaxel will be used in combination with **ANY** of the following:
    a. Daily prednisone
    b. Dexamethasone given on the day of chemotherapy
    c. Carboplatin plus either daily prednisone or dexamethasone given on the day of chemotherapy*

    If used with carboplatin the member must have **EITHER aggressive variant prostate cancer [i.e., **ANY** of the following - visceral metastases, low PSA (<10 ng/mL) with bulky disease, high serum lactate dehydrogenase (LDH) (≥2x ULN), high serum carcinoembryonic antigen (CEA) (≥2x ULN), lytic bone metastases, or neuroendocrine prostate cancer (NEPC) histology]; **OR** unfavorable genomics (i.e., defects in at least two of following three tumor suppressor genes - PTEN, TP53, and RB1)*
4. Member has a neutrophil count of greater than 1,500 cells/mm^3
5. Member does **NOT** have severe hepatic impairment [total bilirubin >3-times the upper limit of normal (ULN)]

6. Dosage of cabazitaxel does not exceed 25 mg/m^2 every 3 weeks (i.e., 25 mg/m^2 once per cycle)
7. Cabazitaxel is not used concomitantly with **ANY** of the following:
    a. Abiraterone (Yonsa, Zytiga)
    b. Apalutamide (Erleada)
    c. Darolutamide (Nubeqa)
    d. Docetaxel (Taxotere)
    e. Enzalutamide (Xtandi)
    f. Mitoxantrone (Novantrone)
    g. Radium-223 (Xofigo)
    h. Sipuleucel-T (Provenge)

Approval duration: 6 months

The continuation of cabazitaxel (Jevtana) **meets the definition of medical necessity** when **ALL** of the following criteria are met ("1" to "5"):

1. An authorization or reauthorization for cabazitaxel has been previously approved by Florida Blue or another health plan in the past 2 years for the treatment of metastatic CRPC, **OR** the member previously met **ALL** indication-specific initiation criteria
2. Cabazitaxel will be used in combination with **ANY** of the following:
    a. Daily prednisone
    b. Dexamethasone given on the day of chemotherapy
    c. Carboplatin plus either daily prednisone or dexamethasone given on the day of chemotherapy
3. Cabazitaxel is not used concomitantly with **ANY** of the following:
    a. Abiraterone (Yonsa, Zytiga)
    b. Apalutamide (Erleada)
    c. Darolutamide (Nubeqa)
    d. Docetaxel (Taxotere)
    e. Enzalutamide (Xtandi)
    f. Mitoxantrone (Novantrone)
    g. Radium-223 (Xofigo)
    h. Sipuleucel-T (Provenge)
4. The member has not had disease progression during treatment with cabazitaxel
5. Dosage of cabazitaxel does not exceed 25 mg/m^2 every 3 weeks (i.e., 25 mg/m^2 once per cycle)

Approval duration: 6 months

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved: Cabazitaxel is indicated, in combination with prednisone, for the treatment of members with metastatic castration-resistant prostate cancer previously treated with a docetaxel-containing treatment regimen. The recommended dosage is based on calculation of Body Surface Area (BSA) and is 20 mg/m^2 every three weeks with oral prednisone 10 mg daily throughout treatment. Per the Jevtana package insert only, a dose of 25 mg/m^2 can be used in select patients at the discretion of the treating healthcare provider. Cabazitaxel is administered as an intravenous (IV) infusion over one hour. PVC equipment should not be used.

Pre-medication, consisting of an antihistamine (e.g., diphenhydramine 25 mg), corticosteroid (e.g., dexamethasone 8 mg), and a histamine-2 receptor antagonist (e.g., ranitidine 50 mg) should be administered 30 minutes prior to each cabazitaxel dose. Antiemetic prophylaxis, either oral or intravenous, is also recommended as needed. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. Consider primary prophylaxis with G-CSF in all patients receiving a dose of 25 mg/m^2.

Dosage Adjustments

- **Renal Impairment:** No dose adjustment is necessary in patients with renal impairment not requiring hemodialysis. Patients presenting with end-stage renal disease (creatinine clearance <5 mL/min/1.73m^2), should be monitored carefully during treatment.
- **Hepatic Impairment:**
    - Mild hepatic impairment (total bilirubin >1 to ≤1.5 × Upper Limit of Normal (ULN) or AST >1.5 × ULN): Administer at a dose of 20 mg/m^2.
    - Moderate hepatic impairment (total bilirubin >1.5 to ≤3 × ULN and AST = any): Reduce starting dose to 15 mg/m^2 based on tolerability data in these patients; however, the efficacy of this dose is unknown.
    - Severe hepatic impairment (total bilirubin >3 × ULN): Cabazitaxel is contraindicated in patients with severe hepatic impairment.
- **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 with these drugs. If patients require co-administration of a strong CYP3A inhibitor, consider a 25% dose reduction of cabazitaxel.
- **Adverse reactions:** the dose of cabazitaxel should be reduced from 25 to 20 mg/m^2 or from 20 to 15 mg/m^2 if members experience the adverse reactions described in Table 1. If the member continues to experience any of these reactions at the 15 mg/m^2 dose, cabazitaxel should be discontinued.

Table 1

Recommended Dosage Adjustments for Adverse Reactions	
Toxicity	**Dosage Modification**
Prolonged grade 3 or greater neutropenia (greater than 1 week) despite appropriate medication including G-CSF	Delay treatment until neutrophil count is greater than 1,500 cells/mm^3, then reduce the dosage by one dose level (i.e., by 5 mg/m^2) Use G-CSF for secondary prophylaxis.
Febrile neutropenia or neutropenic infection	Delay treatment until improvement or resolution, and until neutrophil count is greater than 1,500 cells/mm^3, then reduce the dosage by one dose level. Use G-CSF for secondary prophylaxis
Grade 3 or greater diarrhea or persisting diarrhea despite appropriate medication, fluid and electrolytes replacement.	Delay treatment until improvement or resolution, then reduce the dosage by one dose level.

Grade 2 peripheral neuropathy	Delay treatment until improvement or resolution, then reduce the dosage by one dose level.
Grade ≥3 peripheral neuropathy	Discontinue cabazitaxel treatment
G-CSF = Granulocyte Colony Stimulating Factor	

Drug Availability

- Cabazitaxel Injection (Sandoz) is available as 45 mg/4.5 mL (10 mg/mL) and 60 mg/6 mL (10 mg/mL) multiple-dose vials in a carton
- Jevtana is available as a 60 mg/1.5 mL injection kit consisting of the following:
  - Cabazitaxel injection: 60 mg cabazitaxel in 1.5 mL polysorbate 80
  - Diluent: 5.7 mL of 13% (w/w) ethanol in water for injection

PRECAUTIONS:

CONTRAINDICATIONS

- 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 × ULN)

BOXED WARNING

WARNING: NEUTROPENIA AND HYPERSENSITIVITY

- **Neutropenia**: Neutropenic deaths have been reported. Monitor for neutropenia with frequent blood cell counts. Cabazitaxel is contraindicated in members with neutrophil counts less than or equal to 1,500 cells/mm^3. Primary prophylaxis with G-CSF is recommended in patients with high-risk clinical features. Consider primary prophylaxis with G-CSF in all patients receiving a dose of 25 mg/m^2.
- **Severe hypersensitivity**: Severe hypersensitivity can occur and may include generalized rash/erythema, hypotension and bronchospasm. Severe hypersensitivity reactions require immediate discontinuation of the cabazitaxel infusion and administration of appropriate therapy. Patients should receive premedication. Cabazitaxel is contraindicated in patients who have a history of severe hypersensitivity reactions to cabazitaxel or other drugs formulated with polysorbate 80.

WARNINGS AND PRECAUTIONS

- **Bone Marrow Suppression**: Bone marrow suppression manifested as neutropenia, anemia, thrombocytopenia and/or pancytopenia may occur. Neutropenic deaths have been reported. Closely monitor patients with hemoglobin <10 g/dL. Based on guidelines for the use of G-CSF and the adverse reactions profile of cabazitaxel, 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. Consider primary prophylaxis with G-CSF in all patients receiving cabazitaxel 25 mg/m^2. 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 table 1 for dosage adjustment information.
- **Increased Toxicities in Elderly Patients**: Patients ≥65 years of age are more likely to experience fatal outcomes and 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%).

- **Hypersensitivity Reactions:** Pre-medicate members with an antihistamine, corticosteroid, and histamine-2 receptor antagonist at least 30 minutes prior to each dose of cabazitaxel.
- **Gastrointestinal Adverse Reactions (nausea, vomiting, diarrhea):** Mortality related to diarrhea has been reported. Members should be rehydrated and antiemetics and anti-diarrheals should be administered as needed. If member is experiencing grade ≥ 3 diarrhea, the dosage should be adjusted (refer to Table 1). The incidence of gastrointestinal adverse reactions is greater in patients who have received prior radiation.
- **Renal Failure:** Renal failure, including cases with fatal outcomes, has been reported. The cause should be identified and managed aggressively.
- **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. 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. Interrupt or discontinue cabazitaxel in patients experiencing severe hemorrhagic cystitis. Medical and/or surgical supportive treatment may be required to treat severe hemorrhagic cystitis.
- **Respiratory disorders**: Interstitial pneumonia/pneumonitis, interstitial lung disease and acute respiratory distress syndrome, including fatal outcomes, have been reported. Patients with underlying lung disease may be at higher risk for these events. Interrupt treatment if new or worsening pulmonary symptoms develop.
- **Hepatic Impairment:** Cabazitaxel is contraindicated in patients with severe hepatic impairment (total bilirubin > 3 × ULN). Dose should be reduced for patients with mild and moderate impairment, based on tolerability data in these patients. Administration of cabazitaxel to patients with mild and moderate hepatic impairment should be undertaken with caution and close monitoring of safety.
- **Embryo-Fetal Toxicity**: Based on findings in animal reproduction studies and its mechanism of action, cabazitaxel can cause fetal harm when administered to a pregnant woman.

BILLING/CODING INFORMATION:

HCPCS Coding

J9043	Injection, cabazitaxel, 1 mg
J9064	Injection, cabazitaxel (sandoz), not therapeutically equivalent to j9043, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C61	Malignant neoplasm of prostate

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

Medicare Part D: Not applicable.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Castrate-resistant/recurrent prostate cancer (CRPC): disease progression despite androgen deprivation therapy (ADT) with either medication or surgery (i.e., removal/destruction of testicles), and may present as either a continuous rise in serum prostate-specific antigen (PSA) levels, the progression of pre-existing disease, and/or the appearance of new metastases.

RELATED GUIDELINES:

Abiraterone acetate (Zytiga, Yonsa), 09-J1000-36
Cryosurgical Ablation of the Prostate (CSAP), 02-54000-14
Docetaxel (Taxotere) IV, 09-J0000-95
Gonadotropin Releasing Hormone Analogs and Antagonists, 09-J0000-48
Granulocyte Colony Stimulating Factors, 09-J0000-62
Oral Oncology Medication, 09-J3000-65
Radium Ra 223 (Xofigo) Injection, 09-J2000-01
Sipuleucel-T (Provenge), 09-J1000-29

OTHER:

None.

REFERENCES:

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/08/23.

GUIDELINE UPDATE INFORMATION:

12/15/12	New Medical Coverage Guideline.
04/01/13	Review and revision to guideline; consisting of revising position statement, updating references and adding related guidelines.
04/15/14	Review and revision to guideline; consisting of revising position statement, updating references and program exceptions.
04/15/15	Review and revision to guideline; consisting of description, position statement, related guidelines, and updating of references.
12/15/15	Revision to guideline consisting of updating the position statement.
04/15/16	Review and revision to guideline consisting of updating the description section, position statement, dosage/administration, and references.
04/15/17	Review and revision to guideline consisting of updating the description section, position statement, and references. The total number of treatment cycles must not exceed ten and members must not have severe hepatic dysfunction or neutropenia (both contraindications),
04/15/18	Review and revision to guideline consisting of updating the description section, position statement, dosage/administration, precautions, and references.
10/15/18	Revision to guideline consisting of updating the position statement to permit continuation of therapy until disease progression.
04/15/19	Review and revision to guideline consisting of updating the related guidelines and references.
06/15/21	Revision to guideline consisting of updating the description section, position statement, dosage/administration, precautions, related guidelines, and references based on update to the FDA label and NCCN Guidelines.
04/15/23	Revision to guideline consisting of updating the description section, dosage/administration, billing/coding, and references.
10/01/23	Revision: Added HCPCS code J9064 and deleted code J9999.
06/01/26	Revision: Added Drug Waste Reduction statement to the Position Statement.