09-J3000-76

Original Effective Date: 09/15/20

Reviewed: 03/12/25

Revised: 04/15/25

Subject: Sacituzumab Govitecan-hziy (Trodelvy)

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DESCRIPTION:

Approximately 15% of all breast cancers are caused by triple-negative tumors. Triple negative breast cancer (TNBC) tumors do not carry receptors for estrogen, progesterone, or human epidermal growth factor (HER2). Generally, TNBC is more aggressive and more difficult to treat due to fewer medications.

Sacituzumab govitecan-hziy (Trodelvy), a Trop-2-directed antibody and topoisomerase inhibitor conjugate, was approved by the U.S. Food and Drug Administration (FDA) in April 2020 for the treatment of adult patients with metastatic triple-negative breast cancer (mTNBC) who have received at least two prior therapies for metastatic disease. Sacituzumab works by recognizing the Trop-2 protein located on the surface of tumor cells. Once attached to the tumor, it releases a metabolite of irinotecan that damages the cell DNA.

The safety and efficacy of sacituzumab govitecan were evaluated in patients with advanced epithelial cancer who had received previous therapy. Patients in the study had a variety of different epithelial cancers. The approval for mTNBC was based upon data from a subset of 108 patients with mTNBC. Patients in the study with mTNBC had a median age of 55 years (range, 31–80 years) and 80% had visceral metastases. Patients had an ECOG performance status of 0 or 1, and the median time from metastatic diagnosis to treatment was 1.5 years. Overall, 57 patients had moderate (2+) to strong (3+) Trop-2 expression by immunohistochemistry, and 5 had weak or absent staining for the marker. The data were not available for the remaining patients.

Sacituzumab govitecan was administered at 10 mg/kg on Days 1 and 8 of each 28-day cycle. The median number of prior regimens was 3 (range, 2–10), which included checkpoint inhibitors for 16.7%. Additionally, 41% of patients were treated in the third line setting and 59% were in the fourth-line or greater setting. Patients with bulky disease, defined as a mass >7 cm, were not eligible. Tumor imaging was obtained every 8 weeks, with confirmatory CT/MRI scans obtained 4–6 weeks after an initial partial or complete response, until progression requiring treatment discontinuation.

Endpoints included safety, objective response rate (ORR), duration of response (DOR), clinical benefit, which was defined as a complete or partial response for at least 6 months (stable disease for at least 6 months), progression-free survival (PFS), and overall survival (OS).

The results showed an ORR of 33.3%, with 3 complete responses and 33 partial responses. The median DOR was 7.7 months with a clinical benefit rate of 45.4%. The median PFS was 5.5 months with an OS of

13 months. Median time to respond was 2 months. At the time of data cutoff (December 1, 2017), the median duration of follow up among the 108 patients was 9.7 months (range, 0.3 to 36.5). A total of 100 patients (92.6%) had discontinued treatment, and in 86 of these patients (80%), discontinuation was because of disease progression.

Grade 3/4 adverse events (AEs) were experienced by 85% of patients receiving treatment with sacituzumab. Serious AEs were reported in 35% of patients. Three patients discontinued treatment due to AEs, 2 of which were deemed to have occurred from study-drug-related causes. Dose reductions to 7.5 mg/kg occurred in 25% of patients. The most common (≥10%) grade 3/4 AEs were neutropenia (41.7%), anemia (11%), decreased white cell count (11%), hypophosphatemia (9%), diarrhea (8%), and fatigue and asthenia (8%). Ten patients (9.3%) developed febrile neutropenia during the course of the study. Additionally, 4 deaths occurred during treatment.

National Comprehensive Cancer Network (NCCN) Guidelines for Breast Cancer (Version 1.2024) and Bladder Cancer (Version 1.2024) include recommendations for use of sacituzumab.

POSITION STATEMENT:

Initiation of sacituzumab govitecan-hziy (Trodelvy) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when ALL associated criteria is met:

1. Breast Cancer
    a. Member is diagnosed with recurrent unresectable (local or regional) or stage IV breast cancer or inflammatory breast cancer with no response to preoperative systemic therapy
    b. Member's disease has been confirmed to be triple-negative (TNBC) **OR** hormone receptor positive and human epidermal growth factor receptor 2 (HER2)-negative – laboratory documentation must be provided
    c. Member has received prior treatment:
        i. HR+/HER2- disease: Endocrine therapy, a CDK4/6 inhibitor, and at least two lines of chemotherapy
        ii. TNBC: At least one prior regimen in the metastatic setting
    d. Dose does not exceed 10 mg/kg weekly on days 1 and 8 of a 21-day cycle
2. Bladder Cancer
    a. Member is diagnosed with stage II or higher (i.e., more severe) bladder cancer **OR** metastatic upper GU tract tumor, urothelial carcinoma of the prostate, or primary carcinoma of the urethra
    b. Member has received a first-line platinum-containing chemotherapy and an immune checkpoint inhibitor (e.g., avelumab)
    c. Dose does not exceed 10 mg/kg weekly on days 1 and 8 of a 21-day cycle
3. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. Member meets **ONE** of the following:
        i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) **AND** member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert).

ii. Indication AND usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation.

b. Dose does not exceed 10 mg/kg weekly on days 1 and 8 of a 21-day cycle.

Approval duration: 6 months

Continuation of sacituzumab govitecan-hziy (Trodelvy) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue or another health plan in the past two years for treatment of breast cancer, bladder cancer, upper GU tract tumor, urothelial carcinoma of the prostate, primary carcinoma of the urethra, or other FDA-approved or NCCN supported diagnosis, **OR** the member has previously met all indication-specific criteria.
2. Member's disease has not progressed during treatment with sacituzumab govitecan-hziy.
3. Dose does not exceed 10 mg/kg weekly on days 1 and 8 of a 21-day 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

- For intravenous infusion only. Do not administer as an intravenous push or bolus.
- The recommended dose is 10 mg/kg once weekly on Days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity.

Dose Adjustments

- See FDA approved product labeling.

Drug Availability

- For injection: 180 mg lyophilized powder in single-dose vials for reconstitution.

PRECAUTIONS:

Boxed Warning

- Severe neutropenia may occur. Withhold for absolute neutrophil count below 1500/mm3 or neutropenic fever. Monitor blood cell counts periodically during treatment. Consider G-CSF for secondary prophylaxis. Initiate anti-infective treatment in patients with febrile neutropenia without delay.
- Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. Administer atropine, if not contraindicated, for early diarrhea of any severity. At the onset of late

diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold until resolved to < Grade 1 and reduce subsequent doses.

Contraindications

- Severe hypersensitivity reaction

Precautions/Warnings

- Hypersensitivity: Hypersensitivity reactions including severe anaphylactic reactions have been observed. Monitor patients for infusion-related reactions.
- Nausea/Vomiting: Use antiemetic preventive treatment and withhold for patients with Grade 3 nausea or Grade 3-4 vomiting at the time of scheduled treatment.
- Patients with Reduced UGT1A1 Activity: Individuals who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1) *28 allele are at increased risk for neutropenia following initiation of TRODELVY treatment.
- Embryo-Fetal Toxicity.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding

J9317	Injection, sacituzumab govitecan-hziy, 2.5 mg

ICD-10 Diagnosis Codes That Support Medical Necessity

C50.011–C50.929	Malignant neoplasm of female and male breast
C61	Malignant neoplasm of prostate
C65.1, C65.2, C65.9	Malignant neoplasm of renal pelvis
C66.1, C66.2, C66.9	Malignant neoplasm of ureter
C67.0-C67.9	Malignant neoplasm of bladder
C68.0	Malignant neoplasm of other and unspecified urinary organs
D09.0	Carcinoma in situ of other and unspecified sites

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 Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

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

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:

Adjuvant Treatment: Additional cancer treatment given after the primary treatment to lower the risk that the cancer will return. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy, or biologic therapy. Adjuvant therapy can be used after or in combination with another form of cancer therapy and is commonly used following removal of a cancerous tumor to further help in treatment.

Metastatic cancer: when cancer spreads from the primary site (place where it started) to other places in the body.

Neo-adjuvant treatment: Treatment given as a first step to shrink a tumor before the main treatment, which is usually surgery, is given. Examples of neoadjuvant therapy include chemotherapy, radiation therapy, and hormone therapy. It is a type of induction therapy.

RELATED GUIDELINES:

None

OTHER:

None

REFERENCES:

1. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 02/24/25]. Available from: http://www.clinicalpharmacology.com/.
2. ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine; 2000 Feb 29 - [cited 2/24/25]. Available from: http://clinicaltrials.gov/.
3. DailyMed [Internet]. Bethesda (MD): National Library of Medicine; 2020. Available from: http://dailymed.nlm.nih.gov/dailymed/index.cfm/. Accessed 8/4/20.
4. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2/24/25]. Available from: www.micromedexsolutions.com/.
5. Orphan Drug Designations and Approval [Internet]. Silver Spring (MD): US Food and Drug Administration; 2025 [cited 2/24/25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 03/12/25.

GUIDELINE UPDATE INFORMATION:

09/15/20	New Medical Coverage Guideline.
10/01/20	Revision: Added HCPCS code C9066.
01/01/21	Revision: Added HCPCS code J9317 and deleted codes C9066 and J9999.
06/15/22	Revised position statement per NCCN.
09/15/22	Revised position statement per NCCN.
04/15/23	Review and revision of guideline; updated position statement per NCCN.
04/15/24	Review and revision of guideline; updated position statement per NCCN, coding, and references.
04/15/25	Review and revision of guideline; updated references.