



Trodelvy (sacituzumab govitecan-hziy)
PAM – 029

Table with 4 columns: Iowa Medicaid Program, Revision Number, Reviewed By, Approved By, Prior Authorization, Effective Date, Last Reviewed, Next Review, Approved Date.

Overview

Table with 2 columns: Field (Medication, Brand Name, Pharmacologic Category, FDA-Approved Indication(s), How Supplied, Dosage and Administration, Benefit Category) and Value.

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- Severe or life-threatening neutropenia may occur. Withhold Trodelvy® 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 patient with febrile neutropenia without delay.
Severe diarrhea may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of diarrhea, evaluate for infectious causes and, if negative, promptly initiate loperamide. If severe diarrhea occurs, withhold Trodelvy® until resolved to ≤ Grade 1 and reduce subsequent doses.

Descriptive Narrative

Triple-negative breast cancer (TNBC) describes a set of cancers that lack expression of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), making it more difficult to treat and associated with a poor prognosis. Unlike other subtypes (e.g., ER-positive, HER2-positive subtypes), there are no approved targeted treatments available. However, for a subset of TNBC, immunotherapy (in combination with chemotherapy) is available for those with advanced TNBC that expresses programmed cell death ligand 1 (PD-L1).

TNBC accounts for approximately 15 percent of breast cancers diagnosed worldwide, which amounts to almost 200,000 cases each year. These cancers tend to be more common in women younger than 40 years of age, who are African-American, or who have a BRCA1 mutation.²

Bladder cancer is the most common malignancy involving the urinary system and the ninth most common malignancy worldwide. Urothelial carcinoma is the predominant histologic type in the United States and Western Europe, where it accounts for approximately 90 percent of bladder cancers. In the US, approximately 80,000 new cases and 17,000 deaths occur each year due to bladder cancer. In other areas of the world, such as the Middle East, both urothelial and non-urothelial histologies are seen, with the latter due at least in part to the prevalence of schistosomiasis.

Bladder cancer is typically diagnosed in older individuals. A majority (approximately 73 percent) of patients with bladder cancer are older than 65 years of age. The median age at diagnosis is 69 years of age in males and 71 years of age in females. The incidence increases with age from 142 to 296 per 100,000 in males 65 to 69 years of age and 85 and over, respectively, and from 33 to 74 per 100,000 in females in the same age groups. The age of onset is younger in current smokers than in never smokers. The relative risk for current versus never cigarette smokers is the same in males and females (4.0 and 4.7, respectively), reflecting converging smoking patterns. Although extremely rare, bladder cancer can be seen in children and young adults, where it usually presents with low-grade, noninvasive disease.

There are racial and ethnic variations in bladder cancer incidence. In the US, white males have the highest risk with roughly twice the incidence seen in African American and Hispanic males. In addition to differences in incidence, sex and race also affect the stage at presentation and prognosis. Although the overall incidence of bladder cancer is lower in females and African Americans, these groups have more advanced-stage tumors at presentation compared with white males.³

Abbreviations

- **BRCA1:** breast cancer susceptibility gene 1. Pathogenic variants in BRCA1 and BRCA2 are the strongest hereditary risk factors for the development of breast and ovarian cancer.⁴
- **mUC:** metastatic urothelial cancer
- **PD-1:** programmed cell death 1, a transmembrane protein expressed on T cells, B cells, and NK cells. It is an inhibitory molecule that binds to the programmed cell death ligand 1 (PD-L1) and PD-L2.⁵
- **PD-L1:** programmed cell death ligand 1. Ligands found on both normal and cancer cells. PD-L1 expressed by tumor cells plays a critical role in the induction of inhibitory signals through the interaction with PD-1 expressed on the cell surface of T cells. This PD-1/PD-L1 interaction results in the suppression of tumor-specific T cell responses functioning as a tumor immune evasion mechanism. Immune checkpoint inhibitors targeting the PD-1/PD-L1 interaction have become a successful immunotherapy in treating many advanced cancers and are based on a mechanism of monoclonal antibody binding to and directly disrupting the PD-1/PD-L1 interaction.⁶
- **TNBC:** triple-negative breast cancer, defined as breast cancers that have less than 1 percent expression of the estrogen receptor (ER) and the progesterone receptor (PR) as determined by immunohistochemistry (IHC), and that are, for HER2, either 0 to 1+ by IHC, or IHC 2+ and fluorescence in situ hybridization negative (not amplified), according to American Society of Clinical Oncology/College of American Pathologists guidelines.
- **mTNBC:** metastatic triple-negative breast cancer

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. To view the most recent and complete version of the guidelines, go online to [NCCN.org](https://www.nccn.org). NCCN makes no warranties of any kind whatsoever regarding their content,

use or application and disclaims any responsibility for their application or use in any way.^{7,8}

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):⁹

- Breast Cancer (v.4.2024 – July 3, 2024)
- Bladder Cancer (v.4.2024 – May 9, 2024)

NCCN Guidelines® Recommendation(s) in Breast Cancer	
<p>(1) Recurrent unresectable (local or regional) or Stage IV (M0) breast cancer</p> <p>a. HR-positive and HER2-negative with visceral crisis ^a or endocrine refractory</p> <p>i. Sacituzumab govitecan-hziy: ^b Category 1, Preferred Second-Line Regimen in patients who are not a candidate for fam-trastuzumab deruxtecan-nxki (Enhertu)</p> <p>b. HR-negative and HER2-negative (triple-negative breast cancer; TNBC)</p> <p>i. Sacituzumab govitecan-hziy: ^c Category 1, Preferred Second-Line Regimen (regardless of biomarkers)</p> <p>^a According to the 5th ESO-ESMO international consensus guidelines (Cardoso F, et al. Ann Oncol 2020;31:1625) for advanced breast cancer visceral crisis is defined as: “severe organ dysfunction, as assessed by signs and symptoms, laboratory studies and rapid progression of disease. Visceral crisis is not the mere presence of visceral metastases but implies important organ compromise leading to a clinical indication for the most rapidly efficacious therapy.”</p> <p>^b Sacituzumab govitecan-hziy may be used for adult patients with HR-positive, HER2-negative metastatic/locally advanced unresectable breast cancer after prior treatment including endocrine therapy, a CDK4/6 inhibitor, and at least two lines of chemotherapy, one of which was a taxane, and at least one of which was in the metastatic setting. It may be considered for later line if not used as second line therapy.</p> <p>^c Sacituzumab govitecan-hziy may be used for adult patients with metastatic TNBC who have received at least 2 prior therapies, at least one of which was for metastatic disease. It may be considered for later line if not used as second line therapy.</p>	

NCCN Guidelines® Recommendation(s) in Bladder Cancer	
<p>(1) Locally advanced or metastatic bladder cancer (Stage IV) ^{a, b}</p> <p>a. Subsequent-line systemic therapy</p> <p>i. Sacituzumab govitecan-hziy: Category 2A, Other Recommended Regimen</p> <p>^a Patient should have already received platinum and a checkpoint inhibitor, if eligible.</p> <p>^b Appropriate for patients who received a first-line platinum-containing chemotherapy followed by avelumab maintenance therapy.</p>	

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Criteria

Prior authorization is required.

Breast Cancer

Trodelvy® is considered medically necessary when **ALL** of the following are met:

1. Member meets **ONE** of the following options (a or b):
 - a. Option A: meets all of the following (i and ii):
 - i. Diagnosis of recurrent or metastatic, histologically confirmed triple-negative breast cancer (TNBC); **AND**
 - ii. Confirmation of disease progression after two prior therapies, at least one of which is for metastatic disease; **OR**
 - b. Option B: meets all of the following (i, ii, and iii):
 - i. Diagnosis of unresectable, locally advanced or metastatic, histologically confirmed hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer; **AND**
 - ii. Member has received endocrine-based therapy; **AND**
 - iii. Confirmation of disease progression after two prior lines of therapy; **AND**
2. Member is 18 years of age or older; **AND**
3. Will not be prescribed in combination with irinotecan or its active metabolite SN-38; **AND**
4. Prescribed by, or in consultation with, an oncologist; **AND**
5. Request meets one of the following (a or b):
 - a. Regimen prescribed does not exceed 10 mg/kg once weekly on Days 1 and 8 of a 21-day treatment cycle; or,
 - b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Urothelial Cancer

Trodelvy® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of locally advanced or metastatic urothelial cancer (mUC); **AND**
2. Member continues to have disease progression after **EACH** of the following:
 - a. Platinum-containing therapy; **AND**
 - b. Either an anti-programmed cell death 1 (PD-1) or anti-programmed cell death ligand 1 (PD-L1) agent; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Member is 18 years of age or older; **AND**

5. Will not be prescribed in combination with irinotecan or its active metabolite SN-38; **AND**
6. Request meets one of the following (a or b):
 - a. Regimen prescribed does not exceed 10 mg/kg once weekly on Days 1 and 8 of a 21-day treatment cycle; or,
 - b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Continuation Therapy (all above indications)

Trodelvy® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by tumor response or lack of disease progression, and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
 - a. Regimen prescribed does not exceed 10 mg/kg once weekly on Days 1 and 8 of a 21-day treatment cycle; or,
 - b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	10 mg/kg once weekly on Days 1 and 8 of a continuous 21-day treatment cycle	

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9317	Injection, sacituzumab govitecan-hziy, 2.5 mg

ICD-10	Description
C50.011 – C50.329	Malignant neoplasm of breast
C68.8	Malignant neoplasm of overlapping sites of urinary organs
C79.81	Secondary malignant neoplasm of breast

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
55135-0132-01 (180 mg)	Gilead Sciences, Inc. (55135)	2.5 mg	1	EA	72

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

- ¹ Trodelvy® prescribing information (04/2024). Gilead Sciences, Inc.: Foster City, CA. Available online: www.trodelvyhcp.com. Accessed July 3, 2024.
- ² Anders CK, Carey LA. ER/PR negative, HER2-negative (triple-negative) breast cancer. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 4, 2024.
- ³ Daneshmand S. Epidemiology and risk factors of urothelial (transitional cell) carcinoma of the bladder. Shan S, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 4, 2024.

⁴ Peshkin BN, Isaacs C. Genetic testing and management of individuals at risk of hereditary breast and ovarian cancer syndromes. Vora SR, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 4, 2024.

⁵ Shoushtari AN, Hellmann M. Principles of cancer immunotherapy. Shah S, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed September 4, 2024.

⁶ Park, JJ., Thi, E.P., Carpio, V.H. et al. Checkpoint inhibition through small molecule-induced internalization of programmed death-ligand 1. Nat Commun 12, 1222 (2021).

⁷ National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

⁸ National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

⁹ NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Breast Cancer (v.4.2024 – July 3, 2024)
- Bladder Cancer (v.4.2024 – May 9, 2024)

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]

Signature

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		[#]

Signature

Change Date	Changed By	Description of Change	Version
10/18/2024	CAC	Annual review. Moved from July to October review to align with other policies for breast cancer. Added boxed warning information below Overview table. Added dosing into criteria. Reviewed NCCN Guidelines; no changes. Updated references where applicable.	6

Signature
William (Bill) Jagiello, DO



Change Date	Changed By	Description of Change	Version
07/21/2023	CAC	Annual review. New indication for unresectable locally advanced or metastatic HR-positive, HER2-negative breast cancer approved 2/3/2023. Updated overview table and developed criteria for new indication. Updated NCCN Guidelines.	5

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Change Date	Changed By	Description of Change	Version
07/15/2022	CAC	Added criteria that regimen/dosing prescribed must be in alignment with FDA-approved labeling or supported in NCCN Guidelines. Updated NCCN Guidelines. Formatting.	4

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Change Date	Changed By	Description of Change	Version
07/16/2021	CAC	Annual review.	3

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Change Date	Changed By	Description of Change	Version
04/16/2021	CAC	Implementation of new formatting. Added new indications.	2

Signature
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Change Date	Changed By	Description of Change	Version
01/15/2021	CAC	Criteria implementation.	1

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CAC = Medicaid Clinical Advisory Committee