STATE OF IOWA DEPARTMENT OF
Health AND Human
SERVICES

Trodelvy (sacituzumab govitecan-hziy)
PAM–029

Iowa Medicaid Program:	Prior Authorization	**Effective Date:**	07/01/2021
Revision Number:	5	**Last Rev Date:**	07/21/2023
Reviewed By:	Medicaid Medical Director	**Next Rev Date:**	07/19/2024
Approved By:	Medicaid Clinical Advisory Committee	**Approved Date:**	12/23/2020

Overview

Medication: [1]	sacituzumab govitecan-hziy
Brand Name:	Trodelvy®
Pharmacologic Category:	Trop-2-directed antibody and topoisomerase inhibitor conjugate
FDA-Approved Indication(s):	1. Locally advanced or metastatic breast cancer a. Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) in adult patients who have received two or more prior systemic therapies, at least one of them for metastatic disease. b. Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting. ► **NEW** indication (FDA-approved 02/03/2023) 2. Locally advanced or metastatic urothelial cancer (mUC) in adult patients who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor. ► This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
How Supplied:	180 mg single-dose vial
Dosage and Administration:	• IV infusion: 10 mg/kg once weekly on days 1 and 8 of 21-day treatment cycle • Continue treatment until disease progression or unacceptable toxicity
Benefit Category:	Medical

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

As new and emerging therapies are rapidly coming to market, oncology treatment recommendations and guidelines are constantly changing. To keep up with these changes, the National Comprehensive Cancer Network (NCCN) publishes guidelines which are developed and updated by 60 individual panels, comprising over 1,660 clinicians and oncology researchers from the 31 NCCN Member Institutions.[7]

The NCCN Clinical Practice Guidelines in Oncology (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 of the guidelines, go online to 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.

The information referenced at the time of this policy writing/revision is from:

- NCCN Guidelines® for Breast Cancer (Version 4.2023 – March 23, 2023).[8]
- NCCN Guidelines® for Bladder Cancer (Version 3.2023 – May 25, 2023).[9]

NCCN Guidelines® Recommendation(s) for sacituzumab govitecan-hziy (Trodelvy®) in breast cancer
(1) Recurrent unresectable (local or regional) or Stage IV (M1) disease A. HR-positive and HER2-negative with visceral crisis [a] or endocrine refractory i. Trodelvy®: [b] Category 1, preferred second-line regimen in patients who are not a candidate for fam-trastuzumab deruxtecan-nxki (Enhertu®) B. HR-negative and HER2-negative (triple-negative breast cancer; TNBC) i. Trodelvy®: [c] Category 1, preferred second-line regimen (regardless of biomarkers)
[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." [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. [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.

NCCN Guidelines® Recommendation(s) for sacituzumab govitecan-hziy (Trodelvy®) in bladder cancer
(1) Locally advanced or metastatic disease (Stage IV) [d, e] A. Subsequent-line systemic therapy i. Trodelvy®: Category 2A, other recommended regimen

[d] Patient should have already received platinum and a checkpoint inhibitor, if eligible..

[e] Appropriate for patients who received a first-line platinum-containing chemotherapy followed by avelumab maintenance therapy.

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. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling.

Locally Advanced or Metastatic 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. Member is 18 years of age or older; **AND**
4. Will not be prescribed in combination with irinotecan or its active metabolite SN-38; **AND**
5. Prescribed by, or in consultation with, an oncologist; **AND**
6. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage prescribed does not align with FDA-approved labeling.

Continuation Therapy (all indications above)

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. 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. The regimen prescribed is within the FDA-approved labeling. If dose or schedule exceeds the FDA-approved labeling, therapy regimen (including dosage) must be supported by clinical practice guidelines (i.e., must be recommended in the NCCN Clinical Practice Guidelines®). Supporting clinical documentation must be provided with any request for which the regimen or dosage 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	Labeler	Dosage	Pkg Size	Pkg Qty	Units/Pkg
55135-0132-01	Immunomedics, Inc.	2.5 mg	1	1	72

Compliance

1. Should conflict exist between this 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 (02/2023). Gilead Sciences, Inc.: Foster City, CA. Available online at www.trodelvyhcp.com. Accessed July 10, 2023.

[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 July 10, 2023.

[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 July 10, 2023.

[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 July 8, 2021.

[5] Shoushtari AN, Hellmann M. Principles of cancer immunotherapy. Shah S, ed. UpToDate. Waltham, MA: UpToDate Inc. www.uptodate.com. Accessed July 10, 2023.

[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). Development and Update of Guidelines. Available online at www.nccn.org. Accessed January 19, 2023.

[8] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer (v.4.2022 – June 21, 2022). Accessed June 22, 2022. 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 of the guidelines, go online to NCCN.org.

[9] Referenced from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer (v.2.2022 – May 20, 2022). Accessed July 7, 2022. 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 of the guidelines, go online to NCCN.org.

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
	CAC		
Signature			

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
Signature William (Bill) Jagiello, DO			

Criteria Change History *(continued)*

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
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
07/16/2021	CAC	Annual review.	3
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
04/16/2021	CAC	Implementation of new formatting. Added new indication.	2
Signature William (Bill) Jagiello, DO			
Change Date	**Changed By**	**Description of Change**	**Version**
01/15/2021	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee