Clinical Policy Title:	sacituzumab govitecan-hziy
Policy Number:	RxA.634
Drug(s) Applied:	Trodelvy®
Original Policy Date:	09/14/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of business

Background

Trodelvy® is a Trop-2-directed antibody and topoisomerase inhibitor conjugate indicated for the treatment of adult patients with:

- Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, at least one of them for metastatic disease.
- Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PDL1) inhibitor.[a]

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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
sacituzumab govitecan-hziy (Trodelvy®)	metastatic triple-negative breast cancer (mTNBC)	10 mg/kg intravenously once weekly on days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity.	10 mg/kg
	Locally advanced or metastatic urothelial cancer (mUC)	10 mg/kg once weekly on days 1 and 8 of continuous 21-day treatment cycles until disease progression or unacceptable toxicity.	10 mg/kg

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Metastatic Triple-Negative Breast Cancer

1. Diagnosis of metastatic triple-negative breast cancer (mTNBC);
2. Prescribed by or in consultation with an oncologist;
3. Member is ≥ 18 years of age;
4. Received two or more prior systemic therapies, at least one of them for metastatic disease;
5. ECOG performance status of 0 or 1;
6. Dose does not exceed 10 mg/kg.

Approval Duration
Commercial: 56 days
Medicaid: 56 days

B. Bladder/Urothelial Cancer (must meet all):

1. Diagnosis of locally advanced or metastatic urothelial cancer;
2. Prescribed by or in consultation with an oncologist;
3. Member is ≥ 18 years of age;
4. Member has previously received a platinum-containing chemotherapy (cisplatin, carboplatin and oxaliplatin) and PD-1 and PD-L1 inhibitor (see Appendix D);
5. Trodelvy® is prescribed as a single agent for subsequent line systemic therapy;
6. Request meets one of the following (a or b):
   a. Dose does not exceed 10 mg/Kg;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 56 days
Medicaid: 56 days

II. Continued Therapy Approval

A. Metastatic Triple-Negative Breast Cancer (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. Dose does not exceed 10 mg/kg.

Approval Duration
Commercial: 56 days
Medicaid: 56 days

B. Bladder/Urothelial Cancer (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 10 mg/Kg;

b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 56 days
Medicaid: 56 days

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
mTNBC: metastatic triple-negative breast cancer
mUC: metastatic Urothelial Cancer
PD-1: programmed death receptor-1
PDL1: programmed death-ligand 1
GU: genitourinary

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Daily Dose	Dose Limit/Maximum Dose
fluorouracil	500 mg/m^2 or 600 mg/m^2 intravenously on days 1 and 8, as a component of a cyclophosphamide-based multidrug regimen, every 28 days for 6 cycles	See dosing regimen
epirubicin (Ellence®)	75 mg/m^2 intravenously on day 1 in combination with cyclophosphamide 600 mg/m^2 intravenously on day 1, every 3 weeks for 6 cycles 50 mg/m^2 intravenously on days 1 and 8 in combination with cyclophosphamide 400 mg/m^2 intravenously on days 1 and 8, plus fluorouracil 500 mg/m^2 intravenously on days 1 and 8, every 3 to 4 weeks for 6 to 9 cycles	See dosing regimen
cyclophosphamide IV	600 mg/m^2 intravenously on day 1 in combination with epirubicin 75 mg/m^2 intravenously on day 1, every 3 weeks for 6 cycles 400 mg/m^2 intravenously on days 1 and 8 in combination with epirubicin 50 mg/m^2 intravenously on days 1 and 8, plus fluorouracil 500 mg/m^2	See dosing regimen

Drug Name	Daily Dose	Dose Limit/Maximum Dose
	intravenously on days 1 and 8, every 3 to 4 weeks for 6 to 9 cycles	
paclitaxel (Abraxane®)	100 mg/m^2 intravenously over 30 minutes on days 1, 8, and 15, in combination with atezolizumab 840 mg intravenously over 60 minutes on days 1 and 15, repeated every 28 days until disease progression or unacceptable toxicity	See dosing regimen
Tecentriq®	840 mg intravenously over 60 minutes on days 1 and 15, followed by nab-paclitaxel (100 mg/m^2 intravenously over 30 minutes on days 1, 8, and 15), repeated every 28 days until disease progression or unacceptable toxicity	See dosing regimen
Padcev®	**mUC** 1.25 mg/kg on days 1, 8, and 15 every 28 days until disease progression or unacceptable toxicity	See dosing regimen

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Severe hypersensitivity reaction to Trodelvy®.

- Boxed Warning(s):
  - Severe Neutropenia - 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 patients with febrile neutropenia without delay.
  - Severe Diarrhea – 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 Trodelvy® until resolved to ≤ Grade 1 and reduce subsequent doses.

APPENDIX D: General Information

- Triple-negative breast cancer (TNBC) tumors do not carry receptors for estrogen, progesterone, or human epidermal growth factor (HER2). It is a more aggressive form of breast cancer that is harder to treat and for which there are fewer approved medicines.
- Do not substitute Trodelvy® for or use with other drugs containing irinotecan or its active metabolite SN-

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- PD-1 inhibitor: E.g., Keytruda®, Libtayo®, Opdivo®.
- PD-L1 inhibitor: E.g., Bavencio®, Imfinzi®.

References

1. Trodelvy® Prescribing Information. Morris Plains, NJ: Immunomedics; Issued April 2021. Available at https://www.trodelvy.com/. Accessed June 24, 2021.
2. FDA. https://www.fda.gov/news-events/press-announcements/fda-approves-new-therapy-triple-negative-breast-cancer-has-spread-not-responded-other-treatments. Accessed June 24, 2021.
3. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Accessed June 24, 2021.
4. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed June 24, 2021.
5. National Comprehensive Cancer Network Drugs Guidelines. Bladder Cancer; Version 3.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf . Accessed June 24, 2021.
6. National Comprehensive Cancer Network Drugs Guidelines. Breast Cancer; Version 4.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf . Accessed on June 24, 2021.
7. Enfortumab vedotin. Dosing. Lexicomp. Wolters Kluwer. Hudson, Oh. Available at https://online.lexi.com . Accessed on June 24, 2021.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	9/14/2020	09/14/2020
Policy was reviewed: 1. Background was updated to include "Unresectable locally advanced or…", "Locally advanced or metastatic urothelial cancer (mUC)...", and "This indication is approved under accelerated approval based on tumor response…". 2. Dosing Information was updated to include new indication "Locally advanced or metastatic urothelial cancer (mUC)…" and its respective dosing regimen and maximum dose information. 3. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy. 4. Initial Approval Criteria I.B was updated to include new indication "Bladder/Urothelial Cancer". 5. Initial Approval Criteria and Continued Therapy Approval Criteria approval durations were updated from "8 weeks" to "56 days" for all indications.	06/24/2021	09/14/2021

6. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 7. Continued Therapy Approval Criteria II.B was updated to include new indication“Bladder/Urothelial Cancer”. 8. Appendix A was updated to include abbreviations mUC, PD-1, PDL1 and GU. 9. Appendix B: Therapeutic alternative verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance..". 10. Appendix B: Therapeutic Alternatives was updated to include brand-name drug“Padcev®” and its respective daily dose and maximum dose. 11. Appendix B was updated to remove generic drug "atezolizumab" as it is only available in brand form. 12. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name®...”. 13. Appendix B dosing regimen for "epirubicin (Ellence®)"and "cyclophosphamide IV" was updated from cyclophosphamide 500 mg^2 to “400 mg^2“ and fluorouracil 400 mg^2 to “500 mg^2”; also updated from “depending on patient recovery” to “for 6 to 9 cycles”. 14. Appendix B was updated to remove brand name Adrucil for fluorouracil as it is discontinued. 15. Appendix D was updated to include “Do not substitute Trodelvy®..”. 16. References were reviewed and updated.		