# Sacituzumab govitecan-hziy (TRODELVY) in Breast Cancer
# National Drug Monograph
# August 2024

**VA Pharmacy Benefits Management Services and National Formulary Committee**

*The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. Updates will be made if new clinical data warrant additional formulary discussion. The Product Information or other resources should be consulted for detailed and most current drug information.*

**FDA APPROVAL INFORMATION**

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| **Description / MOA** | Antibody drug conjugate consisting of a humanized antitrophoblast cell-surface antigen 2 (Trop-2) monoclonal antibody with topoisomerase 1 inhibitor, SN-38, through a cleavable linker; After sacituzumab govitecan binds to Trop-2, it is internalized so that SN-38 can be released intracellularly. |
| **Indication Under Review**[1] | • Unresectable locally advanced (LA) or metastatic triple-negative breast cancer (mTNBC) in patients who have received ≥ 2 prior therapies, at least one being for metastatic disease;<br>• Unresectable locally advanced or metastatic HR-positive, HER2-negative (IHC 0, IHC 1+ or IHC 2+/ISH-) breast cancer s/p endocrine-based therapy and ≥ 2 additional systemic therapies in the metastatic setting |
| **Dosage Regimen** | Sacituzumab 10mg/kg once weekly on Days 1 and 8 of a 21-day cycle until progression or unacceptable toxicity |
| **Dosage Forms Under Review** | 180 mg lyophilized power for reconstitution in SDV for injection |

**EFFICACY CONSIDERATIONS**

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| **Trial** | **ASCENT NCT03574455** |
| **Design** | Randomized, phase 3 |
| **Population** | N=468;<br>mTNBC, relapsed or refractory to ≥ 2 standard chemotherapy regimens |
| **Demographics** | mAge 54 yrs; 99.6% female; 79% white; 12% black<br>100% prev rec'd taxanes; 29% rec'd prior PD-1/PD-L1 therapy; ECOG 0-1; 12% stable brain mets |
| **Intervention** | Sacituzumab govitecan 10mg/kg IV on days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity |
| **Comparator** | Clinician choice (eribulin, vinorelbine, capecitabine or gemcitabine) |
| **Results** | **mPFS 5.6 vs. 1.7 mos; HR 0.41; 95% CI 0.32-0.52**<br>mOS 12.1 vs. 6.7 mos; HR 0.48; 95% CI 0.38-0.59<br>ORR 35 vs. 5%<br><br>mPFS and mOS were longer with sacituzumab govitecan than with single agent eribulin, vinorelbine, capecitabine or gemcitabine. |
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| **Trial** | **TROPICS-02 NCT03901339** |
| **Design** | Randomized, open-label, multicenter, phase 3 |
| **Population** | N=543; HR+, HER2-, locally recurrent, inoperable or mBC s/p ≥ 1 prior endocrine therapy, a taxane, a CDK4/6 inhibitor (any setting) and ≥ 2 prior chemo regimens for metastatic disease |
| **Demographics** | mAge 56 years (49-65); median 3 prior LOT (2-3) |
| **Intervention** | Sacituzumab govitecan 10mg/kg IV on days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity |
| **Comparator** | Chemotherapy (eribulin, vinorelbine, capecitabine or gemcitabine) |
| **Results** | **Primary: mPFS 5.5 vs. 4.0 mos; HR 0.66; 95% CI 0.53-0.83; p=0.0003**<br>Secondary: OS, ORR, Patient-Related Outcomes<br>At median 12.5 mos follow-up and 10.7 mos:<br>mOS 14.4 vs. 11.2 mos; HR 0.79; 95% CI 0.65-0.96; p=0.020<br>ORR 21 vs. 14%; odds ratio 1.63; 95% CI 1.03-2.56; p=0.035<br>Time to deterioration global health status, QoL 2.2 vs. 1.4 mos; HR 0.73; p=0.0059<br><br>A modest PFS-benefit was noted; mOS benefit of 3.2 months was demonstrated with sacituzumab; point estimates favor sacituzumab in all subgroups |

**SAFETY CONSIDERATIONS**

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| **Boxed Warnings** | Severe or life-threatening neutropenia.<br>Severe diarrhea. |
| **Contraindications** | Severe hypersensitivity to sacituzumab govitecan |
| **Other Warnings** | Hypersensitivity and infusion-related reactions<br>Nausea and vomiting<br>Patients homozygous for UGT1A1*28 allele are at increased risk for neutropenia, FN and anemia<br>Embryo-fetal toxicity |
| **Top 5 AEs (≥ 25%)** | Leukopenia, Neutropenia, anemia, diarrhea, nausea |
| **Drug Interactions** | Avoid concomitant use of UGT1A1 inhibitors or inducers |
| **ASCENT (≥ gr 3)** | Neutropenia: 51 vs. 33%; leukopenia 10 vs. 5%; diarrhea 10 vs. < 1%; anemia 8 vs. 5%; FN 6 vs. 2% |
| **TROPICS-02** | Neutropenia 51 vs. 39%; diarrhea 10 vs. 1%; FN 5 vs. 4% |

**PLACE IN THERAPY**

| DRUG/VANF/CFU | FDA | VA Pathway | GUIDELINES |
|---|---|---|---|
| Sacituzumab<br>VANF – TBD<br>CFU - TBD | • LA or mTNBC who rec'd ≥ 2 prior therapies, ≥ 1 in metastatic setting<br>• LS or MBC, HR+, HER2- (IHC 0, IHC 1+ or IHC 2+/ISH-) who rec'd ET plus ≥ 2 therapies in metastatic setting | VA Breast Cancer – Stage IV TNBC Pathway<br>• rec'd ≥ 2 prior LOT<br><br>VA Breast Cancer -Stage IV ER+ or PR+/HER2- Pathway<br>• s/p endocrine therapy and who rec'd ≥ 2 prior LOT or 1 prior LOT for MBC if adjuvant tx given w/in prior 12 months | NCCN recurrent unresectable or Stage IV disease<br>• 2L or later in TNBC in patients who rec'd > 1 LOT in the metastatic setting (category 1, preferred)<br>• 2L or later in HR+, HER2- LA or MBC after prior endocrine therapy, a CDK4/6 inhibitor and > 2 prior LOT (one of which was a taxane), and at least one line given in the metastatic setting (category 1, preferred)<br>• Other options, in both settings: doxorubicin, liposomal doxorubicin, paclitaxel, capecitabine, gemcitabine, vinorelbine, eribulin (category 2A) |

**VHA PLACE IN THERAPY**

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| **Potential Use in VHA** | 1. For unresectable, LA or mTNBC s/p ≥ 2 systemic therapies<br>2. For inoperable, LA or mBC, HR+, HER2-negative (defined as IHC 0, IHC 1+ or IHC 2+/ISH-) s/p endocrine therapy (that included a CDK 4/6 inhibitor) and ≥ 2 systemic therapies (including a taxane) in the metastatic setting<br>3. Significant toxicity profile (risk of neutropenia, diarrhea, nausea and vomiting) should be considered in context of the patient and ensure appropriate pre-medications, pertinent labs and monitoring are performed.<br>4. Of note, those known with reduced UGT1A1 activity (homozygous for UGT1A1*28 allele) are at increased risk of neutropenia, febrile neutropenia and anemia |

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Contact person: Berni Heron, Pharm.D., BCOP, National PBM Clinical Pharmacy Program Manager, Formulary Management, VA Pharmacy Benefits Management Services (12PBM)

**References**


1 TRODELVY (Sacituzumab govitecan-hziy) formulation [prescribing information online]. Foster City, CA: Gilead Sciences. February 2023. Available at: 761115s035lbl.pdf (fda.gov) . Accessed July 5, 2024.

2 Bardia A, Hurvitz SA, Tolaney SM, et al. for the ASCENT Investigators. Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. N Engl J Med 2021: 384: 1529-1541.

3 Rugo HS, Bardia A, Marme F, et al. Overall survival with Sacituzumab govitecan in hormone receptor-positive and human epidermal growth factor receptor 2-negative metastatic breast cancer (TROPiCS-02): a randomized, open-label, multicenter, phase 3 trial. Lancet 2023; 402: 1423-1433.