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# Trodelvy® (sacituzumab govitecan-hziy) Use in Patients With Hepatic Impairment

This document is in response to your request for information regarding the use of Trodelvy® (sacituzumab govitecan-hziy [SG]) as monotherapy in patients with hepatic impairment, including patients with hepatic impairment due to liver metastases.

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**The full indication, important safety information, and boxed warnings for neutropenia and diarrhea are available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.**

## Summary


Relevant Product Labeling[1]

Warnings and Precautions: Patients homozygous for *the uridine diphosphate-glucuronosyl transferase 1A1* (*UGT1A1) *28* allele are at increased risk for neutropenia, febrile neutropenia, and anemia; and may be at increased risk for other adverse reactions when treated with SG.

Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue SG based on clinical assessment of the onset, duration, and severity of the observed adverse reactions in patients with evidence of acute early-onset or unusually severe adverse reactions, which may indicate reduced UGT1A1 enzyme activity.

Use in Specific Populations: The safety of SG in patients with moderate (total bilirubin >1.5 to 3 × upper limit of normal [ULN]) or severe (total bilirubin >3 × ULN) hepatic impairment has not been established. SG has not been evaluated in patients with AST or ALT >3 × ULN without liver metastases, or AST or ALT >5 × ULN with liver metastases.

PK in Patients With Hepatic Impairment: The exposure of SG for patients with mild hepatic impairment (total bilirubin ≤ULN with AST >ULN, or bilirubin >1 to ≤1.5 × ULN with any AST) is within range of that of patients with normal hepatic function (total bilirubin and AST <ULN).

SG and free SN-38 exposures are unknown in patients with moderate (total bilirubin >1.5 to 3 × ULN) or severe (total bilirubin >3 × ULN) hepatic impairment.

PopPK Analysis of SG in Patients With Mild Hepatic Impairment

A population pharmacokinetic (PopPK) analysis assessed exposure to SG, free active metabolite of irinotecan (SN-38), and total antibody (tAB) across 3 studies: ASCENT (in metastatic triple-negative breast cancer [mTNBC]), TROPiCS-02 (in hormone receptor-positive/human epidermal growth factor receptor 2-negative [HR+/HER2-] metastatic breast cancer [mBC]), and IMMU-132-01 (in metastatic epithelial cancer).

Exposure to the 3 analytes in patients with mild hepatic impairment (bilirubin >ULN to 1.5 × ULN or AST >ULN [n=257]) relative to those with normal hepatic function (bilirubin and AST ≤ULN [n=525]) were evaluated.[2]

- SG, SN-38, and tAB exposures were similar between patients with mild hepatic impairment and those with normal hepatic function.[2]
- Predicted exposure (90% CI) in the first cycle in patients with mild hepatic impairment relative to normal hepatic function were as follows:
  - 0.976 (0.958–0.994) and 0.983 (0.97–0.996) for the area under the curve (AUC) and maximum concentration ($C_{max}$) with SG, respectively.[2]
  - 0.915 (0.848–0.982) and 0.941 (0.887–0.996) for AUC and $C_{max}$ with SN-38, respectively.[3]
  - 0.931 (0.901–0.962) and 0.961 (0.934–0.989) for AUC and $C_{max}$ with tAB, respectively.[3]

### Phase 3 Clinical Studies of SG Monotherapy: Inclusion Criteria for Hepatic Function

Across five Gilead-sponsored, phase 3 studies of SG monotherapy with results available (ASCENT, ASCENT-03, EVOKE-01, TROPiCS-02, and TROPiCS-04), all patients, including those with liver metastases, were required to have adequate hepatic function.[4-8]

## PopPK Analysis of SG in Patients With Mild Hepatic Impairment

A PopPK analysis using data from ASCENT (253 patients with mTNBC in a second-line or later setting), TROPiCS-02 (260 patients with pretreated HR+/HER2- mBC), and IMMU-132-01 (276 patients with metastatic epithelial cancer) evaluated the impact of clinical covariates on SG exposure. SG exposure was similar in patients with mild hepatic impairment compared to patients with normal hepatic function (Table 1 and Table 2).[2]

**Table 1. PopPK Analysis: Categorical Covariate Relationship to SG Exposure in the First Cycle Relative to Reference[2]**

| Covariate (Reference) | Covariate | Predicted SG Exposure (90% CI) | |
|---|---|---|---|
| | | AUC | $C_{max}$ |
| Hepatic impairment relative to normal (bilirubin and AST ≤ULN; n=525) | Mild hepatic impairment (bilirubin >ULN to 1.5 × ULN or AST >ULN; n=257) | 0.976 (0.958–0.994) | 0.983 (0.97–0.996) |

**Table 2. PopPK Analysis: Continuous Covariate Relationships to SG Exposure in First Cycle Relative to Reference[2]**

| Covariate (Reference) | Percentile | Predicted SG Exposure (90% CI) | |
|---|---|---|---|
| | | AUC | $C_{max}$ |
| AST (27.5 IU/L) | 95$^{th}$ (124 IU/L) | 0.951 (0.925–0.977) | 0.984 (0.965–1) |
| | 5$^{th}$ (14 IU/L) | 1.01 (0.994–1.02) | 1 (0.993–1.01) |
| ALT (21.6 IU/L) | 95$^{th}$ (88.3 IU/L) | 0.985 (0.963–1.01) | 0.996 (0.981–1.01) |
| | 5$^{th}$ (8.84 IU/L) | 1 (0.99–1.02) | 1 (0.991–1.01) |
| Albumin (39 g/L) | 95$^{th}$ (45 g/L) | 1.06 (1.04–1.08) | 1 (0.988–1.01) |
| | 5$^{th}$ (30 g/L) | 0.912 (0.892–0.932) | 0.998 (0.983–1.01) |
| ALP (95 IU/L) | 95$^{th}$ (339 IU/L) | 0.959 (0.939–0.979) | 0.986 (0.971–1) |
| | 5$^{th}$ (51.4 IU/L) | 1.01 (0.995–1.02) | 1 (0.994–1.01) |

| Covariate (Reference) | Percentile | Predicted SG Exposure (90% CI) | |
|---|---|---|---|
| | | AUC | $C_{max}$ |
| Bilirubin (0.4 mg/dL) | 95th (1 mg/dL) | 0.986 (0.965–1.01) | 1 (0.984–1.02) |
| | 5th (0.2 mg/dL) | 1 (0.989–1.02) | 1 (0.989–1.01) |

Abbreviation: ALP=alkaline phosphatase.

A bootstrap analysis confirmed final model estimates for SG, free SN-38, and tAB.[2,3] The correlation between mild hepatic impairment and exposures to free SN-38 and tAB are presented in Table 3, Table 4, and Table 5.[3]

**Table 3. PopPK Analysis: Categorical Covariate Relationship to Free SN-38 and tAB Exposure in the First Cycle Relative to Reference[3]**

| | Covariate (Reference) | Covariate | Predicted Exposure (90% CI) | |
|---|---|---|---|---|
| | | | AUC | $C_{max}$ |
| SN-38 | Hepatic impairment relative to normal (bilirubin and AST ≤ULN; n=514) | Mild hepatic impairment (bilirubin >ULN to 1.5 × ULN or AST >ULN; n=253) | 0.915 (0.848–0.982) | 0.941 (0.887–0.996) |
| tAB | Hepatic impairment relative to normal (bilirubin and AST ≤ULN; n=524) | Mild hepatic impairment (bilirubin >ULN to 1.5 × ULN or AST >ULN; n=256) | 0.931 (0.901–0.962) | 0.961 (0.934–0.989) |

**Table 4. PopPK Analysis: Continuous Covariate Relationships to Free SN-38 Exposure in First Cycle Relative to Reference[3]**

| Covariate (Reference) | Percentile | Predicted SG Exposure (90% CI) | |
|---|---|---|---|
| | | AUC | $C_{max}$ |
| AST (27.8 IU/L) | 95th (124 IU/L) | 0.895 (0.797–0.992) | 0.938 (0.858–1.02) |
| | 5th (14 IU/L) | 1.02 (0.966–1.06) | 1.01 (0.969–1.05) |
| ALT (22 IU/L) | 95th (88.9 IU/L) | 0.994 (0.909–1.08) | 1 (0.934–1.07) |
| | 5th (8.46 IU/L) | 1 (0.952–1.05) | 0.999 (0.959–1.04) |
| Albumin (39 g/L) | 95th (45 g/L) | 1.05 (0.98–1.12) | 1.01 (0.955–1.07) |
| | 5th (30 g/L) | 0.927 (0.848–1.01) | 0.983 (0.919–1.05) |
| ALP (95 IU/L) | 95th (338 IU/L) | 0.917 (0.84–0.995) | 0.948 (0.885–1.01) |
| | 5th (51.6 IU/L) | 1.01 (0.967–1.06) | 1.01 (0.971–1.05) |
| Bilirubin (0.4 mg/dL) | 95th (1 mg/dL) | 0.978 (0.896–1.06) | 0.999 (0.933–1.07) |
| | 5th (0.2 mg/dL) | 1.01 (0.95–1.06) | 1 (0.954–1.05) |

**Table 5. PopPK Analysis: Continuous Covariate Relationships to tAB Exposure in First Cycle Relative to Reference[3]**

| Covariate (Reference) | Percentile | Predicted SG Exposure (90% CI) | |
|---|---|---|---|
| | | AUC | $C_{max}$ |
| AST (27.5 IU/L) | 95th (123 IU/L) | 0.885 (0.84–0.929) | 0.935 (0.896–0.974) |
| | 5th (14 IU/L) | 1.02 (0.994–1.04) | 1.01 (0.99–1.03) |
| ALT (21.6 IU/L) | 95th (87.8 IU/L) | 0.973 (0.934–1.01) | 0.991 (0.957–1.02) |
| | 5th (8.84 IU/L) | 1.01 (0.983–1.03) | 1 (0.982–1.02) |
| Albumin (39 g/L) | 95th (45 g/L) | 1.08 (1.05–1.11) | 1.05 (1.02–1.07) |
| | 5th (30 g/L) | 0.881 (0.846–0.915) | 0.928 (0.897–0.959) |
| ALP (95 IU/L) | 95th (334 IU/L) | 0.91 (0.876–0.944) | 0.934 (0.904–0.964) |
| | 5th (51.3 IU/L) | 1.02 (0.995–1.04) | 1.01 (0.993–1.03) |
| Bilirubin (0.4 mg/dL) | 95th (1 mg/dL) | 0.967 (0.929–1) | 0.969 (0.936–1) |
| | 5th (0.2 mg/dL) | 1.01 (0.985–1.04) | 1.01 (0.987–1.03) |

# Phase 3 Clinical Studies of SG Monotherapy: Inclusion Criteria for Hepatic Function[4-8]

Across five Gilead-sponsored, phase 3 studies of SG monotherapy with results available (ASCENT, ASCENT-03, EVOKE-01, TROPiCS-02, and TROPiCS-04), all patients, including those with liver metastases, were required to have adequate hepatic function. Inclusion criteria regarding hepatic function are summarized in Table 6.

**Table 6. SG Studies: Definitions of Adequate Hepatic Function[4-8]**

| Hepatic Function Test | Value |
|---|---|
| Bilirubin | ≤1.5 × ULN[a] |
| AST and ALT | ≤2.5 × ULN |
| AST and ALT in patients with known liver metastases | ≤5 × ULN |
| Serum albumin | ≥3 g/dL[b] |
| ALP[c] | ≤5 × ULN |

[a]In TROPiCS-02, patients with documented Gilbert's syndrome were required to have a bilirubin level ≤3 × ULN.
[b]In EVOKE-01, serum albumin was required to be >3 g/dL.
[c]Only required in TROPiCS-02 study. If a patient had known bone metastases, liver-specific ALP levels were separated from the total ALP level and were used to assess liver function instead of total ALP.

# Ongoing Study

A phase 1, open-label, dose-escalation study (NCT04617522) is evaluating the safety and dosing of SG (administered on Days 1 and 8 at escalating doses of 5, 7.5, and 10 mg/kg) in patients with advanced or metastatic solid tumors and moderate hepatic impairment (defined as a bilirubin level >1.5 to ≤3 × ULN and any AST level). The estimated enrollment is 30 patients.

# References

1. TRODELVY® Gilead Sciences Inc. Trodelvy (sacituzumab govitecan-hziy) for injection, for intravenous use. U.S. Prescribing Information. Foster City, CA.
2. Sathe AG, Jones AK, Diderichsen PM, et al. Sacituzumab govitecan population pharmacokinetics: updated analyses using HR+/HER2− metastatic breast cancer data from the phase 3 TROPiCS-02 trial. *Clinical and Translational Science.* 2025;18(7):e70291.
3. Sathe AG, Jones AK, Diderichsen PM, et al. Sacituzumab govitecan population pharmacokinetics: updated analyses using HR+/HER2− metastatic breast cancer data from the phase 3 TROPiCS-02 trial [Supplement]. *Clinical and Translational Science.* 2025;18(7):1-41.
4. Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer [Supplementary Appendix]. *N Engl J Med.* 2021;384(16):1529-1541.
5. Cortés J, Punie K, Barrios C, et al. Sacituzumab govitecan in untreated, advanced triple-negative breast cancer [Supplementary Appendix]. *N Engl J Med.* 2025;393(19):1912-1925.
6. Paz-Ares L, Juan-Vidal O, Mountzios GS, et al. Sacituzumab govitecan versus docetaxel for previously treated advanced or metastatic non–small cell lung cancer: the randomized, open-label phase III EVOKE-01 study [Data supplement]. *J Clin Oncol.* 2024:1-13.
7. Rugo HS, Bardia A, Marme F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer [Protocol]. *J Clin Oncol.* 2022;40(29):3365-3376.

8. Powles T, Tagawa S, Vulsteke C, et al. Sacituzumab govitecan in advanced urothelial carcinoma: TROPiCS-04, a phase III randomized trial [Supplementary Appendix]. *Annals of Oncology.* 2025;36(5):561-571.

# Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Trodelvy US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/oncology/trodelvy/trodelvy_pi.

# Follow-Up

For any additional questions, please contact Trodelvy Medical Information at:

☎ 1-888-983-4668 or 🖱 www.askgileadmedical.com

# Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or 🖱 www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🖱 www.accessdata.fda.gov/scripts/medwatch

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