

Drug Monograph

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A - Drug Name

sacituzumab govitecan

COMMON TRADE NAME(S): Trodelvy®

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B - Mechanism of Action and Pharmacokinetics

Sacituzumab govitecan is a Trop-2-directed antibody-drug conjugate (ADC). It is composed of a humanized antibody (sacituzumab) that is covalently attached by a linker (CL2A) to SN-38, a topoisomerase I inhibitor and an active metabolite of irinotecan. After binding to Trop-2-expressing cancer cells, the ADC is internalized. SN-38 is subsequently released via hydrolysis of the linker, leading to DNA damage, apoptosis, and cell death.

Metabolism

No metabolism studies with sacituzumab govitecan have been conducted. The antibody moiety is expected to be catabolized to amino acids. SN-38 is metabolized via UGT1A1.

Inactive metabolites Yes

Elimination

Half-life 15 hours (sacituzumab govitecan); 20 hours (SN-38)

Feces Major route (for SN-38; based on irinotecan elimination)

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C - Indications and Status**Health Canada Approvals:**

- Breast cancer

Refer to the product monograph for a full list and details of approved indications.

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D - Adverse Effects

Emetogenic Potential: Moderate (+ NK-1 RA)

Extravasation Potential: None

The following adverse events were reported in $\geq 5\%$ of patients treated with sacituzumab govitecan in a Phase 3 study of patients with unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who received at least two prior treatments. Other severe or life-threatening adverse effects may also be included.

ORGAN SITE	SIDE EFFECT* (%)	ONSET**
Cardiovascular	QT interval prolonged (5%)	E
Dermatological	Alopecia (47%)	D L
	Rash (12%)	E
Gastrointestinal	Abdominal pain (21%)	E
	Anorexia, weight loss (28%)	E
	Constipation (37%)	E
	Diarrhea (65%) (11% severe)	I E
	Mucositis (10%)	E
	Nausea, vomiting (62%) (3% severe)	I E
General	Edema - limbs (9%)	E
	Fatigue (52%) (4% severe)	E
Hematological	Myelosuppression \pm infection, bleeding (64%) (52% severe)	E
Hepatobiliary	\uparrow LFTs (11%)	E

Hypersensitivity	Hypersensitivity (34%) (1% severe)	I E
	Infusion related reaction (<1%)	I
Metabolic / Endocrine	Abnormal electrolyte(s) (16%) (↓ K, ↓ Mg, ↓ PO4, ↓ Ca, ↓ Na)	E
	Hyperglycemia (7%)	E
Musculoskeletal	Musculoskeletal pain (16%)	E
Nervous System	Dizziness (10%)	E
	Dysgeusia (9%)	E
	Headache (18%)	I E
	Insomnia (11%)	E
Respiratory	Cough, dyspnea (24%)	E

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
 "*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
 D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for sacituzumab govitecan include diarrhea, myelosuppression ± infection, nausea, vomiting, fatigue, alopecia, constipation, hypersensitivity, anorexia, weight loss, cough, dyspnea and abdominal pain.

Diarrhea may be severe with sacituzumab govitecan. This may be due to either early cholinergic syndrome or delayed SN-38-related diarrhea. Patients should be monitored, provided with fluid and electrolytes as required, and evaluated for infectious causes at the onset. If diarrhea is non-infectious, loperamide 4 mg should be initiated, followed by 2 mg with every episode of diarrhea (up to a maximum of 16 mg daily). Discontinue loperamide 12 hours after diarrhea resolves. Similar to irinotecan, patients with severe cholinergic symptoms (e.g. abdominal cramping, salivation, diarrhea) should receive appropriate premedication (e.g. atropine) for subsequent treatments.

Severe neutropenia, including fatal events, has been reported with sacituzumab govitecan. Grade 3-4 neutropenia occurred commonly in clinical trials (51% of patients); febrile neutropenia was reported in 6% of patients. Dose interruption and/or appropriate management including initiation of supportive treatment (e.g. G-CSF, anti-infectives) may be required (see Dosing section). Patients with **known reduced UGT1A1 activity** (e.g. Gilbert's syndrome or homozygous for the UGT1A1*28 allele) may have an increased risk for neutropenia, febrile neutropenia, anemia, or other adverse effects and should be closely monitored. Acute early-onset or unusually severe adverse reactions may indicate reduced UGT1A1 enzyme activity.

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E - Dosing

Refer to protocol by which the patient is being treated.

Screen for hepatitis B virus in all cancer patients starting systemic treatment. Refer to the [hepatitis B virus screening and management](#) guideline.

Patients with **known reduced UGT1A1 activity** (e.g. Gilbert's syndrome or homozygous for the UGT1A1*28 allele) may have an increased risk for neutropenia, febrile neutropenia, anemia, or other adverse effects and should be closely monitored. Acute early-onset or unusually severe adverse reactions may indicate reduced UGT1A1 enzyme activity. Hold or discontinue sacituzumab govitecan as clinically indicated.

Do **NOT** substitute sacituzumab govitecan for or use with other drugs containing irinotecan or its active metabolite, SN-38.

Pre-medications:

- **Prophylaxis for infusion reaction**
 - Administer antipyretics, H1 and H2 blockers prior to infusion.
- **Prophylaxis for cholinergic response**
 - Patients with excessive cholinergic response (e.g., abdominal cramping, diarrhea, salivation) can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Other Supportive Care:

- For non-infectious diarrhea, promptly initiate loperamide 4 mg, followed by 2 mg with every episode of diarrhea (up to a maximum of 16 mg daily). Discontinue loperamide 12 hours after diarrhea resolves.

Adults:

Intravenous: 10 mg/kg Days 1, 8; q21days

Dosage with Toxicity:

Dose Level	Sacituzumab Dose (mg/kg)
0	10
-1	7.5
-2	5
-3	Discontinue

Hematologic Toxicity:

Toxicity	Action
Grade 3 neutropenia	Hold* until resolved. If treatment delayed by 1 week, resume at same dose, consider G-CSF support. If treatment delayed by 2-3 weeks, resume at 1 dose level ↓ and administer G-CSF. Discontinue if 3rd occurrence.
Grade 4 neutropenia	Hold* until resolved. If lasts ≥ 7 days or treatment delayed by 2-3 weeks, resume at 1 dose level ↓ and administer G-CSF. Discontinue if 3rd occurrence.
Febrile neutropenia	Hold* until resolved. Resume at 1 dose level ↓ and administer G-CSF. Discontinue if 3rd occurrence.
Other Grade 3 or 4 hematologic toxicity (e.g., anemia and thrombocytopenia)	Hold* until resolved. If treatment delayed by 2-3 weeks, resume at 1 dose level ↓. Discontinue if 3rd occurrence.

*On **day 1**, do not resume until ANC ≥ 1.5 x 10⁹/L, Platelets ≥ 75 x 10⁹/L, Hgb ≥ 100 g/L, and non-hematologic toxicities recover to ≤ Grade 1.

On **day 8**, do not resume until ANC ≥ 1 x 10⁹/L, Platelets ≥ 75 x 10⁹/L, Hgb ≥ 100 g/L, and non-hematologic toxicities recover to ≤ Grade 1.

Discontinue sacituzumab govitecan if dose is held for > 3 weeks.

Non-hematologic Toxicity:

Toxicity	Action
Grade 3 or 4 nausea / vomiting / diarrhea**	Hold* until resolved. Resume at 1 dose level ↓. Discontinue if 3rd occurrence.
Other Grade 3 non-hematologic toxicity (persisting > 48h despite medical management or requiring dose hold for 2-3 weeks)	Hold* until resolved. Resume at 1 dose level ↓. Discontinue if 3rd occurrence.
Other Grade 4 non-hematologic toxicity	

*On **day 1**, do not resume until ANC $\geq 1.5 \times 10^9/L$, Platelets $\geq 75 \times 10^9/L$, Hgb ≥ 100 g/L, and non-hematologic toxicities recover to \leq Grade 1.

On **day 8**, do not resume until ANC $\geq 1 \times 10^9/L$, Platelets $\geq 75 \times 10^9/L$, Hgb ≥ 100 g/L, and non-hematologic toxicities recover to \leq Grade 1.

Discontinue sacituzumab govitecan if dose is held for > 3 weeks.

**Not controlled with supportive care (antiemetics or anti-diarrheals).

Management of Infusion-related reactions

Also refer to the CCO guideline for detailed description of [Management of Cancer Medication-Related Infusion Reactions](#).

Grade	Management	Re-challenge
1 or 2	<ul style="list-style-type: none"> Stop or slow the infusion rate. Manage the symptoms. <p>Restart:</p> <ul style="list-style-type: none"> Once symptoms have resolved, restart at slower rate. 	<ul style="list-style-type: none"> Consider rechallenge if appropriate. Add a corticosteroid to other pre-medications.
3 or 4	<ul style="list-style-type: none"> Stop treatment. Aggressively manage symptoms. 	<ul style="list-style-type: none"> Discontinue permanently (do not re-challenge).

Dosage with Hepatic Impairment:

Sacituzumab govitecan exposure in patients with mild hepatic impairment is similar to patients with normal hepatic function.

Bilirubin		AST	Sacituzumab Dose
≤ ULN	and	> ULN	No dose adjustment required.
>1 to 1.5 x ULN	and	Any	
>1.5 to 3.0 × ULN	and	Any	Not studied.
> 3 x ULN	and	Any	Avoid; not studied.

Dosage with Renal Impairment:

Renal elimination contributes minimally to the excretion of SN-38. There are no data on the use of sacituzumab govitecan in patients with severe renal impairment (CrCl 15-29 mL/min), or end-stage renal disease (CrCl < 15 mL/min).

Dosage in the elderly:

No dose adjustment is required in patients ≥ 65 years.

Safety and efficacy were similar between patients ≥ 65 years and younger patients with mTNBC.

In patients with HR-positive/HER2-negative breast cancer, there were higher rates of serious adverse reactions and discontinuation in patients ≥ 65 years compared to younger patients.

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F - Administration Guidelines

Do **NOT** substitute sacituzumab govitecan for or use with other drugs containing irinotecan or its active metabolite, SN-38.

- After reconstitution, dilute in an infusion bag with NS to a concentration of 1.1 to 3.4 mg/mL.
- The infusion bag must be made of polyvinyl chloride, polyolefin (polypropylene and/or polyethylene) or ethylene vinyl acetate to minimize foaming.
- Do not shake. Protect the infusion bag from light.
- Administer as an IV infusion only. Do NOT administer as an IV push or bolus.
- Infuse over 3 hours for the first infusion. If well tolerated, infuse over 1-2 hours for subsequent infusions.
- Observe patients during and for at least 30 minutes after each infusion.
- Do not mix or infuse with other agents.
- Flush IV line with 20 mL of NS at the end of infusion.
- Store unopened vials between 2°C to 8°C in the original carton. Protect from light. Do not freeze.

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G - Special Precautions

Contraindications:

- Patients who are hypersensitive to this drug or any of its components

Other Drug Properties:

- Carcinogenicity: Unknown

Pregnancy and Lactation:

- Mutagenicity: Unknown
- Clastogenicity: Yes
- Genotoxicity: Yes
- Embryotoxicity: Probable
- Teratogenicity: Probable

Sacituzumab govitecan is not recommended for use in pregnancy.

- Adequate contraception should be used by patients who can become pregnant and their partners during treatment, and for at least **6 months** after the last dose.
- Adequate contraception should be used by patients who produce sperm and their partners during treatment, and for at least **3 months** after the last dose.

- Excretion into breast milk: Unknown
Breastfeeding is not recommended during treatment and for **1 month** after the last dose.
- Fertility effects: Probable
Female fertility may be affected.

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H - Interactions

No formal drug interaction studies were conducted with sacituzumab govitecan.

SN-38 (the small molecule moiety of sacituzumab govitecan) is primarily metabolized via UGT1A1. Inhibitors or inducers of CYP3A are not anticipated to impact SN-38 exposure.

AGENT	EFFECT	MECHANISM	MANAGEMENT
UGT1A1 inhibitors (e.g., propofol, ketoconazole, EGFR tyrosine kinase inhibitors)	↑ SN-38 toxicity (theoretical)	↓ metabolism of SN-38	Caution
UGT1A1 inducers (e.g., carbamazepine, phenytoin, rifampicin, protease inhibitors)	↓ SN-38 effect (theoretical)	↑ metabolism of SN-38	Caution

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Refer to the [hepatitis B virus screening and management](#) guideline for monitoring during and after treatment.

Closely monitor for toxicity in patients with **known reduced UGT1A1 activity**, or in patients with acute early-onset or unusually severe adverse reactions that may indicate reduced UGT1A1 enzyme activity.

Recommended Clinical Monitoring

Monitor Type	Monitor Frequency
CBC	Baseline and before each dose
Liver function tests	Baseline and as clinically indicated
Renal function tests	Baseline and as clinically indicated
Electrolytes	Baseline and as clinically indicated (especially in patients with diarrhea)
Clinical toxicity assessment for infection, infusion reaction, diarrhea and other GI effects	At each visit

Grade toxicity using the current [NCI-CTCAE \(Common Terminology Criteria for Adverse Events\) version](#)

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J - Supplementary Public Funding

New Drug Funding Program ([NDFP Website](#))

- Sacituzumab Govitecan - Unresectable Locally Advanced or Metastatic Triple Negative Breast Cancer

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K - References

Bardia A, Hurvitz SA, Tolaney SM, et al. Sacituzumab govitecan in metastatic triple-negative breast cancer. *N Engl J Med* 2021;384:1529-41.

European Medicines Agency. Assessment report: Trodelvy. 14 October 2021.

eviQ Cancer Treatments Online. Clinical resource: Gilbert's syndrome. Cancer Institute NSW. 22 Sept 2023 V.5.

Irinotecan drug monograph. Ontario Health (Cancer Care Ontario).

National Comprehensive Cancer Network. Antiemesis: NCCN Guidelines Version 1.2023.

Prescribing information: Trodelvy® (sacituzumab govitecan-hziy). Gilead Sciences, Inc. February 2023.

Product monograph: Trodelvy® (sacituzumab govitecan). Gilead Sciences Canada, Inc. July 19, 2023.

Spring LM, Nakajima E, Hutchinson J, Viscosi E, Blouin G, Weekes C, Rugo H, Moy B, Bardia A. Sacituzumab Govitecan for Metastatic Triple-Negative Breast Cancer: Clinical Overview and Management of Potential Toxicities. *Oncologist*. 2021 Oct;26(10):827-834.

Summary of Product Characteristics: Trodelvy 180 mg powder for concentrate for solution for infusion. Gilead Sciences Ltd. 1 July 2022.

December 2023 Modified Dosage with Toxicity section

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L - Disclaimer

Refer to the [New Drug Funding Program](#) or [Ontario Public Drug Programs](#) websites for the most up-to-date public funding information.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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