**Regimen Monograph**



## A - Regimen Name

# SACI Regimen

**sacituzumab govitecan**

| | |
|---|---|
| **Disease Site** | Breast |
| **Intent** | Palliative |
| **Regimen Category** | **Evidence-Informed :**<br><br>Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use. |
| **Rationale and Uses** | For the treatment of unresectable locally advanced or metastatic triple-negative breast cancer (TNBC), in patients who have received ≥ 2 therapies, with at least 1 therapy used to treat metastatic disease. (See NDFP form for details.) |
| **Supplementary Public Funding** | **sacituzumab govitecan**<br>New Drug Funding Program (Sacituzumab Govitecan - Unresectable Locally Advanced or Metastatic Triple Negative Breast Cancer) (NDFP Website ) |

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## B - Drug Regimen

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| **sacituzumab govitecan** | 10 mg /kg | IV | Days 1 and 8 |

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## C - Cycle Frequency

**REPEAT EVERY 21 DAYS**

Until disease progression or unacceptable toxicity (see NDFP form for details).

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## D - Premedication and Supportive Measures

**Antiemetic Regimen:** Moderate (+ NK-1 RA)

- Also refer to CCO Antiemetic Recommendations.

**Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.

**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.

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## E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

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.

**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.<br>If treatment delayed by 1 week, resume at same dose, consider G-CSF support.<br>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.<br>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. |

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| Other Grade 3 or 4 hematologic toxicity (e.g., anemia and thrombocytopenia) | Hold* until resolved.<br><br>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 $10^9$/L, Platelets ≥ 75 x $10^9$/L, Hgb ≥ 100 g/L, and non-hematologic toxicities recover to ≤ Grade 1.

On **day 8**, do not resume until ANC ≥ 1 x $10^9$/L, Platelets ≥ 75 x $10^9$/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)<br><br>Other Grade 4 non-hematologic toxicity | Hold* until resolved. Resume at 1 dose level ↓. Discontinue if 3rd occurrence. |

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

On **day 8**, do not resume until ANC ≥ 1 x $10^9$/L, Platelets ≥ 75 x $10^9$/L, Hgb ≥ 100 g/L, and non-hematologic toxicities recover to ≤ 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 | • Stop or slow the infusion rate.<br>• Manage the symptoms. | • Consider rechallenge if appropriate.<br>• Add a corticosteroid to other pre-medications. |

| | | |
|---|---|---|
| | **Restart:**<br>• Once symptoms have resolved, restart at slower rate. | |
| 3 or 4 | • Stop treatment.<br>• Aggressively manage symptoms. | • Discontinue permanently (do not re-challenge). |

## 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. |

## 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.

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## F - Adverse Effects

Refer to sacituzumab govitecan drug monograph(s) for additional details of adverse effects.

| Very common (≥ 50%) | Common (25-49%) | Less common (10-24%) | Uncommon (< 10%), but may be severe or life-threatening |
|---|---|---|---|
| • Diarrhea (may be severe)<br>• Myelosuppression ± infection, bleeding (may be severe)<br>• Nausea, vomiting<br>• Fatigue | • Alopecia<br>• Constipation<br>• Hypersensitivity (may be severe)<br>• Anorexia, weight loss | • Cough, dyspnea<br>• Abdominal pain<br>• Headache<br>• Abnormal electrolyte(s)<br>• Musculoskeletal pain<br>• Rash<br>• ↑ LFTs<br>• Insomnia<br>• Dizziness<br>• Mucositis | • QT interval prolonged<br>• Infusion related reactions |

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## G - Interactions

Refer to sacituzumab govitecan drug monograph(s) for additional details.

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## H - Drug Administration and Special Precautions

Refer to sacituzumab govitecan drug monograph(s) for additional details.

### Administration

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.

### Contraindications

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

### Pregnancy/Lactation

- This regimen is **not recommended** for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after treatment the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is **not recommended** during treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if applicable).
- Fertility effects: Female fertility may be affected.

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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

- 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 - Administrative Information

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|---|---|
| Approximate Patient Visit | 2 to 4 hours |
| Pharmacy Workload (average time per visit) | 26.850 minutes |
| Nursing Workload (average time per visit) | 57.333 minutes |

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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 Apr 22;384(16):1529-1541.

CADTH reimbursement recommendation: Sacituzumab govitecan (for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer). February 2022.

Sacituzumab govitecan drug monograph. Ontario Health (Cancer Care Ontario).

**December 2023** Updated Dose modifications section

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## M - Disclaimer

***Regimen Abstracts***

*A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.*

*Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.*

***Regimen Monographs***

*Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.*

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

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*that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.*

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