TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection

Dosing, Administration, and Side Effect Management Guide

INDICATIONS

TRODELVY® (sacituzumab govitecan-hziy) 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.
- Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 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 may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of 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**

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

Preparation, storage, and handling[1]

TRODELVY information

TRODELVY is a sterile, off-white to yellowish lyophilized powder in a single-dose vial for injection. Each vial of TRODELVY is individually boxed. Each box contains one 180-mg vial.

Reconstitution

- TRODELVY is a hazardous drug. Follow applicable special handling and disposal procedures
- Calculate the required dose (mg) of TRODELVY based on the patient's body weight at the beginning of each treatment cycle (or more frequently if the patient's body weight changed by more than 10% since the previous administration)
- Allow the required number of vials to warm to room temperature
- Using a sterile syringe, slowly inject **20 mL of 0.9% Sodium Chloride** Injection, USP, into each 180-mg TRODELVY vial. Each vial contains overfill to compensate for liquid loss during preparation and after reconstitution, the total resulting volume delivers a **concentration of 10 mg/mL**
- Gently swirl vials and allow to dissolve for up to 15 minutes. DO NOT SHAKE
- Inspect for particulate matter and discoloration prior to administration
- The solution should be free of visible particulates, clear and yellow
- Do not use the reconstituted solution if it is cloudy or discolored
- Use immediately to prepare a diluted TRODELVY infusion solution

Dilution

- Calculate the required amount of the reconstituted TRODELVY solution needed to obtain the appropriate dose according to the patient's body weight
- Determine the final volume of the infusion solution to deliver the appropriate dose at a TRODELVY concentration range of 1.1 mg/mL to 3.4 mg/mL
- Use 0.9% sodium chloride injection, USP only since the stability of the reconstituted TRODELVY solution has not been determined with other infusion-based solutions. Use a polyvinyl chloride, polypropylene/polyethylene, polyolefin, or ethylene vinyl acetate infusion bag
- Withdraw and discard the volume of 0.9% Sodium Chloride Injection, USP from the final infusion bag that is necessary to achieve the indicated TRODELVY concentration following the addition of the calculated amount of reconstituted TRODELVY solution
- Withdraw the calculated amount of the reconstituted TRODELVY solution from the vial(s) using a syringe. Discard any unused portion remaining in the vial(s)
- To minimize foaming, slowly inject the calculated amount of reconstituted TRODELVY solution into the infusion bag. Do not shake the contents

Note: Do not freeze or shake. Protect infusion bag from light. Use only 0.9% Sodium Chloride Injection, USP, for dilution.

If not used immediately, the infusion bag containing TRODELVY solution can be refrigerated at 2 °C to 8 °C (36 °F to 46 °F) for up to 24 hours protected from light. After refrigeration, administer diluted solution at room temperature up to 25 °C (77 °F) within 8 hours (including infusion time).

Storage and handling

- Store vials in a refrigerator at **2 °C to 8 °C (36 °F to 46 °F)** in the original carton to protect from light until time of reconstitution
- Do not freeze

The information provided in this guide does not constitute the provision of medical advice and should not substitute for clinical decision making.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

• Severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 on Day 1 of any cycle or neutrophil count below 1000/mm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI.

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

USP, United States Pharmacopoeia.

Dosing and administration

Premedication prior to each dose of TRODELVY[1]

- For the prevention of infusion reactions, premedication with antipyretics and H1 and H2 blockers is recommended. For patients who had prior infusion reactions, consider corticosteroids
- Prevention of chemotherapy-induced nausea and vomiting is recommended and can include premedication with a 2- or 3-drug combination. For example, dexamethasone can be administered with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as outlined below, as well as other drugs as indicated

Examples of 5-HT3 receptor antagonists[2]			
dolasetron	granisetron	ondansetron	palonosetron

Examples of NK_1 receptor antagonists[3]				
aprepitant	fosnetupitant	fosaprepitant	netupitant	rolapitant

- Patients who exhibit an excessive cholinergic response to treatment with TRODELVY (eg, abdominal cramping, diarrhea, salivation, etc) can receive appropriate premedication (eg, atropine) for subsequent treatments

Dosing considerations[1]

TRODELVY is administered at 10 mg/kg as an IV infusion.

Calculate the required dose (mg) of TRODELVY based on the patient's body weight (kg) at the beginning of each treatment cycle (or more frequently if the patient's body weight changes by more than 10% since the previous administration). **For example, a patient who weighs 65 kg would receive an infusion containing 650 mg of TRODELVY.**

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

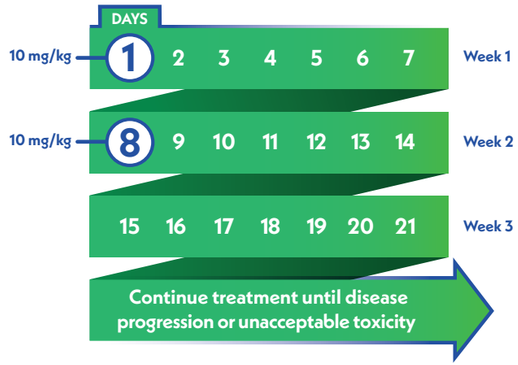
Diarrhea: Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for Grade 3-4 diarrhea and resume when resolved to ≤Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

21-day treatment cycles[1]

The recommended dose of TRODELVY is **10 mg/kg intravenously on days 1 and 8 of 21-day treatment cycles**. Continue treatment until disease progression or unacceptable toxicity.

Note: Do not administer TRODELVY at doses greater than 10 mg/kg. For intravenous infusion only. Do not administer as an intravenous push or bolus. Do NOT substitute TRODELVY for or use with other drugs containing irinotecan or its active metabolite, SN-38.



First infusion[1]

- Administer infusion **over 3 hours**
- Observe patients for signs or symptoms of infusion-related reactions during the infusion and for at least 30 minutes following the initial dose

Subsequent infusions[1]

- Administer infusion **over 1 to 2 hours** if prior infusions were tolerated
- Observe patients during the infusion and for at least 30 minutes after infusion

Dose modifications for adverse reactions[1]

- Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction
- Permanently discontinue TRODELVY for life-threatening infusion-related reactions

See page 7 for additional information on dose modifications for adverse reactions.

Important administration considerations[1]

- Administer TRODELVY as an intravenous infusion. Do not administer as an intravenous push or bolus
- Protect infusion bag from light. The infusion bag should be covered during administration to the patient until dosing is complete. It is not necessary to cover the infusion tubing or to use light-protective tubing during the infusion
- An infusion pump may be used
- Do not mix TRODELVY or co-administer with any other medications
- After infusion, flush IV line with 20 mL 0.9% Sodium Chloride Injection, USP

5-HT3, 5-hydroxytryptamine 3 receptor; H1, histamine receptor 1; H2, histamine receptor 2; IV, intravenous; NK_1, neurokinin-1 receptor; USP, United States Pharmacopoeia.

Side effects and dose modifications[1]

Among patients treated with TRODELVY in the clinical trials, the most common adverse reactions (including lab abnormalities) reported in ≥25% of patients were:

- Decreased leukocyte count
- Decreased neutrophil count
- Decreased hemoglobin
- Diarrhea
- Nausea
- Decreased lymphocyte count
- Fatigue
- Alopecia
- Constipation
- Increased glucose
- Decreased albumin
- Vomiting
- Decreased appetite
- Decreased creatinine clearance
- Increased alkaline phosphatase
- Decreased magnesium
- Decreased potassium
- Decreased sodium

Note: Information provided does not constitute the provision of medical advice and should not substitute for clinical decision making.

Modify or discontinue the TRODELVY dose to manage adverse reactions as described in the following tables. Do not reescalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Develop a side effect management plan to help support your patients.

Before administering TRODELVY

BE AWARE

Learn when side effects can occur and how long they were shown to last in the clinical trials.

PREPARE

Consider which premedications you may need and how to counsel your patients.

After administering TRODELVY

MONITOR

Know how to monitor your patients and what counseling or supportive measures they may need.

MANAGE

Help manage certain adverse reactions with appropriate medications and/or by modifying, withholding, or discontinuing doses of TRODELVY.

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

Dose modifications for adverse reactions[1]

Severe neutropenia

Adverse Reaction	Occurrence	Dose Modification
• **Grade 4 neutropenia ≥7 days,** **OR** • **Grade 3-4 febrile neutropenia,** **OR** • **At time of scheduled treatment, Grade 3-4 neutropenia, which delays dosing by 2 or 3 weeks for recovery to ≤Grade 1**	First	25% dose reduction from the original dose and administer G-CSF
	Second	50% dose reduction from the original dose and administer G-CSF
	Third	Discontinue treatment and administer G-CSF
• **At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤Grade 1**	First	Discontinue treatment and administer G-CSF

See pages 8-9 for additional information on dose modifications for neutropenia.

Severe non-neutropenic toxicity

Adverse Reaction	Occurrence	Dose Modification
• **Grade 4 non-hematologic toxicity of any duration,** **OR** • **Any Grade 3-4 nausea, vomiting or diarrhea due to treatment that is not controlled with antiemetics and antidiarrheal agents,** **OR** • **Other Grade 3-4 non-hematologic toxicity persisting for >48 hours despite optimal medical management,** **OR** • **At time of scheduled treatment, Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, which delays dose by 2 or 3 weeks for recovery to ≤ Grade 1**	First	25% dose reduction from the original dose
	Second	50% dose reduction from the original dose
	Third	Discontinue treatment
• **In the event of Grade 3-4 non-neutropenic hematologic or nonhematologic toxicity, which does not recover to ≤ Grade 1 within 3 weeks**	First	Discontinue treatment

See pages 10-11 for additional information on dose modifications for diarrhea. See pages 12-13 for additional information on dose modifications for hypersensitivity and infusion-related reactions. See pages 14-15 for additional information on dose modifications for nausea and vomiting.

- Modify, withhold, or discontinue TRODELVY to manage adverse reactions as described above
- Do not reescalate the TRODELVY dose after a dose reduction for adverse reactions has been made
- Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction
- Permanently discontinue TRODELVY for life-threatening infusion-related reactions

G-CSF, granulocyte-colony stimulating factor.

Neutropenia side effect management plan

BE AWARE

TRODELVY can cause severe neutropenia.[1]

Severe, life-threatening, or fatal neutropenia can occur in patients treated with TRODELVY.[1]
Among patients treated with TRODELVY in the clinical trials:

- Neutropenia was observed in 64%[1]
- Grade 3-4 neutropenia occurred in 49%[1]
- Febrile neutropenia occurred in 6%[1]
- Neutropenic colitis occurred in 1.4% of patients[1]
- The median time to first onset of neutropenia (including febrile neutropenia) in patients receiving TRODELVY was 16 days, but it has occurred earlier in some patient populations[1,a]
- In a prespecified descriptive analysis of the TROPiCS-02 study,[b] median time to onset for any grade neutropenia[c] related to TRODELVY was 20 days, and the median duration was 8 days[5]
- In a post hoc descriptive analysis of the ASCENT study,[d] median time to onset for any grade neutropenia related to TRODELVY was 20 days, and the median duration was 7 days[6]

PREPARE

It is important to develop a proactive plan for potential neutropenia management. As you start a patient on TRODELVY, ensure that you take the appropriate steps so that you can help manage with G-CSF if needed.

Considerations for management with G-CSF[1]

When starting a patient on TRODELVY, consider:

- Which G-CSF products are covered by the patient's insurance plan?
- Will prior authorization be required?
- When is it prudent to have G-CSF products on hand?
- For G-CSF use with the treatment of TRODELVY, what are other factors to consider?

MONITOR

Important patient counseling information[1]

Advise patients of the risk of neutropenia. Instruct and remind patients to contact their healthcare provider immediately if they experience fever, chills, or other signs of infection.[1]

Monitor blood cell counts periodically during treatment.[1]

Neutropenia grade scale[7]	
Grade 1	ANC <LLN to 1500/mm^3
Grade 2	ANC <1500 to 1000/mm^3
Grade 3	ANC <1000 to 500/mm^3
Grade 4	ANC <500/mm^3
Grade 5	–

Febrile neutropenia grade scale[7]	
Grade 1	–
Grade 2	–
Grade 3	ANC <1000/mm^3 with a single temperature of >38.3 °C (101 °F) or a sustained temperature of ≥38 °C (100.4 °F) for more than 1 hour
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death

[a] Includes patients from 4 trials (IMMU-132-01, TROPHY, ASCENT, and TROPiCS-02).[1]
[b] TROPiCS-02 was a phase 3 study of TRODELVY in pretreated HR+/HER2- metastatic breast cancer.[4]
[c] Events of neutropenia included the preferred terms neutropenia, neutrophil count decreased, and febrile neutropenia.[5]
[d] ASCENT was a phase 3 study of TRODELVY in pretreated metastatic triple-negative breast cancer.[6]

MANAGE

Dose modifications[1]

Doses of TRODELVY can be modified or withheld to help manage adverse reactions.

Note: Do not reescalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

TRODELVY should be withheld if

- ANC is below 1500/mm^3 on day 1 of any cycle, **OR**
- The neutrophil count is below 1000/mm^3 on day 8 of any cycle, **OR**
- Patient develops neutropenic fever

Specific dose modifications are based on severity and occurrence of severe neutropenia.

If the patient experiences:

- **GRADE 4** neutropenia that lasts 7 or more days, **OR**
- **GRADE 3-4** febrile neutropenia, **OR**
- **GRADE 3-4** neutropenia at the time of a scheduled treatment that delays dosing by 2 or 3 weeks to achieve recovery to ≤Grade 1 neutropenia

Then modify the dose of TRODELVY as follows:

1ST OCCURRENCE	2ND OCCURRENCE	3RD OCCURRENCE
25% dose reduction from the original dose and administer G-CSF	50% dose reduction from the original dose and administer G-CSF	Discontinue treatment and administer G-CSF

If Grade 3-4 neutropenia delays dosing at the time of scheduled treatment beyond 3 weeks to achieve recovery to ≤Grade 1 neutropenia, discontinue treatment at first occurrence and administer G-CSF.

If patients experience neutropenia, be ready with G-CSF prophylaxis or support to help patients stay on therapy if clinically indicated/appropriate.[1]

There are different types of G-CSF, including various formulations of [8,9]

- Filgrastim
- Pegfilgrastim (a longer-acting formulation)

Longer-acting G-CSF may be given less frequently than shorter-acting G-CSF.[9]

ANC, absolute neutrophil count; G-CSF, granulocyte-colony stimulating factor; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive; LLN, lower limit of normal.

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

Diarrhea side effect management plan

BE AWARE

TRODELVY can cause severe diarrhea.[1]

Among patients treated with TRODELVY in the clinical trials:

- Diarrhea occurred in 64%[1]
- Grade 3-4 diarrhea occurred in 11%[1]
- One patient had an intestinal perforation following diarrhea[1]
- Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients[1]
- In a prespecified descriptive analysis of the TROPiCS-02 study,[a] median time to onset for any grade diarrhea related to TRODELVY was 15 days, and the median duration was 8 days[5]
- In a post hoc descriptive analysis of the ASCENT study,[b] median time to onset for any grade diarrhea related to TRODELVY was 12 days, and the median duration was 5 days[6]

PREPARE

Important patient counseling information[1]

Be sure to advise patients of the risk of diarrhea. Instruct your patients to contact their healthcare provider immediately if they experience any of the following symptoms

- Diarrhea for the first time
- Black or bloody stools
- Symptoms of dehydration such as light-headedness, dizziness, or faintness
- Inability to take fluids by mouth due to nausea or vomiting
- Inability to control diarrhea within 24 hours

MONITOR

Diarrhea grade scale[7]	
Grade 1	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline
Grade 2	Increase of 4 to 6 stools per day over baseline; moderate increase in ostomy output compared to baseline; limiting instrumental activities of daily living
Grade 3	Increase of ≥7 stools per day over baseline; hospitalization indicated; severe increase in ostomy output compared to baseline; limiting self-care activities of daily living
Grade 4	Life-threatening consequences; urgent intervention indicated
Grade 5	Death

[a] TROPiCS-02 was a phase 3 study of TRODELVY in pretreated HR+/HER2- metastatic breast cancer.[4]
[b] ASCENT was a phase 3 study of TRODELVY in pretreated metastatic triple-negative breast cancer.[6]

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MANAGE

Dose modifications[1]

Doses of TRODELVY can be withheld or modified to help manage adverse reactions.

For patients who experience Grade 3-4 diarrhea at the time of scheduled treatment, withhold the dose of TRODELVY and resume when ≤Grade 1 diarrhea is achieved.

Note: If severe diarrhea occurs, withhold TRODELVY until resolved to ≤Grade 1 and reduce subsequent doses. Do not reescalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Specific dose modifications are based on severity and occurrence of severe diarrhea.

If the patient experiences:

- **GRADE 4** diarrhea of any duration, **OR**
- **GRADE 3-4** diarrhea due to treatment that is not controlled with antidiarrheal agents, **OR**
- **GRADE 3-4** diarrhea that persists >48 hours despite optimal medical management, **OR**
- **GRADE 3-4** diarrhea that at the time of scheduled treatment delays dose by 2 or 3 weeks for recovery to ≤Grade 1

Then modify the dose of TRODELVY as follows:

1ST OCCURRENCE	2ND OCCURRENCE	3RD OCCURRENCE
25% dose reduction from the original dose	50% dose reduction from the original dose	Discontinue treatment

If Grade 3-4 diarrhea does not recover to ≤Grade 1 within 3 weeks, discontinue treatment at first occurrence.

Premedication[1]

Patients who exhibit an excessive cholinergic response to treatment with TRODELVY (eg, abdominal cramping, diarrhea, salivation, etc) can receive appropriate premedication (eg, atropine) for subsequent treatments.

Ongoing supportive care[1]

Should diarrhea occur, evaluate for infectious causes. If no infectious cause is found, initiate 4 mg of loperamide followed by 2 mg with each episode of diarrhea (up to 16 mg/day). Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures such as fluid and electrolyte support may be added as needed.

HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive.

Hypersensitivity and infusion-related reactions side effect management plan

BE AWARE

TRODELVY can cause hypersensitivity and infusion-related reactions.[1]

Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms include cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions.

Among patients treated with TRODELVY in the clinical trials:

- Hypersensitivity reactions occurred within 24 hours of dosing in 35%[1]
- Grade 3-4 hypersensitivity occurred in 2%[1]
- Hypersensitivity reactions leading to permanent discontinuation of TRODELVY occurred in 0.2%[1]
- Anaphylactic reactions occurred in 0.2%[1]
- In a prespecified descriptive analysis of the TROPiCS-02 study,[a] median time to onset for any grade hypersensitivity and infusion-related reactions related to TRODELVY was 29 days, and the median duration was 15 days[5]

PREPARE

Premedication [1]

Premedication for infusion reactions is recommended. Premedicate with antipyretics, H1 and H2 blockers prior to infusion. Corticosteroids may be used for patients who had prior infusion reactions.

Note: Be sure to advise patients of the risk of serious infusion reactions and anaphylaxis.

Have medications and emergency equipment immediately available to treat infusion-related reactions, including anaphylaxis.

MONITOR

Closely monitor patients for hypersensitivity and infusion-related reactions during each infusion and for **at least 30 minutes after the infusion** is complete.[1]

30 minutes

Important patient counseling information[1]

Instruct patients to self-monitor during their infusion and for 24 hours after their infusion and to immediately contact their healthcare provider if they experience

- Swelling of the face, lips, tongue, or throat
- Urticaria (hives)
- Difficulty breathing
- Lightheadedness
- Dizziness, feeling faint, or pass out
- Chills
- Rigors (shaking chills)
- Wheezing
- Rash, itching, or flushing of skin
- Hypotension
- Fever

MANAGE

Dose modifications[1]

- Infusion of TRODELVY may be modified or withheld to help infusion-related reactions
- Slow or interrupt the infusion rate of TRODELVY if the patient develops an infusion-related reaction
- Permanently discontinue TRODELVY for Grade 4 infusion-related reactions

Have medications and emergency equipment immediately available to treat infusion-related reactions, including anaphylaxis.

[a] TROPiCS-02 was a phase 3 study of TRODELVY in pretreated HR+/HER2- metastatic breast cancer.[4]

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

H1, histamine receptor 1; H2, histamine receptor 2; HER2-, human epidermal growth factor receptor 2-negative; HR+, hormone receptor-positive.

Nausea and vomiting side effect management plan

BE AWARE

TRODELVY is emetogenic, or a substance that may cause vomiting in some patients.[1,10]

Among patients treated with TRODELVY in the clinical trials:

- Nausea and vomiting occurred in 64% and 35%, respectively[1]
- Grade 3-4 nausea occurred in 3%[1]
- Grade 3-4 vomiting occurred in 2%[1]
- In a post hoc descriptive analysis of the ASCENT study, median time to onset for any grade nausea reactions related to TRODELVY was 8 days, and the median duration was 5.5 days. The median time to onset for any grade vomiting related to TRODELVY was 24.5 days, and the median duration was 1.5 days[6]

PREPARE

Premedication[1]

- Prior to each dose of TRODELVY, premedication for prevention of CINV is recommended
- Premedicate with a 2- or 3-drug combination (eg, dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as needed)
- Additional antiemetics, sedatives, and other supportive measures may also be employed as clinically indicated
- All patients should be given take-home medications with clear instructions for prevention and treatment of delayed nausea and vomiting

MONITOR

Important patient counseling information[1]

- Be sure to advise patients of the risk of nausea and vomiting
- Instruct patients to immediately contact their healthcare provider if they experience uncontrolled nausea or vomiting

Nausea and vomiting grade scales[7]

	Nausea	Vomiting
Grade 1	Loss of appetite without alteration in eating habits	Intervention not indicated
Grade 2	Oral intake decreased without significant weight loss, dehydration, or malnutrition	Outpatient IV hydration; medical intervention indicated
Grade 3	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	Tube feeding, TPN, or hospitalization indicated
Grade 4	–	Life-threatening consequences
Grade 5	–	Death

[a] ASCENT was a phase 3 study of TRODELVY in pretreated metastatic triple-negative breast cancer.[6]

MANAGE

Dose modifications[1]

Doses of TRODELVY can be withheld or modified to help manage adverse reactions.

Doses of TRODELVY should be withheld for Grade 3 nausea or Grade 3-4 vomiting at the time of scheduled treatment administration and resume with additional supportive measures when resolution to ≤Grade 1 is achieved.

Note: Do not reescalate the TRODELVY dose after a dose reduction for adverse reactions has been made.

Specific dose modifications are based on severity and occurrence of severe nausea and vomiting.

If the patient experiences:

- **GRADE 4** nausea or vomiting of any duration, **OR**
- **GRADE 3-4** nausea or vomiting that is not controlled with antiemetics, **OR**
- **GRADE 3-4** nausea or vomiting that persists >48 hours despite optimal medical management, **OR**
- **GRADE 3-4** nausea or vomiting that at the time of scheduled treatment delays dose by 2 or 3 weeks for recovery to ≤Grade 1

Then modify the dose of TRODELVY as follows:

1ST OCCURRENCE	2ND OCCURRENCE	3RD OCCURRENCE
25% dose reduction from the original dose	50% dose reduction from the original dose	Discontinue treatment

If Grade 3-4 nausea or vomiting does not recover to ≤Grade 1 within 3 weeks, discontinue treatment at first occurrence.

5-HT3, 5-hydroxytryptamine 3 receptor; CINV, chemotherapy-induced nausea and vomiting; IV, intravenous; NK_1, neurokinin-1 receptor; TPN, total parenteral nutrition.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

Drug interactions

Drug interactions with UGT1A1 inhibitors[1]

Concomitant administration of TRODELVY with UGT1A1 inhibitors may increase the incidence of adverse reactions due to a potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

Examples of UGT1A1 inhibitors include[11,12]

- protease inhibitors (eg, atazanavir, efavirenz, ritonavir)
- tyrosine kinase inhibitors (eg, lapatinib, nilotinib, sorafenib)
- SGLT2 inhibitors (eg, canagliflozin, dapagliflozin)
- gemifibrozil
- levothyroxine
- ketoconazole
- diclofenac
- entacapone
- everolimus
- vitamin A
- zafirlukast

Note: This is not an inclusive list of all UGT1A1 inhibitiors.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Nausea and Vomiting: Nausea occurred in 64% of all patients treated with TRODELVY and Grade 3-4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and Grade 3-4 vomiting occurred in 2% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting (CINV). Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to Grade ≤1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

Drug interactions with UGT1A1 inducers[1]

Exposure to SN-38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

Examples of UGT1A1 inducers include[13-15]

- carbamazepine
- rifampicin
- phenobarbital
- phenytoin

Note: This is not an inclusive list of all UGT1A1 inducers.

Important patient counseling information[1]

Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY 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.

SGLT2, sodium-glucose cotransporter-2; UGT1A1, uridine diphosphate-glucuronosyl transferase 1A1.

IMPORTANT SAFETY INFORMATION (cont'd)

WARNINGS AND PRECAUTIONS (cont'd)

Increased Risk of Adverse Reactions in Patients with Reduced UGT1A1 Activity: 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 with TRODELVY. The incidence of Grade 3-4 neutropenia was 58% in patients homozygous for the UGT1A1*28, 49% in patients heterozygous for the UGT1A1*28 allele, and 43% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 21% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 9% in patients homozygous for the wild-type allele. Closely monitor patients with known reduced UGT1A1 activity for adverse reactions. Withhold or permanently discontinue TRODELVY 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 function.

Please see full Important Safety Information on pages 18-19 and click to see full Prescribing Information, including BOXED WARNING.

INDICATIONS

TRODELVY® (sacituzumab govitecan-hziy) 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.
- Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least two additional systemic therapies in the metastatic setting.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: NEUTROPENIA AND DIARRHEA

- **Severe or life-threatening neutropenia may occur. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 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 may occur. Monitor patients with diarrhea and give fluid and electrolytes as needed. At the onset of 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.**

CONTRAINDICATIONS

- Severe hypersensitivity reaction to TRODELVY.

WARNINGS AND PRECAUTIONS

Neutropenia: Severe, life-threatening, or fatal neutropenia can occur and may require dose modification. Neutropenia occurred in 64% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 49% of patients. Febrile neutropenia occurred in 6%. Neutropenic colitis occurred in 1.4%. Withhold TRODELVY for absolute neutrophil count below 1500/mm^3 on Day 1 of any cycle or neutrophil count below 1000/mm^3 on Day 8 of any cycle. Withhold TRODELVY for neutropenic fever. Administer G-CSF as clinically indicated or indicated in Table 1 of USPI.

Diarrhea: Diarrhea occurred in 64% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 11% of patients. One patient had intestinal perforation following diarrhea. Diarrhea that led to dehydration and subsequent acute kidney injury occurred in 0.7% of all patients. Withhold TRODELVY for Grade 3-4 diarrhea and resume when resolved to ≤Grade 1. At onset, evaluate for infectious causes and if negative, promptly initiate loperamide, 4 mg initially followed by 2 mg with every episode of diarrhea for a maximum of 16 mg daily. Discontinue loperamide 12 hours after diarrhea resolves. Additional supportive measures (e.g., fluid and electrolyte substitution) may also be employed as clinically indicated. Patients who exhibit an excessive cholinergic response to treatment can receive appropriate premedication (e.g., atropine) for subsequent treatments.

Hypersensitivity and Infusion-Related Reactions: Serious hypersensitivity reactions including life-threatening anaphylactic reactions have occurred with TRODELVY. Severe signs and symptoms included cardiac arrest, hypotension, wheezing, angioedema, swelling, pneumonitis, and skin reactions. Hypersensitivity reactions within 24 hours of dosing occurred in 35% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.2%. The incidence of anaphylactic reactions was 0.2%. Pre-infusion medication is recommended. Have medications and emergency equipment to treat such reactions available for immediate use. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

Nausea and Vomiting: Nausea occurred in 64% of all patients treated with TRODELVY and Grade 3-4 nausea occurred in 3% of these patients. Vomiting occurred in 35% of patients and Grade 3-4 vomiting occurred in 2% of these patients. Premedicate with a two or three drug combination regimen (e.g., dexamethasone with either a 5-HT3 receptor antagonist or an NK_1 receptor antagonist as well as other drugs as indicated) for prevention of chemotherapy-induced nausea and vomiting (CINV). Withhold TRODELVY doses for Grade 3 nausea or Grade 3-4 vomiting and resume with additional supportive measures when resolved to Grade ≤1. Additional antiemetics and other supportive measures may also be employed as clinically indicated. All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting.

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Embryo-Fetal Toxicity: Based on its mechanism of action, TRODELVY can cause teratogenicity and/or embryo-fetal lethality when administered to a pregnant woman. TRODELVY contains a genotoxic component, SN-38, and targets rapidly dividing cells. Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with TRODELVY and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with TRODELVY and for 3 months after the last dose.

ADVERSE REACTIONS

In the pooled safety population, the most common (≥ 25%) adverse reactions including laboratory abnormalities were decreased leukocyte count (84%), decreased neutrophil count (75%), decreased hemoglobin (69%), diarrhea (64%), nausea (64%), decreased lymphocyte count (63%), fatigue (51%), alopecia (45%), constipation (37%), increased glucose (37%), decreased albumin (35%), vomiting (35%), decreased appetite (30%), decreased creatinine clearance (28%), increased alkaline phosphatase (28%), decreased magnesium (27%), decreased potassium (26%), and decreased sodium (26%).

In the ASCENT study (locally advanced or metastatic triple-negative breast cancer), the most common adverse reactions (incidence ≥25%) were fatigue, diarrhea, nausea, alopecia, constipation, vomiting, abdominal pain, and decreased appetite. The most frequent serious adverse reactions (SAR) (>1%) were neutropenia (7%), diarrhea (4%), and pneumonia (3%). SAR were reported in 27% of patients, and 5% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the ASCENT study were reduced neutrophils, leukocytes, and lymphocytes.

In the TROPiCS-02 study (locally advanced or metastatic HR-positive, HER2-negative breast cancer), the most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, nausea, alopecia, and constipation. The most frequent serious adverse reactions (SAR) (>1%) were diarrhea (5%), febrile neutropenia (4%), neutropenia (3%), abdominal pain, colitis, neutropenic colitis, pneumonia, and vomiting (each 2%). SAR were reported in 28% of patients, and 6% discontinued therapy due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the TROPiCS-02 study were reduced neutrophils and leukocytes.

DRUG INTERACTIONS

UGT1A1 Inhibitors: Concomitant administration of TRODELVY with inhibitors of UGT1A1 may increase the incidence of adverse reactions due to potential increase in systemic exposure to SN-38. Avoid administering UGT1A1 inhibitors with TRODELVY.

UGT1A1 Inducers: Exposure to SN-38 may be reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

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Gilead Oncology Support

Do your patients have questions about cost or coverage for their prescribed medication? We can help your patients understand their options.[a]

Support is available Monday through Friday, 9 AM to 7 PM EST

1-844-TRODELVY (1-844-876-3358)

[a] Support may vary based on application criteria and is subject to change or discontinuation. Physician office must submit Prior Authorizations and appeals.

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References: 1. Trodelvy. Package insert. Gilead Sciences, Inc; April 2024. **2.** Schwartzberg L, Barbour SY, Morrow GR, Ballinari G, Thorn MD, Cox D. Pooled analysis of phase III clinical studies of palonosetron versus ondansetron, dolasetron, and granisetron in the prevention of chemotherapy-induced nausea and vomiting (CINV). *Support Care Cancer.* 2014;22(2):469-477. https://doi.org/10.1007/s00520-013-1999-9 **3.** Hesketh PJ, Kris MG, et al. Antiemetics: ASCO guideline update. *J Clin Oncol.* 2020;38(24):2782-2797. doi:10.1200/JCO.20.01296 **4.** Rugo HS, Bardia A, Marmé F, et al. Sacituzumab govitecan in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer. *J Clin Oncol.* 2022;40(29):3365-3376. https://doi.org/10.1200/JCO.22.01002 **5.** Data on file. Gilead Sciences, Inc.; June 2022. **6.** Rugo HS, Tolaney SM, Loirat D, et al. Safety analyses from the phase 3 ASCENT trial of sacituzumab govitecan in metastatic triple-negative breast cancer. *NPJ Breast Cancer.* 2022;8(1):98. doi:10.1038/s41523-022-00467-1 **7.** National Cancer Institute, Division of Cancer Treatment & Diagnosis (DCTD). *Common Terminology Criteria for Adverse Events (CTCAE).* Version 5.0. National Institutes of Health. Published November 27, 2017. Accessed June 5, 2024. **8.** National Cancer Institute. Granulocyte colony-stimulating factor. National Institutes of Health. Accessed June 5, 2024. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/granulocyte-colony-stimulating-factor **9.** National Cancer Institute. Pegfilgrastim. National Institutes of Health. Accessed June 5, 2024. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/pegfilgrastim **10.** National Cancer Institute. Emetogenic. National Institutes of Health. Accessed June 5, 2024. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/emetogenic **11.** Lv X, Xia Y, Finel M, Wu J, Ge G, Yang L. Recent progress and challenges in screening and characterization of UGT1A1 inhibitors. *Acta Pharm Sin B.* 2019;9(2):258-278. https://doi.org/10.1016/j.apsb.2018.09.005 **12.** You BH, Gong EC, Choi YH. Inhibitory effect of sauchinone on UDP-glucuronosyltransferase (UGT) 2B7 activity. *Molecules.* 2018;23(2):366. https://doi.org/10.3390/molecules23020366 **13.** Song I, Weller S, Patel J, et al. Effect of carbamazepine on dolutegravir pharmacokinetics and dosing recommendation. *Eur J Clin Pharmacol.* 2016;72:665-670. https://doi.org/10.1007/s00228-016-2020-6 **14.** Marques SC, Ikediobi ON. The clinical application of UGT1A1 pharmacogenetic testing: gene-environment interactions. *Hum Genomics.* 2010;4(4):238-249. https://doi.org/10.1186/1479-7364-4-4-238 **15.** Hirashima R, Michimae H, Takemoto H, et al. Induction of the UDP-glucuronosyltransferase 1A1 during the perinatal period can cause neurodevelopmental toxicity. *Mol Pharmacol.* 2016;90(3):265-274. https://doi.org/10.1124/mol.116.104174

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TRODELVY®
sacituzumab govitecan-hziy
180 mg for injection