# TRODELVY™

## sacituzumab govitecan-hziy

180 mg for injection

# DOSING, RECONSTITUTION, AND ADMINISTRATION GUIDE

*180 mg off-white to yellowish lyophilized powder in a single-dose vial*

## INDICATION

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.
- Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

## 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. Administer atropine, if not contraindicated, for early diarrhea of any severity. At the onset of late 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 61% of patients treated with TRODELVY. Grade 3-4 neutropenia occurred in 47% of patients. Febrile neutropenia occurred in 7%. 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.

**Diarrhea:** Diarrhea occurred in 65% of all patients treated with TRODELVY. Grade 3-4 diarrhea occurred in 12% of patients. One patient had intestinal perforation following diarrhea. Neutropenic colitis occurred in 0.5% of 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 additional Important Safety Information on the following pages, and click to see full Prescribing Information, including BOXED WARNING.**

# RECOMMENDED DOSING AND PREPARATION FOR TRODELVY

## Dosing[1]

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

- The recommended dose of TRODELVY is 10 mg/kg administered as an intravenous infusion once weekly on Days 1 and 8 of 21-day treatment cycles. Continue treatment until disease progression or unacceptable toxicity. Do not administer TRODELVY at doses greater than 10 mg/kg. Administer TRODELVY as an intravenous infusion only. Do not administer as an intravenous push or bolus
- **First infusion:** Administer infusion over 3 hours. Observe patients during the infusion and for at least 30 minutes following the initial dose for signs or symptoms of infusion-related reactions
- **Subsequent infusions:** Administer infusion over 1 to 2 hours if prior infusions were tolerated. Observe patients during the infusion and for at least 30 minutes after the infusion
- **Prior to each dose of TRODELVY:** Premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended
  - -Premedicate with antipyretics, H1 and H2 blockers prior to infusion, and corticosteroids may be used for patients who had prior infusion reactions
  - -Premedicate with a 2- or 3-drug combination regimen (eg, dexamethasone with either a 5-HT3 receptor antagonist or an $NK_1$ receptor antagonist, as well as other drugs as indicated)
- **For infusion-related reactions:** 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. Medication to treat infusion-related reactions, as well as emergency equipment, should be available for immediate use
- **For dose modifications for adverse reactions: Please see Table 1 in full Prescribing Information for more information.** Do not re-escalate the TRODELVY dose after a dose reduction for adverse reactions has been made

## Reconstitution[1,2]

TRODELVY is a cytotoxic drug. Follow applicable special handling and disposal procedures.

1. 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 previous administration).
2. Allow the required number of vials to warm to room temperature.
3. Using a sterile syringe, slowly inject 20 mL of 0.9% Sodium Chloride Injection, USP, into each 180 mg TRODELVY vial. The resulting concentration is 10 mg/mL.

   Please note, the target fill amount of drug product is 200 mg per each TRODELVY vial. The amount of drug indicated on the FDA-approved label (180 mg/vial) represents the minimum amount of drug possibly contained in the vial based on filling and extraction variability. Based on the target fill amount of 200 mg per vial, upon reconstitution with 20 mL of Sodium Chloride Injection, USP, following labeled instructions contained in the TRODELVY Prescribing Information, the resulting target concentration is 10 mg/mL.
4. Gently swirl vials and allow to dissolve for up to 15 minutes. Do not shake. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. The solution should be free of visible particulates, clear and yellow. Do not use the reconstituted solution if it is cloudy or discolored.
5. Use immediately to prepare a diluted TRODELVY infusion solution.

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## Dilution[1]

6. Calculate the required volume of the reconstituted TRODELVY solution needed to obtain the appropriate dose according to patient's body weight. Withdraw this amount from the vial(s) using a syringe. Discard any unused portion remaining in the vial(s).
7. Adjust the volume in the infusion bag as needed with 0.9% Sodium Chloride Injection, USP, to obtain a concentration of 1.1 mg/mL to 3.4 mg/mL (total volume should not exceed 500 mL). For patients whose body weight exceeds 170 kg, divide the total dosage of TRODELVY equally between two 500 mL infusion bags and infuse sequentially via slow infusion.
8. Slowly inject the required volume of reconstituted TRODELVY solution into a polyvinyl chloride, polypropylene or ethylene/propylene copolymer infusion bag, to minimize foaming. Do not shake the contents.
9. Only normal saline (0.9% Sodium Chloride Injection, USP) should be used since the stability of the reconstituted product has not been determined with other infusion-based solutions.
10. Use the diluted solution in the infusion bag immediately.

## If not used immediately:

**The infusion bag containing TRODELVY solution can be stored refrigerated 2°C to 8°C (36°F to 46°F) for up to 4 hours**

After refrigeration, administer diluted solution within 4 hours (including infusion time)

**Do not freeze or shake. Protect from light.**

## Administration[1]

- Administer TRODELVY as an intravenous infusion. Protect infusion bag from light
- An infusion pump may be used
- Do not mix TRODELVY, or administer as an infusion, with other medicinal products
- Upon completion of the infusion, flush the intravenous line with 20 mL 0.9% Sodium Chloride Injection, USP

## IMPORTANT SAFETY INFORMATION *(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 37% of patients. Grade 3-4 hypersensitivity occurred in 2% of patients. The incidence of hypersensitivity reactions leading to permanent discontinuation of TRODELVY was 0.3%.
The incidence of anaphylactic reactions was 0.3%. Pre-infusion medication is recommended. Observe patients closely for hypersensitivity and infusion-related reactions during each infusion and for at least 30 minutes after completion of each infusion. Medication to treat such reactions, as well as emergency equipment, should be available for immediate use. Permanently discontinue TRODELVY for Grade 4 infusion-related reactions.

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## IMPORTANT SAFETY INFORMATION *(cont'd)*

**Nausea and Vomiting:** Nausea occurred in 66% of all patients treated with TRODELVY and Grade 3 nausea occurred in 4% of these patients. Vomiting occurred in 39% of patients and Grade 3-4 vomiting occurred in 3% 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.

**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 67% in patients homozygous for the UGT1A1*28, 46% in patients heterozygous for the UGT1A1*28 allele and 46% in patients homozygous for the wild-type allele. The incidence of Grade 3-4 anemia was 25% in patients homozygous for the UGT1A1*28 allele, 10% in patients heterozygous for the UGT1A1*28 allele, and 11% 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.

**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 ASCENT study (IMMU-132-05)**, the most common adverse reactions (incidence ≥25%) were fatigue, neutropenia, diarrhea, nausea, alopecia, anemia, 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 TROPHY study (IMMU-132-06)**, the most common adverse reactions (incidence ≥25%) were diarrhea, fatigue, neutropenia, nausea, any infection, alopecia, anemia, decreased appetite, constipation, vomiting, abdominal pain, and rash. The most frequent serious adverse reactions (SAR) (≥5%) were infection (18%), neutropenia (12%, including febrile neutropenia in 10%), acute kidney injury (6%), urinary tract infection (6%), and sepsis or bacteremia (5%). SAR were reported in 44% of patients, and 10% discontinued due to adverse reactions. The most common Grade 3-4 lab abnormalities (incidence ≥25%) in the TROPHY study were reduced neutrophils, leukocytes, and lymphocytes.

### 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 substantially reduced in patients concomitantly receiving UGT1A1 enzyme inducers. Avoid administering UGT1A1 inducers with TRODELVY.

**Please click to see full Prescribing Information, including BOXED WARNING.**

**References: 1.** TRODELVY [package insert]. Foster City, CA: Gilead Sciences, Inc.; April 2021. **2.** Data on file. Gilead Sciences, Inc. 2021.

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