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PRACTICAL GUIDE TO TRODELVY®▼

(sacituzumab govitecan)

Dosing, administration, and management of key adverse events

Trodelvy® is 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 lines of systemic therapies, at least one of them given for unresectable locally advanced or metastatic disease[1]

TRODELVY®▼
sacituzumab govitecan
180 mg powder for concentrate for solution for infusion

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Information About Trodelvy®

What is Trodelvy®?[1]

Trodelvy® is a medicinal product also known as sacituzumab govitecan - or SG

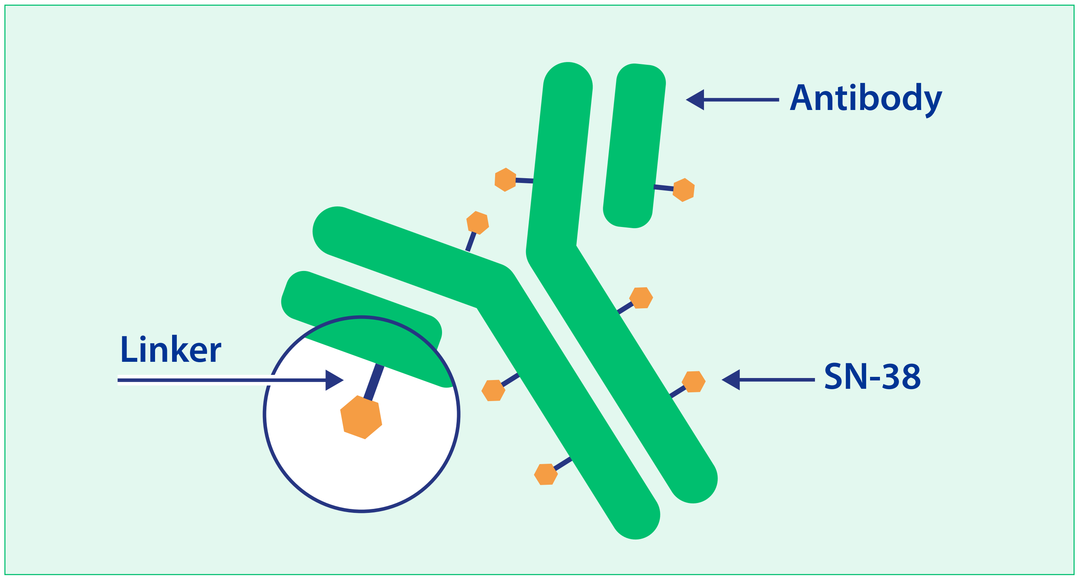
Trodelvy® is used to treat a type of breast cancer called metastatic triple-negative breast cancer (mTNBC)

Trodelvy® is indicated for the treatment of adult patients with unresectable locally advanced or mTNBC who have received two or more prior lines of systemic therapies, at least one of them given for unresectable locally advanced or metastatic disease

What is Trodelvy® made of?[1-4]

Trodelvy® is a type of medicine called an antibody-drug conjugate (ADC). Unlike traditional chemotherapy, Trodelvy® is made up of 3 parts:

- an antibody which recognises a protein called Trop-2
- an anticancer drug called SN-38
- a linker which connects the two other parts together



Adapted from Rugo H, et al. *Future Oncol*. 2020;16:705-715.

How does Trodelvy® work?[3]

Many triple-negative breast cancer cells have a higher-than-normal level of a protein called Trop-2 on their surface, which stimulates them to grow

Trodelvy® attaches to the Trop-2 proteins and delivers the chemotherapy drug SN-38 directly into the breast cancer cells to kill them

Trodelvy® also has a 'bystander effect'. This means it can kill neighbouring cancer cells, even if they do not have a higher level of Trop-2 on their surface

Proposed treatment pathway for Trodelvy®

In your adult patients with unresectable locally advanced or metastatic TNBC (not including *de novo* diagnoses):

Early stage TNBC

Any systemic neoadjuvant and/or adjuvant therapy

Locally advanced unresectable or metastatic TNBC

1st line — **Any systemic therapy**

2nd line — **Trodelvy®** **from 2nd line onwards for mTNBC, irrespective of time to progression or disease-free period following neoadjuvant/adjuvant therapy**

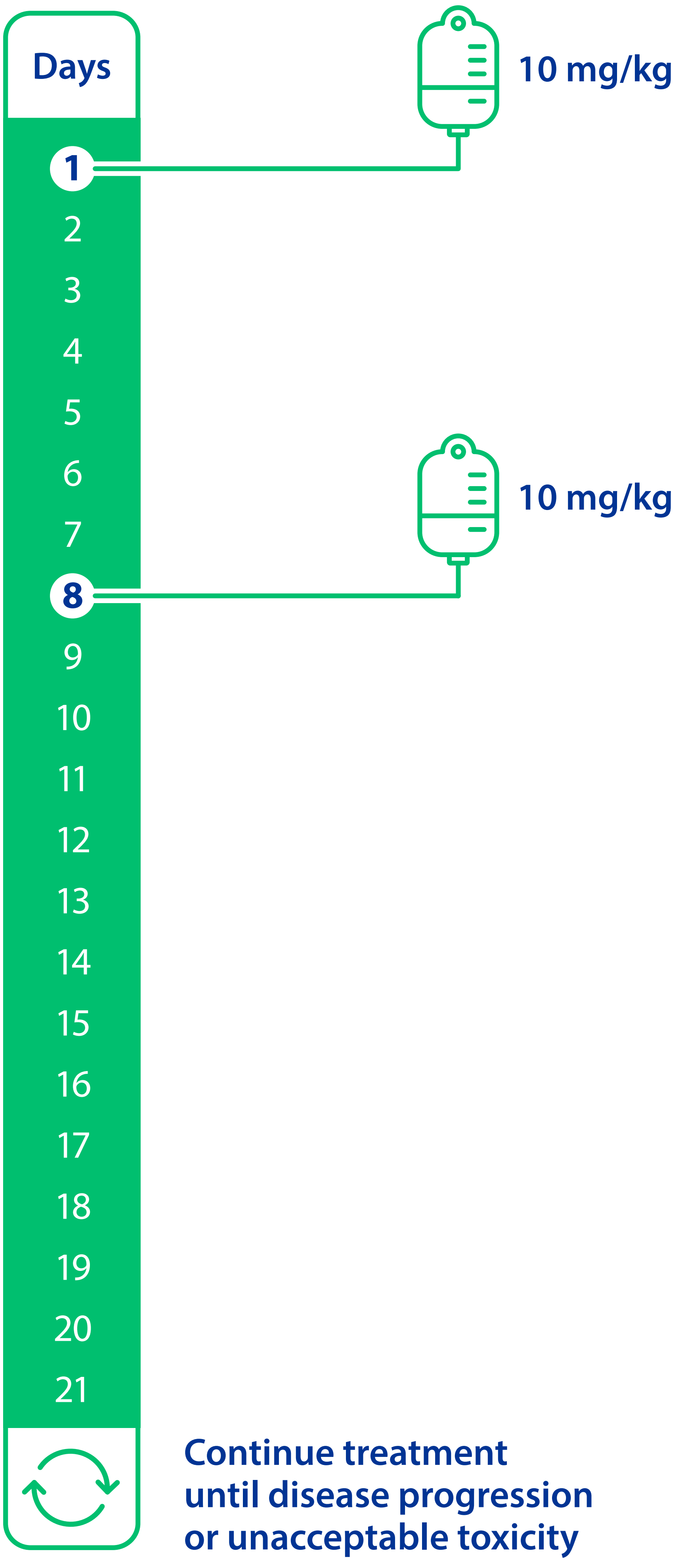
3rd line and later

For *de novo* locally advanced unresectable or metastatic TNBC patients, 2 prior lines of therapy must be given in this setting before Trodelvy®.

Dosing

The recommended dose of Trodelvy® is 10 mg/kg administered as an intravenous (IV) infusion once weekly on Days 1 and 8 of 21-day treatment cycles[1]. Continue treatment until disease progression or unacceptable toxicity

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 changed by more than 10% since the previous administration)[1]



Premedication

Prior to each dose of Trodelvy®, premedication for prevention of infusion reactions and prevention of chemotherapy-induced nausea and vomiting (CINV) is recommended[1]

Infusion Reactions

Pre-infusion medication for patients receiving Trodelvy® is recommended[1]

- Antipyretics
- H1 and H2 blockers prior to infusion
- Corticosteriods may be used for patients who had prior infusion reactions

Trodelvy® should be permanently discontinued if life-threatening infusion-related reactions occur[1]

Chemotherapy-Induced Nausea and Vomiting

Premedication with a 2- or 3-drug combination regimen is recommended to prevent chemotherapy-induced nausea and vomiting[1]

- E.g. dexamethasone with either a 5-HT3 receptor antagonist or an NK-1 antagonist, and other drugs as indicated

Additional antiemetics and other supportive measures may also be employed as clinically indicated[1]

All patients should be given take-home medications with clear instructions for prevention and treatment of nausea and vomiting[1]

Administration

Trodelvy® must only be prescribed and administered to patients by healthcare professionals experienced in the use of anti-cancer therapies and should be administered in an environment where resuscitation facilities are available

		Protect the infusion bag from sunlight An infusion pump may be used	
		First Infusion	**Subsequent Infusions**
Infusion Period		**3 hours**	**1-2 hours** (if prior infusions were tolerated)
Observation Period		Observe patients during the infusion and for ≥30 minutes after	
On Completion		Upon completion of the infusion, flush the intravenous line with 20 mL sodium chloride 0.9% solution for injection	

Special Warnings and Precautions

Neutropenia[1]

Trodelvy® can cause severe or life-threatening neutropenia

Trodelvy® should not be administered if the absolute neutrophil count is below 1500/mm^3 on Day 1 of any cycle or if the neutrophil count is below 1000/mm^3 on Day 8 of any cycle. Therefore, it is recommended that patients' blood counts are routinely tested prior to each dose of Trodelvy® and as clinically indicated

Trodelvy® should not be administered in case of neutropenic fever. Administration of G-CSF and dose reduction are required due to severe neutropenia or febrile neutropenia. Consider G-CSF for secondary prophylaxis

Hypersensitivity[1]

Trodelvy® can cause severe and life-threatening hypersensitivity

Anaphylactic reactions have been observed in clinical trials with Trodelvy® and the use of Trodelvy® is contraindicated in patients with a known hypersensitivity to sacituzumab govitecan

Other hypersensitivity events observed during and within 24 hours following the infusion included dyspnoea; rash; pruritus; hypotension; wheezing; oedema including facial and tongue; urticaria; and bronchospasm. Inform patients of the risk of serious infusion reactions and anaphylaxis

Medication to treat life-threatening hypersensitivity, as well as emergency equipment, should be available for immediate use

Instruct patients

- of the risk of severe and life-threatening hypersensitivity
- to immediately contact their healthcare team if they experience these signs and symptoms

Infusion-related reactions[1]

Pre-infusion medication for patients receiving Trodelvy® is recommended

Patients should be closely observed for infusion-related reactions during each Trodelvy® 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

The infusion rate of Trodelvy® should be slowed down or infusion interrupted if the patient develops an infusion-related reaction. Trodelvy® should be permanently discontinued if life-threatening infusion-related reactions occur

Special Warnings and Precautions continued...

Use in patients with reduced UGT1A1 activity[1]

Individuals who are homozygous for the uridine diphosphate-glucuronosyl transferase 1A1 (UGT1A1)*28 allele are at increased risk of severe neutropenia, severe diarrhoea, febrile neutropenia, and anaemia and may be at increased risk for other adverse reactions following initiation of Trodelvy® treatment

Patients with known reduced UGT1A1 activity should be closely monitored 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 activity

Traceability[1]

In order to improve traceability of biological medicinal products, clearly record the name and batch number of the administered product

Diarrhoea[1]

Trodelvy® can cause severe diarrhoea. Diarrhoea in some cases was observed to have led to dehydration and subsequent acute kidney injury

Trodelvy® should not be administered in case of Grade 3-4 diarrhoea at the time of scheduled treatment and treatment should only be continued when resolved to ≤ Grade 1

For information on the management of diarrhoea, see the practical management section included in this booklet

Patients who exhibit an excessive cholinergic response to treatment with Trodelvy® (e.g. abdominal cramping, diarrhoea, salivation, etc.) can receive appropriate premedication (e.g. atropine) for subsequent treatments

Instruct patients:[1]

- of the risk of diarrhoea and the need to be closely monitored
- to immediately contact their healthcare team if they experience diarrhoea for the first-time during treatment
- to immediately contact their healthcare team if they experience melena, haematochezia, dehydration, an inability to tolerate oral fluids or an inability to manage diarrhoea within 24 hours

Special Warnings and Precautions continued…

Nausea and vomiting[1]

Trodelvy® is emetogenic

Trodelvy® should not be administered in case of Grade 3 nausea or Grade 3-4 vomiting at the time of scheduled treatment administration and treatment should only be continued with additional supportive measures when resolved to ≤ Grade 1

For information on premedication management of nausea and vomiting, see the practical management section included in this booklet. 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

Pregnancy[1]

Trodelvy® is not recommended during pregnancy

Based on its mechanism of action, Trodelvy® can cause teratogenicity and /or embryo-foetal lethality when administered during pregnancy

Instruct female patients:

- to contact their healthcare team if they are pregnant or become pregnant
- of the risk to the foetus and potential loss of a pregnancy

Women of Childbearing Potential / Contraception in Males and Females[1]

The pregnancy status of women of childbearing potential should be verified prior to the initiation of Trodelvy®

Instruct female patients:

- to use effective contraception during treatment and for 6 months after the last dose

Instruct male patients:

- to use effective contraception during treatment with Trodelvy® and for 3 months after the last dose, with female partners of childbearing potential

Special Warnings and Precautions continued…

Breast-feeding[1]

It is unknown whether Trodelvy® or metabolites are excreted in human milk

Instruct female patients:

- breast-feeding should be discontinued during treatment with Trodelvy® and for 1 month after the last dose

Fertility[1]

Based on findings in animals, Trodelvy® may impair fertility in females of reproductive potential

Practical Management of Diarrhoea

1 Talk to patients about the possibility of experiencing diarrhoea while on Trodelvy®

- Encourage patients to immediately notify their hospital team if they experience diarrhoea for the first time during treatment[1]

2 Trodelvy® should not be administered if the patient is experiencing grade ≥3 diarrhoea at the time of scheduled treatment

- Treatment should only be continued when diarrhoea has resolved to Grade ≤ 1[1]

3 Initiate loperamide at the onset of diarrhoea unless an infectious cause is identified

- Promptly initiate loperamide 4 mg initially followed by 2 mg with every episode of diarrhoea for a maximum of 16 mg daily
- Discontinue loperamide 12 hours after diarrhoea resolves[1,4]

4 Dose modifications or interruptions may be required to manage persistent Grade ≥3 diarrhoea[1]

- Do not re-escalate the Trodelvy® dose after a dose reduction for toxicity has been made[1]

5 Initiate other supportive measures such as administration of fluids or electrolytes as clinically indicated[1]

No patients discontinued Trodelvy® due to diarrhoea in the ASCENT trial[1]

- No Grade 4 diarrhoea was reported[1]

Median time to onset of first diarrhoea (any grade) was 12 days[5]

Median duration of diarrhoea (any grade) was 5 days[5]

Practical Management of Nausea and Vomiting[1]

1 **Talk to patients about the possibility of experiencing nausea and/or vomiting while on Trodelvy®**

2 **All patients should receive take-home medications for preventing and treating nausea and vomiting, with instructions**

3 **Dose modifications may be required to manage severe nausea and vomiting[1]**

- Trodelvy® should not be administered in case of Grade 3 nausea or Grade 3-4 vomiting at the time of scheduled treatment
- Administration and treatment should only be continued with additional supportive measures when resolved to ≤ Grade 1
- Do not re-escalate the Trodelvy® dose after a dose reduction for toxicity has been made

4 **Additional antiemetics and other supportive measures may also be given as clinically indicated[1]**

Median time to onset of first nausea (any grade) was 8 days[5]

Median duration of nausea (any grade) was 5.5 days[5]

Median time to onset of first vomiting (any grade) was 24.5 days[5]

Median duration of vomiting (any grade) was 1.5 days[5]

Dose Modifications for Non-Neutropenic Toxicities

Dose modifications for severe non-neutropenic toxicity (diarrhoea, nausea and vomiting)[1]

Grade 4 non-hematologic toxicity which recovers to ≤ Grade 1 within 3 weeks

OR

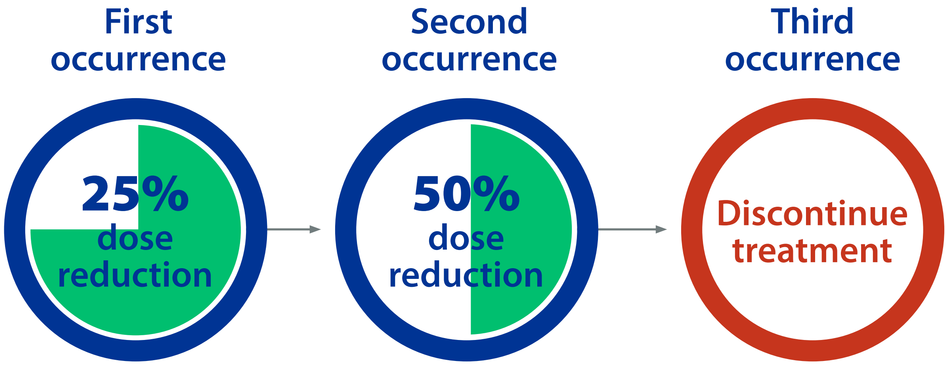
Any Grade 3-4 nausea, vomiting, or diarrhoea due to treatment that is not controlled with antiemetics and anti-diarrheal agents

OR

Other Grade 3-4 non-hematologic toxicity persisting >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



The Trodelvy® dose should not be re-escalated after a dose reduction for adverse reactions has been made

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In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, Grade 3 nausea or Grade 3-4 vomiting, which does not recover to ≤ Grade 1 within 3 weeks[1]

Practical Management of Neutropenia

1 **Talk to patients about the possibility of experiencing neutropenia while on Trodelvy®**

2 **Encourage patients to notify their healthcare team if they experience fever, chills or other signs of infection**

3 **Consider use of G-CSF to manage neutropenia**

- In ASCENT, G-CSF was not recommended prophylactically at the first dose and was used as needed in 49% of patients who received Trodelvy® vs 23% of those treated with SAC[4]

4 **Dose modifications may be required to manage severe neutropenia[1]**

- Trodelvy® should not be administered if the absolute neutrophil count is below 1500/mm^3 on Day 1 of any cycle or if the neutrophil count is below 1000/mm^3 on Day 8 of any cycle
- Trodelvy® shouldn't be administered in case of neutropenic fever

No patients permanently discontinued Trodelvy® due to neutropenia in the ASCENT trial[1]

- No patients had febrile neutropenia leading to permanent discontinuation[1]

Median time to onset of first neutropenia (any grade, including febrile neutropenia) was 20 days*[5]

Median duration of neutropenia (any grade) was 7 days[5]

*Neutropenia has occurred earlier in some patient populations (see SmPC for full details)

Dose modifications for Neutropenia

Dose modifications for severe neutropenia[1]

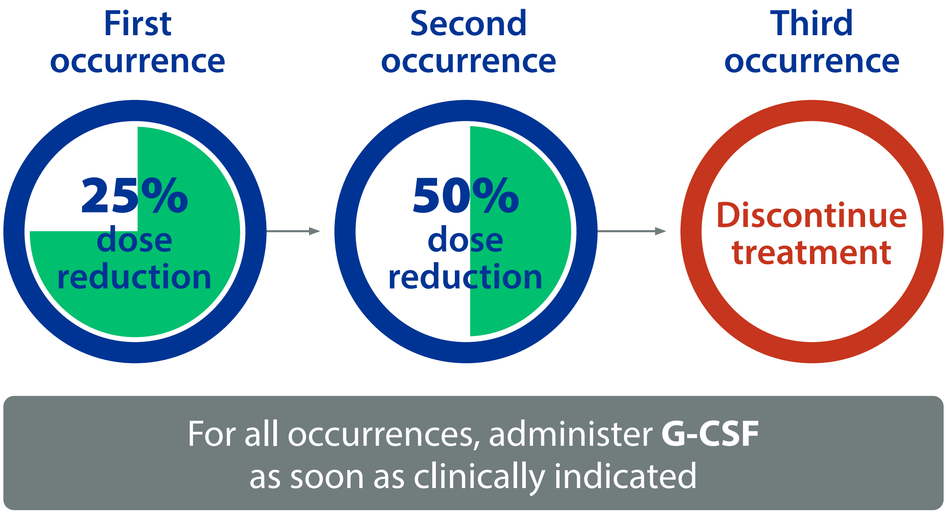
Grade 4 neutropenia ≥7 days or less if clinically indicated

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



For all occurrences, administer **G-CSF** as soon as clinically indicated

The Trodelvy® dose should not be re-escalated after a dose reduction for adverse reactions has been made[1]

At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤ Grade 1

Administer **G-CSF** as soon as clinically indicated

Dosing and administration checklist[1]

- Only administer Trodelvy® in an environment where resuscitation facilities and emergency anaphylactic equipment are available
- Record the name and batch number of Trodelvy®
- Check patients weight and adapt dose as necessary
- Administer pre-infusion medication to patient to prevent infusion related reactions and nausea and vomiting
- Check patients neutrophil count – to administer Trodelvy® the absolute neutrophil count should not be below 1500/mm^3 on Day 1 of any cycle and below 1000/mm^3 on Day 8 of any cycle
- Protect the infusion bag from sunlight and observe patients during the infusion, and for at least 30 minutes following the initial dose, for signs or symptoms of infusion-related reactions
- Check take-home medications with clear instructions for prevention and treatment of nausea and vomiting are available
- Go through patient checklist

Patient discussion checklist

At the end of the appointment, it might be helpful to use the checklist below to confirm you have covered all the necessary information with your patient, that they have understood the information given, and have had a chance to ask any questions they may have

A patient guide to treatment with Trodelvy® is additionally available for you to pass onto your patients

Ask your patient if they understand the following:

- **What treatment they have been recommended and why**
- **How they will receive treatment i.e. IV infusion**
- **How often they will get their treatment, and how much time each treatment will take**
- **How long they will be on treatment**
- **Where they will need to go to have their treatment**
- **What are the possible side effects of treatment and when they should contact their hospital team**
  - Include hypersensitivity, neutropenia, diarrhoea, nausea and vomiting as well as contraception, fertility, and pregnancy
  - It's important to reassure patients that in most cases adverse events can be managed with dose modifications and routine management strategies
- **Who to contact for help and support, and in case of emergencies**

Summary of recommended dose modifications for adverse reactions[1]

Adverse Reaction	Occurrence	Dose Modification
Severe Neutropenia		
Grade 4 neutropenia ≥ 7 days or less if clinically indicated **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	**1st**	25% dose reduction Administer G-CSF as soon as clinically indicated
	2nd	50% dose reduction Administer G-CSF as soon as clinically indicated
	3rd	Discontinue treatment Administer G-CSF as soon as clinically indicated
At time of scheduled treatment, Grade 3-4 neutropenia which delays dosing beyond 3 weeks for recovery to ≤ Grade 1	**1st**	Discontinue treatment
Severe Non-Neutropenic Toxicity		
Grade 4 non-hematologic toxicity which recovers to ≤ Grade 1 within 3 weeks **OR** Any Grade 3-4 nausea, vomiting or diarrhoea due to treatment that is not controlled with antiemetics and anti-diarrheal agents **OR** Other Grade 3-4 non-hematologic toxicity persisting > 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	**1st**	25% dose reduction
	2nd	50% dose reduction
	3rd	Discontinue treatment
In the event of Grade 3-4 non-neutropenic hematologic or non-hematologic toxicity, Grade 3 nausea or Grade 3-4 vomiting, which does not recover to ≤ Grade 1 within 3 weeks	**1st**	Discontinue treatment

Grading according to NCI-CTCAE v.4.03

Important Information[1]

The Trodelvy® dose should not be re-escalated after a dose reduction for adverse reactions has been made

The infusion rate of Trodelvy® should be slowed down or infusion interrupted if the patient develops an infusion related reaction

Trodelvy® should be permanently discontinued if life-threatening infusion-related reactions occur

References and Abbreviations

1. Trodelvy® (sacituzumab govitecan) Summary of Product Characteristics. Gilead Sciences Ltd. Available at: https://www.medicines.org.uk/emc/product/12880. Accessed: November 2023.
2. Goldenberg DM, et al. *Oncotarget*. 2015;6(26):22496-22512
3. Rugo HS, et al. *Future Oncol.* 2020;16(12):705-715
4. Bardia A, et al. *N Engl J Med*. 2021;384(16):1529-1541
5. Rugo H, et al. Poster. SABCS [virtual meeting]. 2020 (abstr PS11-09)

1L, first line; 2L, second line; ADC, antibody-drug conjugate; ASCENT, Trial of sacituzumab govitecan in participants with refractory/relapsed metastatic triple-negative breast cancer; G-CSF, Granulocyte-colony stimulating factor; IV, intravenous; mTNBC, metastatic triple-negative breast cancer; NCI-CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; Trop-2, trophoblast cell surface antigen 2

TRODELVY®
(sacituzumab govitecan)
prescribing information
is available **here**

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report suspected adverse reactions. Reporting suspected adverse reactions after authorisation of the medical product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

Adverse events should be reported.
For the UK, reporting forms and information can be found at www.mhra.gov.uk/yellowcard or via the Yellow Card app (download from the Apple App Store or Google Play Store).
Adverse events should also be reported to Gilead: safety_fc@gilead.com or +44 (0) 1223 897500
Trodelvy® is a biological medicine, healthcare professionals **should report adverse reactions by brand name and batch number**

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180 mg powder for concentrate for solution for infusion

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