Swiss Public Summary of the Risk Management Plan (RMP)

for

Trodelvy®180 mg, Powder for concentrate for solution for infusion

(Sacituzumab govitecan)

Version 3.0 (September 2024)
Based on EU RMP version 4.0 (Mar 2024)

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SUMMARY OF RISK MANAGEMENT PLAN FOR TRODELVY® (SACITUZUMAB GOVITECAN)

The Risk Management Plan (RMP) is a comprehensive document submitted as part of the application dossier for market approval of a medicine. The RMP summary contains information on the medicine's safety profile and explains the measures that are taken in order to further investigate and follow the risks as well as to prevent or minimize them.

The RMP summary of TRODELVY is a concise document and does not claim to be exhaustive.

As the RMP is an international document, the summary might differ from the „Arzneimittelinformation / Information sur le médicament“ approved and published in Switzerland, e.g. by mentioning risks occurring in populations or indications not included in the Swiss authorization.

Please note that the reference document which is valid and relevant for the effective and safe use of TRODELVY in Switzerland is the „Arzneimittelinformation / Information sur le médicament“ (see www.swissmedic.ch) approved authorized by Swissmedic. Gilead Sciences Switzerland Sàrl is fully responsible for the accuracy and correctness of the content of the here published summary RMP of TRODELVY.

I. The Medicine and What Is It Used For

TRODELVY is authorized as a monotherapy for the treatment of adult patients with unresectable or metastatic triple-negative breast cancer (mTNBC) who have received two or more prior systemic therapies, including at least one of them for advanced disease and for the treatment of adult patients with unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer who have received endocrine-based therapy, and at least two additional systemic therapies in the advanced setting (see SmPC for the full indication). It contains sacituzumab govitecan as the active substance and it is given as an intravenous infusion. Further information about the evaluation of TRODELVY’s benefits can be found in TRODELVY’s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine’s webpage https://www.ema.europa.eu/en/medicines/human/EPAR/trodelvy.

II. Risks Associated With the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of TRODELVY, together with measures to minimise such risks and the proposed studies for learning more about TRODELVY’s risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific Information, such as warnings, precautions, and advice on correct use, in the package leaflet (PL) and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;

- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the public (eg, with or without prescription) can help to minimise its risks.

Together, these measures constitute routine risk minimisation measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including periodic safety update report (PSUR) assessment, so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

If important information that may affect the safe use of TRODELVY is not yet available, it is listed under 'missing information' below.

II.A. List of Important Risks and Missing Information

Important risks of TRODELVY are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of TRODELVY. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (eg, on the long-term use of the medicine)

Table Part VI.1. List of Important Risks and Missing Information

Important Identified Risks	Serious infections secondary to neutropenia
Important Potential Risks	None
Missing Information	Use in patients with moderate or severe hepatic impairment
	Immunogenicity

II.B. Summary of Important Risks

TRODELVY has been assigned legal status of a medicine subject to medical prescription in the European Union (EU), whereby therapy should only be prescribed and administered by a healthcare professional experiences in the use of anti-cancer therapies (as described in section 4.2 of the SmPC).

Table Part VI.2. Summary of Important Risks and Missing Information

Important identified risk	**Serious infections secondary to neutropenia**
Evidence for linking the risk to the medicine	In the clinical studies 67.6% of 688 patients had neutropenia and in 50.7% of patients the neutropenia was severe. The dose of sacituzumab govitecan (SG) was interrupted in 44.2% and reduced in 12.4% of patients. Three patients (0.4%) discontinued SG because of neutropenia.

	Infections potentially associated with neutropenia occurred in 10.6% of 688 patients in the Overall Targeted metastatic breast cancer (mBC) population. Serious infections potentially associated with neutropenia occurred in 2.8% of 688 patients. The dose of SG was interrupted in 1.5% of patients, reduced in 0.4% if patients, and was discontinued in 0.3% of patients. Neutropenia was one of the main toxicities seen in animal studies. Clinical studies can provide an estimation of the frequency and nature of a side effect that is expected to occur in clinical practice. Findings from studies in animals may be relevant for humans and in the absence of data in humans suggest a potential safety concern that awaits clinical confirmation.
Risk factors and risk groups	Risk factors for neutropenia caused by cancer chemotherapies include increasing age, abnormal liver enzyme laboratory values, female gender, underweight, radiation therapy to the bone marrow, type of prior chemotherapy, and type of current treatment [Fontanella et al, 2014]. When SG is metabolised in the body, the active metabolite SN-38 is inactivated by an enzyme called uridine 5'-diphospho (UDP)-glucuronosyltransferase (UGT). Patients with reduced activity of this enzyme, such as patients who are homozygous for the *28 allele of UGT1A1, who are treated with SG have an increased risk of neutropenia and accordingly, an increased risk of serious infection.
Risk minimisation measures	Routine risk minimisation measures: • Dose modifications based on severity and occurrence in SmPC section 4.2 • Warnings of severe or life-threatening neutropenia, including fatal infections in the setting of neutropenia observed in clinical studies, in SmPC section 4.4 • Warning for UGTA1A1*28 allele homozygous patients in SmPC section 4.4 • Adverse reaction in SmPC section 4.8 • Guidance for treating severe neutropenia relating to overdose in SmPC section 4.9 • Warning in PL section 2 • Side effect in PL section 4 • Restricted medical prescription Additional risk minimisation measures: • None
Missing information	**Use in patients with moderate or severe hepatic impairment**
Risk minimisation measures	Routine risk minimisation measures: • Guidance that no dose adjustment is necessary for mild hepatic impairment in SmPC section 4.2 • Guidance that TRODELVY should be avoided in patients with moderate or severe hepatic impairment in SmPC section 4.2 • Information on SG exposure in patients with hepatic impairment in SmPC section 5.2 • Guidance for the patient to talk to their doctor or nurse if they have liver problems in PL section 2 • Restricted medical prescription Additional risk minimisation measures:

	• None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: • Study IMMU-132-15 See Section II.C of this summary for an overview of the postauthorisation development plan.
Missing information	**Immunogenicity**
Risk minimisation measures	Routine risk minimisation measures • Available clinical data on SG immunogenicity in SmPC section 4.8 • Restricted medical prescription Additional risk minimisation measures: • None

II.C. Postauthorisation Development Plan

II.C.1. Studies Which Are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of TRODELVY.

II.C.2. Other Studies in Postauthorisation Development Plan

Table Part VI.3. Other Studies in Postauthorisation Development Plan

Short Study Name	Purpose of the Study
Study IMMU-132-15 A Phase 1, Open-Label, Dose-Escalation Study to Determine an Appropriate Starting Dose of Sacituzumab Govitecan in Subjects with Advanced or Metastatic Solid Tumour and Moderate Liver Impairment	The purpose of this study is: To identify the safe starting dose of TRODELVY in subjects with solid tumour and moderate hepatic impairment. To evaluate the pharmacokinetics of TRODELVY, free SN-38, total SN-38, and SN-38G in subjects with solid tumour and moderate hepatic impairment. To assess the occurrences of human antibodies against TRODELVY in subjects with solid tumour and moderate hepatic impairment.

List of references for the RMP Public Summary

Fontanella C, Bolzonello S, Lederer B, et al. Management of breast cancer patients with chemotherapy-induced neutropenia or febrile neutropenia. Breast Care. 2014;9:239-245.

Gomes ER, Kuyucu S. Epidemiology and risk factors in drug hypersensitivity reactions. Curr Treat Options Allergy. 2017;4:239-257.

Stein A, Voigt W, Jordan K. Chemotherapy-induced diarrhea: pathophysiology, frequency and guideline-based management. Ther Adv Med Oncol. 2010;2(1):51-63.