Swiss Summary of the Risk Management Plan (RMP)

Tepkinly®

(Epcoritamab)

4 mg/0.8 ml and 48 mg/0.8 ml

Concentrate for solution for injection and
Solution for injection

Version 1 (15 February 2024)

Based on EU RMP, version 1.4, dated July 2023

AbbVie AG, Cham

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 minimise them. The RMP summary of Tepkinly® 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 Tepkinly® in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see www.swissmedic.ch) approved and authorized by Swissmedic. AbbVie AG is fully responsible for the accuracy and correctness of the content of the published summary RMP of Tepkinly®.

Part VI: Summary of the Risk Management Plan

I The Medicine and What it Is Used For

Epcoritamab as monotherapy is indicated for the treatment of adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL) after 2 or more lines of systemic therapy (see SmPC for the full indication). It contains epcoritamab as the active substance and it is given by subcutaneous injection.

Further information about the evaluation of epcoritamab's benefits can be found in Epcoritamab's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage.

II Risks Associated with the Medicine and Activities to Minimize or Further Characterize the Risks

Important risks of epcoritamab, together with measures to minimize such risks and the proposed studies for learning more about epcoritamab risks, are outlined below.

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

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and HCPs;
- Important advice on the medicine's packaging;
- The authorized 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 patient (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute **routine risk minimization** measures.

In the case of epcoritamab, these measures are supplemented **with additional risk minimization measures** mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including 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 epcoritamab is not yet available, it is listed under "missing information" below.

II.A List of Important Risks and Missing Information

Important risks of epcoritamab are risks that need special risk management activities to further investigate or minimize 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 epcoritamab. 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 (e.g., on the long-term use of the medicine).

List of Important Risks and Missing Information	
Important identified risks	CRS
	ICANS
	Serious Infections
Important potential risks	Risk of overdose due to medication errors
Missing information	Long-term safety

II.B Summary of Important Risks

Important identified risk: CRS	
Evidence for linking the risk to the medicine	Most frequent AE across epcoritamab clinical trials and literature (Salvaris 2021).
Risk factors and risk groups	No risk factors and no risk groups were identified in epcoritamab trials. Risks identified in literature include but not limited to: High disease burden, preexisting thrombocytopenia and endothelial activation, lymphodepleting therapy with fludarabine and cyclophosphamide, previous cardiovascular disease or organ dysfunction (Schubert 2021, Xiao 2021). Children seem to be at a higher risk of developing CRS than adults (Shimabukuro-Vornhagen 2018).
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.2 - Posology and method of administration includes Recommended Dose Modifications for CRS and CRS Grading and Management Guidance • SmPC Section 4.4 - Special warnings and precautions for use • SmPC Section 4.8 - Undesirable effects • Prescription-only medicine Additional risk minimization measure: • Patient Card
Additional PV activities	Additional PV activities: • Study GCT3013-05 See Section II.C of this summary for an overview of the post-authorization development plan.

Important identified risk: ICANS	
Evidence for linking the risk to the medicine	Epcoritamab clinical trials and literature (Salvaris 2021)
Risk factors and risk groups	No risk factors and no risk groups were identified in epcoritamab trials. Risks identified in literature include but not limited to: Early and severe CRS with high levels of inflammatory cytokines, high disease burden, preexisting thrombocytopenia and endothelial activation, lymphodepleting therapy with fludarabine and cyclophosphamide, preexisting neurologic comorbidities (Schubert 2021, Xiao 2021).
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.2 - Posology and method of administration includes Recommended Dose Modifications for ICANS and ICANS Grading and Management Guidance • SmPC Section 4.4 - Special warnings and precautions for use • SmPC Section 4.8 - Undesirable effects • Prescription-only medicine Additional risk minimization measure: • Patient Card
Additional PV activities	Additional PV activities: • Study GCT3013-05 See Section II.C of this summary for an overview of the post-authorization development plan.

Important identified risk: Serious Infections	
Evidence for linking the risk to the medicine	Epcoritamab clinical trials and literature (Longhitano 2021, Salvaris 2021)
Risk factors and risk groups	No risk factors and no risk groups were identified in epcoritamab trials. The epidemiology and risks for infections amongst patients managed with bispecific antibodies remain unclear (Longhitano 2021). Infections are more common in patients with advanced stage of disease, prolonged leukopenia, hypogammaglobulinemia, low granulocyte count, defective monocytes, reduced serum complement levels, longer length of disease, steroid use, bone marrow transplant recipients, and renal dysfunction. Patients with CRS are at a high risk of infection and the immunosuppressive treatment that is administered for the treatment of CRS can mask some of the signs of infection thereby delaying diagnosis and treatment of infections. The mechanism that is responsible for the increased incidence of infection in patients with CRS is unknown (Longhitano 2021, Shimabukuro-Vornhagen 2018).
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.4 - Special warnings and precautions for use • SmPC Section 4.8 - Undesirable effects • Prescription-only medicine
Additional PV activities	Additional PV activities: • Study GCT3013-05 See Section II.C of this summary for an overview of the post-authorization development plan.

Important potential risk: Risk of overdose due to medication errors	
Evidence for linking the risk to the medicine	Epcoritamab clinical trials
Risk factors and risk groups	No risk factors and no risk groups were identified in epcoritamab clinical trials.
Risk minimization measures	Routine risk minimization measures: • SmPC Section 4.2 - Posology and method of administration • SmPC Section 4.9 – Overdose • SmPC Section 6.6 – Special precautions for disposal and other handling • Prescription-only medicine

Missing information: Long-term safety	
Risk minimization measures	Routine risk minimization measures: • Prescription-only medicine
Additional PV activities	Additional PV activities: • Study GCT3013-01 • Study GCT3013-05 See Section II.C of this summary for an overview of the post-authorization development plan.

II.C Post-Authorization Development Plan

II.C.1 Studies Which are Conditions of the Marketing Authorization

The following studies are conditions of the marketing authorization:

GCT3013-01 summary

Purpose of the study:

The purpose of the dose escalation part of this trial is to establish the MTD of GEN3013 and the RP2D of GEN3013 in patients with R/R or progressive BCL.

The purpose of the expansion part of this trial is to evaluate the efficacy and safety of GEN3013 at the RP2D in patients with the following B-NHL with limited therapeutic options:

- Aggressive R/R B-NHL (aNHL cohort) including:
    - DLBCL
    - HGBCL
    - PMBCL
    - FL grade 3b
- Indolent R/R B-NHL (iNHL cohort) including:
    - FL grade 1 to 3a
    - MZL
    - SLL
- MCL

GCT3013-05 summary

Purpose of the study: The primary objective of this trial is to evaluate the efficacy of epcoritamab compared to IC of chemotherapy in subjects with R/R DLBCL, who have failed or are ineligible for HDT-ASCT.

II.C.2 Other Studies in Post-Authorization Development Plan

None