Swiss Public Summary of the Risk Management Plan (RMP)

for

TECARTUS®

(Brexucabtagene autoleucel)

Version 3.0 (September 2023)
Based on EU RMP Version 3.0 (May 2023)

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SUMMARY OF RISK MANAGEMENT PLAN FOR TECARTUS® (BREXUCABTAGENE AUTOLEUCEL)

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 Tecartus 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 Tecartus 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 Tecartus.

VI.2. The Medicine and What is it Used for

Tecartus is authorized for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) after two or more lines of systemic therapy including a Bruton’s tyrosine kinase (BTK) inhibitor and for the treatment of adult patients 26 years of age and above with relapsed or refractory B-cell acute lymphoblastic leukaemia (ALL) (see SmPC for the full indication). It contains brexucabtagene autoleucel as the active substance and it is given as a single infusion product for autologous and intravenous use only.

Further information about the evaluation of Tecartus’s benefits can be found in Tecartus’s EPAR, including in its plain-language summary, available on the European Medicines Agency (EMA) website, under the medicine’s webpage link to the EPAR summary landing page:

https://www.ema.europa.eu/en/medicines/human/EPAR/tecartus

VI.3. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Tecartus, together with measures to minimise such risks and the proposed studies for learning more about Tecartus’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 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 the case of Tecartus, these measures are supplemented with additional risk minimisation measures mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed (eg, via the periodic safety update report [PSUR]) 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 Tecartus is not yet available, it is listed under 'missing information' below.

VI.3.A List of Important Risks and Missing Information

Important risks of Tecartus 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 Tecartus. 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 neurologic events, including cerebral oedema
	Cytokine release syndrome (CRS)
	Cytopenias
	Infections
	Hypogammaglobulinaemia
Important Potential Risks	Secondary malignancy
	Immunogenicity
	Replication-competent retrovirus (RCR)
	Tumour lysis syndrome (TLS)
	Aggravation of graft versus host disease (GvHD)
Missing Information	New occurrence or exacerbation of an autoimmune disorder
	Long-term safety

VI.3.B Summary of Important Risks

Tecartus has been assigned the legal status of a medicine subject to medical prescription in the European Union (EU), whereby therapy must be administered in a qualified clinical setting, and be initiated by a doctor experienced in the management of haematological malignancies (as described in section 4.2 of the SmPC).

Table Part VI. 2. Summary of Important Risk(s) and Missing Information

Important Identified Risk	**Serious Neurologic Events including Cerebral Oedema**
Evidence for linking the risk to the medicine	Serious neurologic adverse events were reported in clinical trials, post-marketing surveillance, and in patients treated with other CAR T therapies.
Risk factors and risk groups	Female patients and subjects with higher ECOG performance status had a higher incidence of neurologic events.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC sections: 4.2, 4.4, 4.7,4.8 Package Leaflet (PL): 2, 4 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** HCP educational material Patient Alert Card (PAC) Controlled distribution
Additional Pharmacovigilance activities	KT-EU-472-5966: Q2 2024 ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan.
Important Identified Risk	**Cytokine Release Syndrome**

Evidence for linking the risk to the medicine	CRS was reported in clinical trials, post-marketing surveillance, and in patients treated with other CAR T therapies.
Risk factors and risk groups	A higher disease burden, older age, organ dysfunction and female gender were associated with a higher rate of CRS.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC sections: 4.2, 4.4, 4.8 PL section: 2, 4 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** HCP educational material PAC Controlled distribution program
Additional Pharmacovigilance activities	KT-EU-472-5966: Q2 2024 ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan.
Important Identified Risk	**Cytopenias**
Evidence for linking the risk to the medicine	Cytopenias were reported in clinical trials, post-marketing surveillance, and in patients treated with other CAR T therapies.
Risk factors and risk groups	Prior exposure to chemotherapy or radiation.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC sections: 4.4, 4.8 PL section: 2, 4 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan
Important Identified Risk	**Infections**
Evidence for linking the risk to the medicine	Infections were reported in clinical trials, post-marketing surveillance, and in patients treated with other CAR T therapies.
Risk factors and risk groups	Patient factors: Underlying immune deficiencies, medical comorbidities, past infections, poor nutritional status, and psychological stress. Additive or synergistic factors: Surgery, radiation, immunosuppressant therapies, antimicrobial use, and invasive procedures.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC sections: 4.4, 4.8

	PL section: 2, 4 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan
Important Identified Risk	**Hypogammaglobulinaemia**
Evidence for linking the risk to the medicine	Hypogammaglobinemia was reported in clinical trials and in patients treated with other CAR T therapies.
Risk factors and risk groups	Prior treatment with rituximab and concomitant use of other drugs (eg, steroids) that can induce hypogammaglobulinaemia.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC sections: 4.4, 4.8 PL section: 4 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan
Important Potential Risk	**Secondary Malignancy**
Evidence for linking the risk to the medicine	No secondary malignancies were attributed to brexucabtagene autoleucel in clinical trials or post-marketing experience.
Risk factors and risk groups	Patient factors: Age Additive or synergistic factors: Chemotherapy and immunosuppressive treatments
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC section: 4.4 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan.
Important Potential Risk	**Immunogenicity**

Evidence for linking the risk to the medicine	No brexucabtagene autoleucel related confirmed cases of immunogenicity were seen in ZUMA-2. In ZUMA-3, 2 subjects were confirmed to have antibodies to the anti CD19 CAR after brexucabtagene autoleucel infusion. One of these subjects was confirmed to be antibody-positive after retreatment with brexucabtagene autoleucel.
Risk factors and risk groups	None known.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC section: 4.8 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan
Important Potential Risk	**RCR**
Evidence for linking the risk to the medicine	There is no evidence for the occurrence of RCR in patients treated with Tecartus.
Risk factors and risk groups	Not applicable
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan.
Important Potential Risk	**TLS**
Evidence for linking the risk to the medicine	There have been low numbers of reports of TLS in clinical trials and none reported postmarketing.
Risk factors and risk groups	Patient factors: Tumor size and presence of bulky tumor, wide metastatic dispersal, and organ and/or bone marrow involvement. Patients' health status, including presence of hypotension, dehydration, acidic urine, oliguria, pre-cancer nephropathy, and previous experience with nephrotoxic agents. Additive or synergistic factors: Medications and other compounds that tend to increase uric acid levels.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC section: 4.4 PL section: 2 Use restricted to physicians experienced in the treatment of haematological cancers

	Additional risk minimisation measures: None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan.
Important Potential Risk	**Aggravation of Graft versus Host Disease (GvHD)**
Evidence for linking the risk to the medicine	There have been low numbers of reports of GvHD in clinical trials and none reported postmarketing.
Risk factors and risk groups	Patients who had undergone a prior allo-HSCT and then received donor derived CAR T cells (from prior allo-HSCT donor) appear to be at an increased risk of developing aggravation of GvHD or GvHD.
Risk Minimisation Measure(s)	**Routine risk minimisation measures:** SmPC section: 4.4 PL section: 2 Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan
Missing information	**New occurrence or exacerbation of an autoimmune disorder**
Risk Minimization Measures	**Routine risk minimisation measures:** Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan
Missing information	**Long term safety**
Risk Minimisation Measures	**Routine risk minimisation measures:** Use restricted to physicians experienced in the treatment of haematological cancers **Additional risk minimisation measures:** None
Additional Pharmacovigilance activities	ZUMA-8: Dec 2036 See section VI.3.C of this summary for an overview of the post-authorisation development plan

VI.3.C Post-authorization Development Plan

VI.3.C.1. Studies Which Are Conditions of the Marketing Authorization

Table Part VI. 3. Studies as Condition of the Marketing Authorization

Short Study Name	Purpose of the Study
KT-EU-472-6036	A prospective study to confirm the long-term efficacy and safety of Tecartus in adult patients with all indications and the Benefit/Risk in subgroups: elderly, females, patients with severe disease. Further evaluation of efficacy, additional characterisation of the identified risks, further evaluation of potential risks and missing information. This study will be designed as an efficacy and safety long-term follow up study.
ZUMA-3	Primar objective of Phase 1: To evaluate the safety of brexucabtagene autoleucel Primary objective of Phase 2: To evaluate the efficacy of brexucabtagene autoleucel, as measured by the overall complete remission rate defined as complete remission and complete remission with incomplete hematologic recovery in adult subjects with relapsed/refractory ALL. Secondary objectives: Assessing the safety and tolerability of brexucabtagene autoleucel, additional efficacy endpoints, and change in EQ-5D scores.
Specific obligation for ALL	Long-term efficacy and safety of Tecartus in adult patients with relapsed/refractory ALL.

VI.3.C.2 Other Studies in Post-authorisation Development Plan

Table Part VI. 4. Other Studies in Post-Authorisation Development Plan

Short Study Name	Purpose of the Study
KT-EU-472-5966	Evaluating the effectiveness of risk minimisation activities: HCP educational material and Patient Alert Card
KTE-C19-108 (ZUMA-8)	To evaluate the safety and tolerability of brexucabtagene autoleucel in adult subjects with relapsed/refractory CLL and SLL

This summary was last updated in September 2023.