SWISS SUMMARY OF THE RISK MANAGEMENT PLAN

FOR

TUKYSA™ (TUCATINIB)

50 mg film-coated tablets
150 mg film-coated tablets

Swissmedic Authorisation Number: 67798

Marketing authorisation holder:Seagen International GmbH , Dammstrasse 23, 6300 Zug , Switzerland

Based on Swiss RMP Version 1.0, dated 16June 2021, derived from company core RMP (DLP 16April2021)

DISCLAIMER:

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 TUKYSA 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 authorisation. Please note that the reference document which is valid and relevant for the effective and safe use of TUKYSA in Switzerland is the „Arzneimittelinformation/Information sur le médicament“ (see www.swissmedicinfo.ch) approved and authorised by Swissmedic.

Seagen International GmbH is fully responsible for the accuracy and correctness of the content of this published summary RMP of TUKYSA.

SUMMARY OF THE RISK MANAGEMENT PLAN

Summary of Risk Management Plan for TUKYSA™

This is a summary of the risk management plan (RMP) for TUKYSA. The RMP details how additional safety information will be obtained about TUKYSA's risks and uncertainties (missing information) on an ongoing basis over time.

This summary of the RMP for TUKYSA should be read in the context of other relevant safety information including the assessment report of the evaluation and its plain-language summary, all of which is part of the SwissPAR.

Important new concerns or changes to the current ones will be included in updates of TUKYSA's RMP.

I. The medicine and what it is used for

TUKYSA is authorised in combination with trastuzumab and capecitabine for the treatment of patients with metastatic HER2-positive breast cancer, who have previously received 2 or more anti-HER2 regimens in any setting, including trastuzumab, pertuzumab and trastuzumab-emtansine (T-DM1).

It contains tucatinib (INN) as the active substance and it is given orally.

Further information about the evaluation of TUKYSA's benefits can be found in TUKYSA's SwissPAR, including in its plain-language summary, available on Swissmedic Website (www.swissmedic.ch).

II. Risks associated with the medicine and activities to minimise or further characterize the risks

Important risks of TUKYSA, together with measures to minimise such risks and the proposed studies for learning more about TUKYSA'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 Information for Healthcare Professionals addressed to subjects and healthcare professionals, such as warnings, precautions, and advice on correct use;
- 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.

In addition to these measures, information about adverse events is collected continuously, regularly analyzed, and included in periodic safety update reports (PSURs) so that immediate action can be taken if necessary. These measures constitute routine pharmacovigilance activities.

II.A. List of Important Risks and Missing Information

Important risks of TUKYSA 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. Important identified risks are concerns for which there is sufficient proof of a link with the use of tucatinib. Important 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).

List of Important Risks and Missing Information	
Important identified risks	Diarrhoea Hepatotoxicity
Important potential risks	Embryo-foetal toxicity
Missing information	Patients with prior cumulative anthracycline doses equivalent to >360 mg/m^2 doxorubicin Patients who are known carriers of hepatitis B and/or hepatitis C, or who have auto-immune hepatitis, sclerotizing cholangitis, or other known chronic liver disease Long-term safety

II.B. Summary of Important Risks

Important identified risk: Diarrhoea	
Risk minimisation measures	Routine risk communication: • Swiss Information for Healthcare Professionals: "Warnings and precautions", "Dosage/administration", and "Undesirable effects" sections Routine risk minimisation activities recommending specific clinical measures to address the risk: • Recommendation for diagnostic tests clinically indicated to exclude infectious causes are included in Swiss Information for Healthcare Professionals: "Warnings and precautions" section Other risk minimisation measures beyond the Information for Healthcare Professionals: • None
Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • Standard Adverse Experience Reporting Form Additional pharmacovigilance activities: • SGNTUC-016 and SGNTUC-017 See Section II.C of this summary for an overview of the post-authorisation development plan.

Important identified risk: Hepatotoxicity	
Risk minimisation measures	Routine risk communication: • Swiss Information for Healthcare Professionals: "Warnings and precautions", "Dosage/administration", and "Undesirable effects" sections Routine risk minimisation activities recommending specific clinical measures to address the risk: • Recommendations for liver function monitoring are included in Swiss Information for Healthcare Professionals: "Warnings and precautions" section Other risk minimisation measures beyond the Information for Healthcare Professionals: • None
Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • Hepatic Event Questionnaire Additional pharmacovigilance activities: • SGNTUC-016 and SGNTUC-017 See Section II.C of this summary for an overview of the post-authorisation development plan.

Important potential risk: Embryo-foetal toxicity	
Risk minimisation measures	Routine risk communication:

Important potential risk: Embryo-foetal toxicity	
	• Swiss Information for Healthcare Professionals: "Warnings and precautions", "Pregnancy, lactation" sections Routine risk minimisation activities recommending specific clinical measures to address the risk: • Recommendation for verification of pregnancy status in women of childbearing potential prior to initiating treatment with tucatinib is included in Swiss Information for Healthcare Professionals: "Pregnancy, lactation" section • Recommendation for males and females of reproductive potential to use contraception during and up to at least 1 week after treatment is included in Swiss Information for Healthcare Professionals: "Warnings and precautions", "Pregnancy, lactation" sections Other risk minimisation measures beyond the Information for Healthcare Professionals: • None
Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • None Additional pharmacovigilance activities: • SGNTUC-016 and SGNTUC-017 See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing information: Patients with prior cumulative anthracycline doses equivalent to >360 mg/m^2 doxorubicin	
Risk minimisation measures	Routine risk communication: • None Routine risk minimisation activities recommending specific clinical measures to address the risk: • None Other risk minimisation measures beyond the Information for Healthcare Professionals : • None
Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • Standard Adverse Experience Reporting Form Additional pharmacovigilance activities: • SGNTUC-016 See Section II.C of this summary for an overview of the post-authorisation development plan.

Missing information: Patients who are known carriers of hepatitis B and/or hepatitis C, or who have auto-immune hepatitis, sclerotizing cholangitis, or other known chronic liver disease	
Risk minimisation measures	Routine risk communication for hepatotoxicity:

	• Swiss Information for Healthcare Professionals: "Warnings and precautions", "Dosage/administration", and "Undesirable effects" sections Routine risk minimisation activities recommending specific clinical measures for hepatotoxicity to address the risk: • Recommendations for liver function monitoring are included in Swiss Information for Healthcare Professionals: "Warnings and precautions" section Other risk minimisation measures beyond the Information for Healthcare Professionals: • None
Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • Hepatic Event Questionnaire Additional pharmacovigilance activities: • None

Missing information: Long term safety	
Risk minimisation measures	Routine risk communication: • None Routine risk minimisation activities recommending specific clinical measures to address the risk: • None Other risk minimisation measures beyond the Information for Healthcare Professionals: • None
Pharmacovigilance activities	Routine pharmacovigilance activities beyond adverse reactions reporting and signal detection: • None Additional pharmacovigilance activities: • SGNTUC-016 and SGNTUC-017 See Section II.C of this summary for an overview of the post-authorisation development plan.**Error! Reference source not found.**

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 TUKYSA.

II.C.2 Other Studies in Postauthorisation Development Plan

SGNTUC-016 (HER2CLIMB-02)

This is a randomized, double-blind, placebo-controlled, international, multicenter, phase 3 study designed to evaluate the efficacy and safety of tucatinib in combination with T-DM1 in subjects with unresectable locally advanced/metastatic HER2+ breast cancer who have had prior treatment with a taxane and trastuzumab in any setting.

SGNTUC-017 (MOUNTAINEER)

This is a multicenter, randomized, open-label, Phase 2 study of tucatinib, administered as monotherapy and in combination with trastuzumab, in subjects with HER2-positive, RAS wild-type, unresectable or metastatic colorectal cancer.