Tezspire®

Solution for injection in pre-filled syringe
210 mg/1.91 ml (110 mg/ml)

Summary of the Risk Management Plan (RMP) for Tezspire® (tezepelumab)

Document version: 2.0

Document date: 5 May 2023

Based on EU RMP version 1.4 (DLP 9 Dec 2021)

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

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN FOR TEZSPIRE™ (TEZEPELUMAB)

This is a summary of the risk management plan (RMP) for TEZSPIRE™. The RMP details important risks of TEZSPIRE, how these risks can be minimised, and how more information will be obtained about TEZSPIRE's risks and uncertainties (missing information).

TEZSPIRE's Summary of Product Characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how tezepelumab should be used.

This summary of the RMP for TEZSPIRE should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

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

I.1 THE MEDICINE AND WHAT IT IS USED FOR

The proposed indication of TEZSPIRE is as an add-on maintenance treatment in adults with severe asthma (see SmPC for the full indication). It contains tezepelumab as the active substance and it is given/self-administered by subcutaneous injection.

I.2 RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS

Important risks of TEZSPIRE, together with measures to minimise such risks and the proposed studies for learning more about TEZSPIRE'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 patient (e.g. 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 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 tezepelumab is not yet available, it is listed under 'missing information' below.

I.2.1 List of Important Risks and Missing Information

Important risks of TEZSPIRE 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 TEZSPIRE. 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 I-1 List of Important Risks and Missing Information

Important identified risks	None
Important potential risks	Serious infections Serious cardiac events Malignancy
Missing information	Use in pregnant and breastfeeding women Long-term use (> 1 year)

I.2.2 Summary of Important Risks

Table I-2 Important Potential Risk: Serious Infections

Evidence for linking the risk to the medicine	Although there is a theoretical risk of infection based on the mechanism of action of tezepelumab, there were no imbalances in the incidence of serious infections observed in the tezepelumab and placebo groups in the Primary Safety Pool or the long-term extension study D5180C00018.
Risk factors and risk groups	No specific factors or subgroups of patients have been identified in respect of increased potential risk of infection with tezepelumab.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section Warnings and precautions and Package Leaflet Section When is caution required when using TEZSPIRE? Additional risk minimisation measures: None
Additional pharmacovigilance activities	Study D5180C00024 - 28-week OCS-reduction study in severe asthma Study D5180C00021 - 52-week China/Asia regional efficacy and safety study in severe asthma

SmPC, Summary of Product Characteristics.

Table I-3 Important Potential Risk: Serious Cardiac Events

Evidence for linking the risk to the medicine	A numeric imbalance in serious cardiac events was observed in Study D5180C00018, however, there were no imbalances in overall cardiac events (serious and non-serious) in the Primary Safety Pool or the long-term extension study D5180C00018.
Risk factors and risk groups	There is no evidence of a specific factor that would increase the risk of fatal cardiac events in subjects receiving tezepelumab, and no specific subgroup of patients who may be at an increased risk of serious cardiac events has been identified.
Risk minimisation measures	Routine risk minimisation measures: SmPC Section Warnings and precautions and Package Leaflet Section When is caution required when using TEZSPIRE? Additional risk minimisation measures: None
Additional pharmacovigilance activities	Study D5180C00024 - 28-week OCS-reduction study in severe asthma Study D5180C00021 - 52-week China/Asia regional efficacy and safety study in severe asthma Serious cardiac events post-authorisation safety study

SmPC, Summary of Product Characteristics.

Table I-4 Important Potential Risk: Malignancy

Evidence for linking the risk to the medicine	Malignancies have been reported in the completed asthma studies of tezepelumab. The incidence of malignancies reported was low and similar across tezepelumab and placebo treatment groups in the Primary Safety Pool and in the long-term study D5180C00018 including up to 2 years of treatment. However, longer-term exposure data are not available, and a potential theoretical risk of malignancy remains.
Risk factors and risk groups	No specific risk factors or subgroups of patients have been identified in respect of potential malignancy risk for patients treated with tezepelumab.
Risk minimisation measures	None
Additional pharmacovigilance activities	Study D5180C00024 - 28-week OCS-reduction study in severe asthma Study D5180C00021- 52-week China/Asia regional efficacy and safety study in severe asthma

SmPC, Summary of Product Characteristics.

Table I-5 Missing Information: Use in Pregnant and Breastfeeding Women

Risk minimisation measures	Routine risk minimisation measures: SmPC Section Pregnancy, lactation and Package Leaflet Section Can TEZSPIRE be used during pregnancy or breast feeding? Additional risk minimisation measures: None
Additional pharmacovigilance activities	Study D5180R00010 - Database study of the use (and safety) of tezepelumab in women with severe asthma during pregnancy

SmPC, Summary of Product Characteristics.

Table I-6 Missing Information: Long-term Use (> 1 Year)

Risk minimisation measures	Routine risk minimisation measures: None Additional risk minimisation measures: None
Additional pharmacovigilance activities	Study D5180C00018 (DESTINATION) - Phase 3 safety extension study to evaluate the safety and tolerability of tezepelumab in adults and adolescents with severe uncontrolled asthma.

I.2.3 Post-Authorisation Development Plan

I.2.3.1 Studies Which Are Conditions of the Marketing Authorisation

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

I.2.3.2 Other Studies in Post-authorisation Development Plan

Tezepelumab Pregnancy Study (D5180R00010)

Study title: Study of the Use (and Safety) of Tezepelumab in Women with Severe Asthma During Pregnancy

Purpose of the study: The proposed study has the following objectives:

- Stage 1: To monitor the use of tezepelumab in pregnant women with severe asthma to inform the initiation of Stage 2.
- Stage 2:
  - To describe pregnancy and delivery outcomes in pregnancies among women with severe asthma exposed to tezepelumab at any time during pregnancy. Outcomes will be assessed by trimester of exposure as a secondary objective.
  - To compare frequency of outcomes in pregnant women exposed to tezepelumab with that in those not exposed to tezepelumab.

DESTINATION - Long-term Extension Study (D5180C00018)

Study title: A Multicentre, Double-blind, Randomized, Placebo Controlled, Parallel Group, Phase 3, Safety Extension Study to Evaluate the Safety and Tolerability of Tezepelumab in Adults and Adolescents with Severe Uncontrolled Asthma

Purpose of the study: The primary objective of this long-term extension study is to evaluate the long-term safety and tolerability of 210 mg tezepelumab SC Q4W in severe asthma subjects. The secondary objective is to assess the long-term effect of 210 mg tezepelumab subcutaneously administered every 4 weeks on asthma exacerbations in adult and adolescent subjects with severe uncontrolled asthma compared with placebo.

(This study is not classified as a post-authorisation safety study.)

SUNRISE – OCS reduction study in severe asthma (D5180C00024)

Study Title: A Randomised, Double-Blind, Parallel-Group, Placebo-Controlled 28-week Phase 3 Efficacy and Safety Study of Tezepelumab in Reducing Oral Corticosteroid Use in Adults with Oral Corticosteroid Dependent Asthma

Purpose of the study: To demonstrate the ability of tezepelumab, compared with placebo, to reduce OCS use in adults with severe asthma being treated with maintenance OCS in combination with high dose ICS and LABA, with or without other asthma controller therapies, while maintaining asthma control.

DIRECTION – China/Asia regional efficacy and safety study in severe asthma (D5180C00021)

Study Title: A Regional, Multicentre, Randomized, Double-Blind, Placebo Controlled, Parallel Group, 52-week Phase 3 Study to Evaluate the Efficacy and Safety of Tezepelumab in Adults with Severe Uncontrolled Asthma

Purpose of the study: To confirm the efficacy and safety of 210 mg dose of tezepelumab administered SC Q4W in adults (18 to 80 years of age inclusive) with a history of asthma exacerbations and severe, uncontrolled asthma receiving medium or high dose ICS plus at least one additional asthma controller medication with or without OCS. The study will evaluate the incidence of asthma exacerbations and other efficacy parameters such as lung function, asthma control and quality of life as well as a safety evaluation to further characterise the benefit-risk profile of the drug.

Serious cardiac events post-authorisation safety study

Study title: A Non-Interventional Multi-Country Post-Authorisation Safety Study (PASS) to Assess the Incidence of Serious Cardiac Events in Patients with Severe Uncontrolled Asthma Exposed to Tezepelumab

Purpose of the study: To evaluate possible effects of tezepelumab exposure in patients with severe asthma on serious cardiac events. The overall objective of the study is to compare the incidence of serious cardiac events in patients with severe uncontrolled asthma newly exposed to tezepelumab with the incidence in comparable severe uncontrolled asthma patients exposed to other standard of care regimens.