# Summary of Risk Management Plan

**CINQAERO®** (reslizumab)

Concentrate for solution for infusion, 100mg/10ml and 25mg/2.5ml

Teva Pharma AG

RMP Version: 4.1

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

# Part VI: Summary of the Risk Management Plan

## Summary of Risk Management Plan for Reslizumab (CINQAERO®)

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

Reslizumab's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Reslizumab should be used.

This summary of the RMP for Reslizumab 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 Reslizumab's RMP.

## I. The Medicine and What It is used for

Reslizumab (CINQAERO®) is authorised for treatment of severe eosinophilic asthma in adult patients, 18 years of age and over, when the condition is not well controlled despite treatment with high dose inhaled corticosteroids together with another asthma medicine (see SmPC for the full indication). It contains Reslizumab as the active substance and it is given intravenously.

Further information about the evaluation of Reslizumab (CINQAERO®)'s benefits can be found in Reslizumab (CINQAERO®)'s EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage*:*
*https://www.ema.europa.eu/en/medicines/human/EPAR/cinqaero.*

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

Important risks of Reslizumab, together with measures to minimise such risks and the proposed studies for learning more about Reslizumab'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 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 Reslizumab (CINQAERO®) is not yet available, it is listed under 'missing information' below.

## II.A List of Important Risks and Missing Information

Important risks of Reslizumab 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 Reslizumab. 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);

**Table 24: Summary of Safety Concerns**

| **List of important risks and missing information** | |
|---|---|
| **Important identified risks** | • Severe hypersensitivity reactions, including anaphylactic or anaphylactoid reactions |
| **Important potential risks** | • Malignancy<br>• Medication errors related to possible confusion between the two vial presentations |
| **Missing information** | • Use during pregnancy<br>• Use in breastfeeding |

## II.B Summary of Important Risks

**Table 25: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern**

| **Important identified risk: Severe hypersensitivity reactions, including anaphylactic or anaphylactoid reactions** | |
|---|---|
| Evidence for linking the risk to the medicine | Acute systemic reactions, including anaphylactic reactions, have been reported in association with reslizumab. These adverse reactions were observed during or within 20 minutes after completion of the infusion. Patients should be monitored during and for an appropriate time after administration of reslizumab. If an anaphylactic reaction occurs, administration of reslizumab should be stopped immediately and appropriate medical treatment should be provided; reslizumab must be discontinued permanently. |
| Risk factors and risk groups | Limited data suggested that patients with history of multiple drug allergies, history of NSAID pseudo-anaphylaxis, or multiple allergic hypersensitivities may be at increased risk.<br>Female patients may be at increased risk. |

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|---|---|
| Risk minimisation measures | Routine risk minimisation measures<br>SmPC section 4.2, 4.3, 4.4, 4.8 and 6.6.<br>PL section 2, 3 and 4.<br>Prescription only medicine.<br>Reslizumab (CINQAERO®) should be prescribed by physicians experienced in the diagnosis and treatment of severe eosinophilic asthma.<br>Additional risk minimisation measures<br>None. |
| **Important potential risk: Malignancy** | |
| Evidence for linking the risk to the medicine | A literature search indicated that the risk of cancer in asthma patients may be elevated compared to the general population.<br>In placebo-controlled clinical studies, 6 out of 1,028 patients (0.6%) receiving 3 mg/kg reslizumab had at least one malignant neoplasm reported compared to 2 out of 730 patients (0.3%) in the placebo group. The malignancies observed in reslizumab-treated patients were diverse in nature and without clustering of any particular tissue type. |
| Risk factors and risk groups | No specific group identified. |
| Risk minimisation measures | Routine risk minimisation measures<br>SmPC section 4.8.<br>Prescription only medicine.<br>Reslizumab (CINQAERO®) should be prescribed by physicians experienced in the diagnosis and treatment of severe eosinophilic asthma.<br>Additional risk minimisation measures<br>None. |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>Assessment of potential risk of malignancy in patients with severe asthma treated with reslizumab: a cohort study using secondary administrative healthcare data.<br>See section II.C of this summary for an overview of the post-authorisation development plan. |
| **Important potential risk: Medication errors related to possible confusion between the two vial presentations** | |
| Evidence for linking the risk to the medicine | No data regarding this potential risk is currently available, however risk of medication errors related to possible confusion between the two vial presentations cannot be excluded if both are available in that market. |
| Risk factors and risk groups | It is evaluated that the risk of confusion between vial sizes for reslizumab is similar to risk of such errors presented by other parenteral drugs with multiple presentations and has similar triggers. However, it is acknowledged that HCPs involved in reslizumab prescribing and administration that have previously used reslizumab 100 mg vial with the weight-based dosing regimen and now have to switch to the new VBD, are more prone to errors due to their previous awareness of one-vial availability only. |
| Risk minimisation measures | Routine risk minimisation measures<br>SmPC section 2, 4.2 and 6.6.<br>Prescription only medicine.<br>Reslizumab (CINQAERO®) should be prescribed by physicians experienced in the diagnosis and treatment of severe eosinophilic asthma.<br>Artwork and product design. |

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|---|---|
| | Additional risk minimisation measures<br>None. |
| **Missing information: Use during pregnancy** | |
| Risk minimisation measures | Routine risk minimisation measures<br>SmPC section 4.6.<br>PL section 2.<br>Prescription only medicine<br>Additional risk minimisation measures<br>None. |
| Additional pharmacovigilance activities | Additional pharmacovigilance activities:<br>Active Pregnancy Surveillance Programme<br>See section II.C of this summary for an overview of the post-authorisation development plan. |
| **Missing information: Use in breastfeeding** | |
| Risk minimisation measures | Routine risk minimisation measures<br>SmPC section 4.6.<br>PL section 2.<br>Prescription only medicine.<br>Additional risk minimisation measures<br>None. |

## II.C Post-Authorisation 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 Reslizumab (CINQAERO®).

### II.C.2 Other Studies in Post-Authorisation Development Plan

**Table 26: List of Studies in Post Authorisation Development Plan**

| Study/Status | Purpose of the study |
|---|---|
| Active Pregnancy Surveillance Programme | The primary objective of this study is to examine pregnant women exposed to reslizumab during pregnancy and to evaluate pregnancy outcomes of major birth defects. The secondary objective is to characterise other maternal and foetal outcomes, including pre-term birth, spontaneous abortions, and stillbirth. |
| Assessment of potential risk of malignancy in patients with severe asthma treated with reslizumab: a cohort study using secondary administrative healthcare data | The primary objective of this study is to assess the risk of malignancy in patients with severe asthma comparing patients treated with reslizumab and patients treated with non-reslizumab asthma medications in a real-world clinical practice setting. |