

## **ACTEMRA®**

**Konzentrat zur Herstellung einer Infusionslösung, Zul.-Nr. 58'868**

**Injektionslösung zur subkutanen Anwendung, Zul.-Nr. 63'166**

**Injektionslösung zur subkutanen Anwendung, Fertigpen, Zul.-Nr. 66'931**

### *Public Risk Management Plan (RMP) Summary*

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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 medicinal products. 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 "Actemra" 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 "Actemra" in Switzerland is the "Arzneimittelinformation / Information sur le médicament" (see [www.swissmedic.ch](http://www.swissmedic.ch)) approved and authorized by Swissmedic. "Roche Pharma (Schweiz) AG" is fully responsible for the accuracy and correctness of the content of the published summary RMP Actemra.

## **PART VI: SUMMARY OF THE RISK-MANAGEMENT PLAN FOR ROACTEMRA (TOCILIZUMAB)**

This is a summary of the Risk Management Plan for RoActemra. The RMP details important risks of RoActemra, how these risks can be minimized, and how more information will be obtained about RoActemra risks and uncertainties (missing information).

RoActemra Summary of Product Characteristics and its package leaflet give essential information to healthcare professionals and patients on how RoActemra should be used.

This summary of the RMP for RoActemra 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 RoActemra RMP.

### **I. THE MEDICINE AND WHAT IT IS USED FOR**

RoActemra is authorized for rheumatoid arthritis, systemic juvenile idiopathic arthritis, juvenile idiopathic polyarthritis, giant cell arteritis, cytokine release syndrome induced by CAR T cell therapies, and COVID-19 (see SmPC for the full indication). It contains tocilizumab as the active substance and it is given by intravenous infusion or subcutaneous injection.

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

### **II. RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMISE OR FURTHER CHARACTERISE THE RISKS**

Important risks of RoActemra, together with measures to minimize such risks and the proposed studies for learning more about RoActemra 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 healthcare professionals;
- 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 (e.g., with or without prescription) can help to minimize its risks.

Together, these measures constitute *routine risk minimization* measures. In the case of RoActemra, these measures are supplemented with *additional risk minimization* measures mentioned under relevant risks, below.

In addition to these measures, information about adverse events 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 RoActemra is not yet available, it is listed under ‘missing Information’ below.

## II.A LIST OF IMPORTANT RISKS AND MISSING INFORMATION

Important risks of RoActemra 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 RoActemra. 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                      | <ul style="list-style-type: none"> <li>• Serious infection *</li> <li>• Complications of diverticulitis *</li> <li>• Neutropenia</li> <li>• Hepatotoxicity</li> </ul>                           |
| Important potential risks                       | <ul style="list-style-type: none"> <li>• Elevated lipid levels and the potential risk of cardiovascular and cerebrovascular events</li> <li>• Malignancies</li> <li>• Immunogenicity</li> </ul> |
| Missing information                             | None                                                                                                                                                                                            |

\* The safety concerns “serious infection” and “complications of diverticulitis” are considered important identified risks for chronic TCZ dosing, but are assessed as important potential risks for the indication of COVID-19.

## II.B Summary of Important Risks

| <b>Important Identified Risk: Serious infections *</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
|--------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Evidence for linking the risk to the medicine          | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Risk factors and risk groups                           | Patients with diabetes reported a higher rate of serious infections compared to patients without diabetes. Patients treated with TCZ and taking background corticosteroids reported a higher rate of serious infections compared to patients not taking background corticosteroids. The rate of serious infections appears to increase by body weight. Healthcare professionals should exercise caution when considering the use of TCZ in patients with a history of recurring or chronic infections or with underlying conditions (e.g., diverticulitis, diabetes, and ILD which may predispose patients to infections).                                                                                                                                                                                                                                                                      |
| Risk minimization measures                             | <p><b>Routine risk measure:</b><br/> <b><u>SmPC</u></b><br/> <b>IV and SC formulation:</b><br/>           Section 4.3 Contraindications Active, severe infections (see Section 4.4)<br/>           Section 4.4 Special warnings and precautions for use<br/>           Section 4.8 Undesirable effects</p> <p><b><u>Patient Information Leaflet:</u></b><br/> <b>IV and SC Formulation</b><br/>           Section 2. What you need to know before you are given TCZ<br/>           Section 4 Possible serious side effects: tell a doctor straightaway.</p> <p><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b><br/>           None</p> <p><b>Other risk minimization measures beyond the Product Information:</b><br/>           Pack size: None<br/>           Medicine's legal status: RoActemra is a prescription only medicine</p> |

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|                                                                     | <b>Additional risk minimization measures:</b> Patient Card                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Additional pharmacovigilance activities                             | <b>Additional pharmacovigilance activities:</b><br>Epidemiology data <ul style="list-style-type: none"> <li>• EU registries (Ongoing: WA29358)</li> <li>• EU registries :(Completed: RABBIT)</li> </ul><br>See Section <a href="#">II.C</a> of this summary for an overview of the post-authorization development plan.                                                                                                                                                                                                                                                                                                                             |
| <b>Important Identified Risk: Complications of Diverticulitis *</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Evidence for linking the risk to the medicine                       | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Risk factors and risk groups                                        | TCZ should be used with caution in patients with previous history of intestinal ulceration or diverticulitis.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Risk minimization measures                                          | <b>Routine risk minimization measure:</b><br><b><u>SmPC</u></b><br>Section 4.4 Special warnings and precautions for use<br>Section 4.8 Undesirable effects<br><b><u>Patient Information Leaflet:</u></b><br>Section 2 Warnings and precautions<br>Section 4 Possible side effects<br><br><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b><br>None<br><br><b>Other risk minimization measures beyond the Product Information:</b><br>Pack size: None<br>Medicine's legal status: RoActemra is a prescription only medicine<br><br><b>Additional risk minimization measures:</b> Patient Card |
| Additional pharmacovigilance activities                             | <b>Additional pharmacovigilance activities:</b><br>Epidemiology data <ul style="list-style-type: none"> <li>• EU registries (Ongoing: WA29358)</li> <li>• EU registries :(Completed: RABBIT)</li> </ul><br>See Section <a href="#">II.C</a> of this summary for an overview of the post-authorization development plan.                                                                                                                                                                                                                                                                                                                             |

| <b>Important Identified Risk: Neutropenia</b>    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
|--------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Evidence for linking the risk to the medicine    | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Risk factors and risk groups                     | None identified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Risk minimization measures                       | <p><b>Routine risk communication:</b><br/> <b>SmPC</b><br/>           Section 4.2 Posology and method of administration<br/>           Section 4.4 Special warnings and precautions for use<br/>           Section 4.8 Undesirable effects/Laboratory evaluations</p> <p><b>Patient Information Leaflet</b><br/>           Section 4 Possible Side Effects</p> <p><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b><br/>           None</p> <p><b>Other risk minimization measures beyond the Product Information:</b><br/>           Pack size: None<br/>           Medicine's legal status: RoActemra is a prescription only medicine</p> <p>Additional risk minimization measures: NA</p> |
| Additional pharmacovigilance activities          | <p><b>Additional pharmacovigilance activities:</b></p> <ul style="list-style-type: none"> <li>• EU registries (Ongoing: WA29358)</li> <li>• EU registries :(Completed: RABBIT)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| <b>Important Identified Risk: Hepatotoxicity</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Evidence for linking the risk to the medicine    | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Risk factors and risk groups                     | Treatment with other hepatotoxic drugs (e.g., MTX).                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Risk minimization measures                       | <p><b>Routine risk communication:</b><br/> <b>SmPC</b><br/>           Section 4.2 Posology and method of administration (IV formulation)<br/>           Section 4.4 Special warnings and precautions for use</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |

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|                                                                                                                            | <p>Section 4.8 Undesirable effects</p> <p><b>Patient Information Leaflet</b><br/>(IV/SC formulation)<br/>Section 2 Warning and precautions<br/>Section 4 Possible side effects</p> <p><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b><br/>In patients with RA, GCA, pJIA, sJIA, ALT and AST should now be monitored every 4 to 8 weeks for the first 6 months of treatment followed by every 12 weeks thereafter.</p> <p><b>Other risk minimization measures beyond the Product Information:</b><br/>Pack size: None<br/>Medicine's legal status: RoActemra is a prescription only medicine</p> <p><b>Additional risk minimization measures:</b> Patient Card</p> |
| Additional pharmacovigilance activities                                                                                    | <p><b>Additional pharmacovigilance activities:</b></p> <ul style="list-style-type: none"> <li>• EU registries (Ongoing: WA29358)</li> <li>• EU registries :(Completed: RABBIT)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| <p><b>Important Potential Risk : Elevated Lipid Levels and Potential Risk of Cardiovascular/Cerebrovascular Events</b></p> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Evidence for linking the risk to the medicine                                                                              | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Risk factors and risk groups                                                                                               | Not identified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Risk minimization measures                                                                                                 | <p><b>Routine risk minimization measures:</b><br/><b>SmPC</b><br/>Section 4.4 Special warnings and precautions for use<br/>Section 4.8 Undesirable effects<br/><b>Patient Information Leaflet</b><br/>Section 2 Warnings and precautions<br/>Section 4 Possible side effects</p> <p><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b></p>                                                                                                                                                                                                                                                                                                                           |

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|-----------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                               | <p>None</p> <p><b>Other risk minimization measures beyond the Product Information:</b><br/> Pack size: None<br/> Medicine's legal status: RoActemra is a prescription only medicine</p> <p><b>Additional risk minimization measures: NA</b></p>                                                                                                                                                                                                                                                                         |
| Additional pharmacovigilance activities       | <p><b>Additional pharmacovigilance activities:</b></p> <ul style="list-style-type: none"> <li>• EU registries (Ongoing: WA29358)</li> <li>• EU registries :(Completed: RABBIT)</li> </ul> <p>See Section <a href="#">II.C</a> of this summary for an overview of the post-authorization development plan.</p>                                                                                                                                                                                                           |
| <b>Important Potential Risk: Malignancies</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Evidence for linking the risk to the medicine | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                                                                                              |
| Risk factors and risk groups                  | None identified                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Risk minimization measures                    | <p><b>Routine risk communication:</b><br/> <b>SmPC</b><br/> Section 4.4 Special warnings and precautions for use<br/> Section 4.8 Undesirable effects</p> <p><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b><br/> None</p> <p><b>Other risk minimization measures beyond the Product Information:</b><br/> Pack size: None<br/> Medicine's legal status: RoActemra is a prescription only medicine</p> <p><b>Additional risk minimization measures: NA</b></p> |

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| Additional pharmacovigilance activities          | <b>Additional pharmacovigilance activities:</b> <ul style="list-style-type: none"> <li>• EU registries (Ongoing: WA29358)</li> <li>• EU registries :(Completed: RABBIT)</li> </ul> <p>See Section <a href="#">II.C</a> of this summary for an overview of the post-authorization development plan.</p>                                                                                                                                               |
| <b>Important Potential Risk : Immunogenicity</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Evidence for linking the risk to the medicine    | Adequate and well-controlled clinical trials and their long-term extensions, as described within this RMP, provide the strongest evidence.                                                                                                                                                                                                                                                                                                           |
| Risk factors and risk groups                     | Not identified                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| Risk minimization measures                       | <b>Routine risk minimization measures:</b><br><b>SmPC</b><br>Section 4.8 Undesirable effects<br><br><b>Routine risk minimization activities recommending specific clinical measures to address the risk:</b><br>None<br><br><b>Other risk minimization measures beyond the Product Information:</b><br>Pack size: None<br>Medicine's legal status: RoActemra is a prescription only medicine<br><br><b>Additional risk minimization measures:</b> NA |
| Additional pharmacovigilance activities          | <b>Additional pharmacovigilance activities:</b><br>None<br><br>See Section <a href="#">II.C</a> of this summary for an overview of the post-authorization development plan.                                                                                                                                                                                                                                                                          |

IV=Intravenous; SC=Subcutaneous; SmPC=Summary of Product Characteristics; TCZ=Tocilizumab.

\* The safety concerns “serious infection” and “complications of diverticulitis” are considered important identified risks for chronic TCZ dosing, but are assessed as important potential risks for the indication of COVID-19.

## **II.C POST-AUTHORIZATION DEVELOPMENT PLAN**

### **II.C.1 Studies That Are Conditions of the Marketing Authorization**

There are no studies which are conditions of the marketing authorization or specific obligation of RoActemra.

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

#### **Study short name: WA29358**

Purpose of the study: To provide long-term safety and efficacy data from the use of TCZ in pJIA patients.