

Summary of the Risk Management Plan (RMP) for SARCLISA®

SARCLISA® (Isatuximab)

Marketing Authorisation Holder : sanofi-aventis (suisse) sa

RMP version 1.6

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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 minimize them. The RMP summary of SARCLISA® 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 SARCLISA® in Switzerland is the "Arzneimittelinformation/ Information sur le médicament" (see www.swissmedicinfo.ch) approved and authorized by Swissmedic. Sanofi-aventis (suisse) sa is fully responsible for the accuracy and correctness of the content of this published summary RMP of SARCLISA®.

I.THE MEDICINE AND WHAT IT IS USED FOR

According to Swiss label

SARCLISA is indicated in:

- in combination with pomalidomide and dexamethasone for the treatment of relapsed and refractory multiple myeloma in adult patients who have received at least two prior lines of therapy, including lenalidomide and a proteasome inhibitor, and who have experienced disease progression on the last line of therapy.
- in combination with carfilzomib and dexamethasone for the treatment of multiple myeloma in adult patients who have received at least 1 to 3 prior lines of therapy.

According to EU SmPC

SARCLISA is authorized:

- in combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor and have demonstrated disease progression on the last therapy.
- in combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.

It contains isatuximab as the active substance and it is given by intravenous infusion.

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

<https://www.ema.europa.eu/en/medicines/human/EPAR/sarclisa>

II.RISKS ASSOCIATED WITH THE MEDICINE AND ACTIVITIES TO MINIMIZE OR FURTHER CHARACTERIZE THE RISKS

Important risks of SARCLISA, together with measures to minimize such risks and the proposed studies for learning more about SARCLISA's risks, are outlined in the next sections.

Measures to minimize the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the PL and SmPC addressed to patients and HCP;
- 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 (eg, with or without prescription) can help to minimize its risks.

Together, these measures constitute routine risk minimization measures.

In the case of SARCLISA, these measures are supplemented with additional risk minimization measures (aRMMs) mentioned under relevant important risks, outlined in the next sections.

In addition to these measures, information about adverse reactions is collected continuously and regularly analyzed, including periodic safety update report (PSUR) assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

II.A List of important risks and missing information

Important risks of SARCLISA 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 SARCLISA. 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 1 - List of important risks and missing information

Important identified risks	Interference for blood typing (minor antigen) (positive indirect Coombs' test)
Important potential risks	Viral reactivation
Missing information	None

II.B Summary of important risks

Table 2 - Important identified risk: Interference for blood typing (minor antigen) (positive indirect Coombs' test) with corresponding risk minimization activities and additional pharmacovigilance activities

Interference for blood typing (minor antigen) (positive indirect Coombs' test)	
Evidence for linking the risk to the medicine	Class effect: isatuximab binds to RBCs and may interfere with routine blood bank compatibility tests. Interference for blood typing has occurred during clinical trials.

Interference for blood typing (minor antigen) (positive indirect Coombs' test)	
Risk factors and risk groups	Patients with MM may require blood transfusions (as it has occurred in 30% of the patients in the isatuximab arm of study EFC14335 and in 26% of the patients in the isatuximab arm of the study EFC15246), because of morbidity from MM and its treatment.
Risk minimization measures	<p>Routine risk minimization measures:</p> <p>SmPC sections 4.4 and 4.5.</p> <p>PL section 2.</p> <p>Legal status: Available only on prescription. Isatuximab should be administered by a HCP, in an environment where resuscitation facilities are available (SmPC section 4.2).</p> <p>Additional risk minimization measures:</p> <p>Healthcare Professionals and blood banks educational material (brochure) and patient card.</p>

HCP: Healthcare Professional; MM: Multiple Myeloma; PL: Package Leaflet; RBC: Red Blood Cell; SmPC: Summary of Product Characteristics.

Table 3 - Important potential risk: Viral reactivation with corresponding risk minimization activities and additional pharmacovigilance activities

Viral reactivation	
Evidence for linking the risk to the medicine	Viral reactivation has been identified for another anti-CD38 antibody approved for the treatment of MM.
Risk factors and risk groups	<p><u>Documented previous viral exposure:</u></p> <ul style="list-style-type: none"> •For HBV: serology; •For Herpes Zoster: clinical evidence of Herpes simplex exposure (eg, shingles); •Any other viruses: standard evidence of viral exposure. <p><u>Immunosuppression:</u></p> <ul style="list-style-type: none"> •History of previous treatment with immunosuppressive drugs such as high dose corticosteroids; (33) •Clinical or laboratory data supportive of immunosuppression.

Risk minimization measures	Routine risk minimization measures: SmPC and PL: Not labeled. Additional risk minimization measures: None
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CD: Cluster of Differentiation; HBV: Hepatitis B Virus; MM: Multiple Myeloma; PL: Package Leaflet; SmPC: Summary of Product Characteristics.

VI II.C Post-authorization development plan

II.C.I *Studies which are conditions of the marketing authorization*

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

II.C.II *Other studies in post-authorization development plan*

There are no studies for SARCLISA.