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

SARCLISA® (isatuximab)
Marketing Autorisation Holder : sanofi-aventis (suisse) sa
RMP version 1.2
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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. This RMP summary 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 medicament" 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 the product in Switzerland is the "Arzneimittelinformation/ Information sur le medicament" (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 RMP summary.

1. THE MEDICINE AND WHAT IT IS USED FOR

According to Swiss label

SARCLISA is indicated, in combination with pomalidomide and dexamethasone, for the treatment of adult patients with relapsed and refractory multiple myeloma (MM) who have received at least two prior lines of therapy including lenalidomide and a proteasome inhibitor (PI) and have demonstrated disease progression on the last 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 (see section 5.1).

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 (EMA) website, under the medicine's webpage:

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

2. 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 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 (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 mentioned under relevant important risks, outlined in the next sections.

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

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

2.2. 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.
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.

Interference for blood typing (minor antigen) (positive indirect Coombs' test)	
Risk minimization measures	**Routine risk minimization measures:** SmPC Sections 4.4 and 4.5. PL Section 2. **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). **Additional risk minimization measures**: Healthcare Professionals and blood banks educational material (including brochure and patient card).
Additional pharmacovigilance activities	○ Non-interventional PASS survey to evaluate the effectiveness of the isatuximab educational materials, to minimize the risk of interference for blood typing (minor antigen) (positive indirect Coombs' test). ○ Study TED16414

HCP: Healthcare Professional; MM: Multiple Myeloma; PASS: Post-Authorization Safety Study; 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	Documented previous viral exposure: ○ For HBV: serology; ○ For Herpes Zoster: clinical evidence of Herpes simplex exposure (eg, shingles); ○ Any other viruses: standard evidence of viral exposure. Immunosuppression: ○ History of previous treatment with immunosuppressive drugs such as high dose corticosteroids; (1) ○ Clinical or laboratory data supportive of immunosuppression.
Risk minimization measures	**Routine risk minimization measures**: SmPC and PL: not labeled **Additional risk minimization measures**: None

CD: Cluster of Differentiation; HBV: Hepatitis B Virus; MM: Multiple Myeloma; PL: Package Leaflet; SmPC: Summary of Product Characteristics.

2.3. Post-authorisation development plan

2.3.1. Studies which are conditions of the marketing authorisation

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

2.3.2. Other studies in post-authorisation development plan

Table 4 - Other studies in post-authorization development plan

Non-interventional PASS survey to evaluate the effectiveness of the isatuximab educational materials, to minimize the risk of interference for blood typing (minor antigen) (positive indirect Coombs' test)
Purpose of the study: To assess HCP's/Blood banks awareness, knowledge and behaviour with respect to the minimization of the risk of interference for blood typing with isatuximab.

HCP: Healthcare Professional; PASS: Post-Authorization Safety Study

A Phase 1b/2 study to evaluate the safety, pharmacokinetics, and preliminary efficacy of isatuximab (SAR650984) in patients awaiting kidney transplantation (Study TED16414)
Purpose of the study: • Phase 1: to characterize the safety and tolerability of isatuximab in kidney transplant candidates. • Phase 2: to evaluate the efficacy of isatuximab in desensitization of patients awaiting kidney transplantation.

REFERENCES

1. Asthana A, Lubel J. Reactivation of latent viruses after treatment with biological therapies. Virus Adaptation and Treatment. 2014 Jun;6:1-10.