Summary of risk management plan for SARCLISA (Isatuximab)

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

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

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

1. THE MEDICINE AND WHAT IT IS USED FOR

SARCLISA is an anti-cancer medicine that contains the active substance isatuximab. It belongs to a group of medicines called "monoclonal antibodies". SARCLISA is used to treat "multiple myeloma (MM)". This is a type of cancer of your bone marrow.

SARCLISA is used together with two other medicines called pomalidomide and dexamethasone. This treatment is for adult patients with relapsed and refractory MM who have received at least two treatments for MM before and have demonstrated disease progression on the last 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 (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 minimisation measures.

In the case of SARCLISA, these measures are supplemented with additional risk minimisation 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 with indirect antiglobulin test (indirect Coombs test) and possible resulting adverse clinical consequences for the patient (bleeding due to transfusion delay, transfusion haemolysis)
Important potential risk	Viral reactivation
Missing information	None

2.2. Summary of important risks

Table 2 – Important identified risk: Interference with indirect antiglobulin test (indirect Coombs test) and possible resulting adverse clinical consequences for the patient (bleeding due to transfusion delay, transfusion haemolysis) with corresponding risk minimization activities and additional pharmacovigilance activities

Interference with indirect antiglobulin test (indirect Coombs test) and possible resulting adverse clinical consequences for the patient (bleeding due to transfusion delay, transfusion haemolysis)	
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 study EFC14335), because of morbidity from MM and its treatment.
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 PAC).
Additional pharmacovigilance activities	• Non-interventional PASS survey to measure the effectiveness of the isatuximab educational materials, to minimize the risk of interference with indirect antiglobulin test and possible resulting adverse clinical consequences for the patient (bleeding due to transfusion delay, transfusion haemolysis) • Study TED16414

HCP: Healthcare Professional; MM: Multiple Myeloma; PAC: Patient Alert Card; 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 [a] • Clinical or laboratory data supportive of immunosuppression

Viral reactivation	
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.

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

2.3. Post-authorization development plan

2.3.1. Studies which are conditions of the marketing authorization

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

2.3.2. Other studies in post-authorization development plan

Table 4 - Other studies in post-authorization development plan

Non-interventional PASS survey to measure the effectiveness of the isatuximab educational materials, to minimize the risk of interference with indirect antiglobulin test and possible resulting adverse clinical consequences for the patient (bleeding due to transfusion delay, transfusion haemolysis)
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.