Sarclisa® (isatuximab) Abbreviated Prescribing Information

This Abbreviated Prescribing Information is based on the EU Summary of Product Characteristics (SPC). **Name and Presentation:** SARCLISA 20mg/mL concentrate for solution for infusion. Each vial contains 500 mg of isatuximab in 25 mL of concentrate (500 mg/25mL). Isatuximab is an immunoglobulin G1 (IgG1) monoclonal antibody (mAb). **Therapeutic indications:** 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 therapies including lenalidomide and a proteasome inhibitor (PI) 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. In combination with bortezomib, lenalidomide, and dexamethasone, for the treatment of adult patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplant. **Dosage and administration:** SARCLISA should be administered by a healthcare professional, in an environment where resuscitation facilities are available. Premedication should be used 15-60 minutes prior to SARCLISA infusion with the following medicinal products to reduce the risk and severity of infusion reactions: Dexamethasone 40 mg oral or intravenous (or 20 mg oral or intravenous for patients ≥75 years of age): when administered in combination with isatuximab and pomalidomide; 20 mg (intravenous on the days of isatuximab and/or carfilzomib infusions, and oral on the other days): when administered in combination with isatuximab and carfilzomib; 20 mg (intravenous on the days of isatuximab infusion, and oral on the other days): when administered in combination with isatuximab, bortezomib, and lenalidomide. The recommended dose of dexamethasone (oral or intravenous) corresponds to the total dose to be administered only once before the infusion, as part of the premedication and the backbone treatment, before isatuximab and pomalidomide, before isatuximab and carfilzomib, and before isatuximab, bortezomib, and lenalidomide administration; Acetaminophen 650 mg to 1000 mg oral (or equivalent), Diphenhydramine 25 mg to 50 mg intravenous or oral (or equivalent), H2 antagonists (ranitidine 50 mg IV or equivalent [e.g., cimetidine]), or oral proton pump inhibitors (e.g., omeprazole, esomeprazole). Patients who do not experience an infusion reaction upon their first 4 administrations of SARCLISA may have their need for subsequent premedication reconsidered. **Posology:** The recommended dose of SARCLISA is 10 mg/kg body weight administered as an intravenous infusion in combination with pomalidomide and dexamethasone or in combination with carfilzomib and dexamethasone or in combination with bortezomib, lenalidomide, and dexamethasone. Dosing schedule in combination with pomalidomide and dexamethasone or in combination with carfilzomib and dexamethasone: cycle 1: days 1, 8, 15 and 22 (weekly), cycle 2 and beyond: days 1, 15 (every 2 weeks). Each treatment cycle consists of a 28- day period. Dosing schedule in combination with bortezomib, lenalidomide, and dexamethasone for transplant ineligible patients: cycle 1: days 1, 8, 15, 22 and 29, cycles 2 to 4: days 1, 15 and 29 (every 2 weeks), cycles 5 to 17: days 1 and 15 (every 2 weeks), cycles 18 and beyond: day 1 (every 4 weeks). Each treatment cycle consists of a 42-day period from cycle 1 to 4, and of a 28-day period from cycle 5. Treatment is repeated until disease progression or unacceptable toxicity. **Method of administration:** SARCLISA is for intravenous use. For details on preparation and infusion rate see full SmPC. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. See full SmPC for full list of excipients. **Warnings and precautions:** Infusion reactions, mostly mild or moderate, were observed in 38.2% of patients treated with SARCLISA in ICARIA, and in 45.8% in IKEMA but resolved on the same day in 98% of infusions, and in 24.0% of patients treated with Isa-VRd in IMROZ and resolved the same day in 97.3% of patients. The most common symptoms of an IR included dyspnoea and chills. The most common severe sign and symptom was hypertension. Vital signs should be frequently monitored during the entire infusion and when required infusion should be interrupted or permanently discontinued in case symptoms that do not improve to grade ≤1 after infusion interruption. Serious infusion reactions including severe anaphylactic reactions have also been observed after SARCLISA administration. Most of the grade 3-4 neutropenia was reported as laboratory abnormalities. In patients treated with Isa-VRd, in IMROZ, neutropenia was reported as a laboratory abnormality in 87.5% of patients and as an adverse reaction in 30% of patients. A higher incidence of infections including grade ≥ 3 infections occurred with SARCLISA. Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) according to treatment guidelines should be considered during treatment. Patients receiving SARCLISA should be closely

monitored for signs of infection. Physicians should carefully evaluate patients before and during treatment as per International Myeloma Working Group (IMWG) guidelines for occurrence of secondary primary malignancies (SPM) and treatment should be initiated as indicated. Patients should be monitored closely, and appropriate precautions taken for tumor lysis syndrome. Isatuximab binds to CD38 on red blood cells (RBCs) and may result in a false positive indirect antiglobulin test (indirect Coombs test). This interference with the indirect Coombs test may persist for at least 6 months after the last infusion of SARCLISA. Patient should have blood type and screen tests performed prior to the first infusion of Isatuximab and should be monitored for theoretical risk of hemolysis. For details in tests interference see full SmPC. **Drug interactions:** Isatuximab has no impact on the pharmacokinetics of pomalidomide or carfilzomib, or bortezomib, or lenalidomide and vice versa. Isatuximab may interfere with serological testing and with Serum Protein Electrophoresis and Immunofixation assays. In patients with persistent very good partial response, where isatuximab interference is suspected, consider using a validated isatuximab- specific IFE assay to distinguish isatuximab from any remaining endogenous M protein in the patient's, to facilitate determination of complete response. **Fertility, pregnancy and lactation:** Women of childbearing potential treated with isatuximab should use effective contraception during treatment and for 5 months after cessation of treatment. The use of isatuximab in pregnant women is not recommended since there are no available data. **Undesirable effects:** Observed in patients treated with isatuximab in combination with pomalidomide and dexamethasone: Infections/infestations: very common: pneumonia, upper respiratory tract infection, bronchitis: common: Herpes zoster. Neoplasms benign, malignant and unspecified: common: skin cancer, solid tumor (non-skin cancer): uncommon: hematology malignancy. Blood/lymphatic system disorders: very common: neutropenia, thrombocytopenia, common: febrile neutropenia, anaemia, unknown frequency: lymphopenia. Metabolism and nutrition disorders: very common: decreased appetite. Cardiac disorders: common: atrial fibrillation. Respiratory, thoracic and mediastinal disorders: very common: dyspnoea. Gastrointestinal disorders: very common: diarrhoea, nausea, vomiting. Investigations: common: weight decreased. Injury, poisoning and procedural complications: very common: infusion reaction. Immune system disorders: uncommon: anaphylactic reaction. Observed in patients treated with isatuximab in combination with carflizomib and dexamethasone: Infections/infestations: very common: pneumonia, upper respiratory tract infection, bronchitis: common: Herpes Zoster. Vascular disorder: very common: hypertension. Neoplasms benign, malignant and unspecified: common: Skin cancers and solid tumors non- skin cancers. Blood/lymphatic system disorders: common: neutropenia, anaemia, thrombocytopenia, unknown frequency: lymphopenia. Respiratory, thoracic and mediastinal disorders: very common: dyspnoea and cough. Gastrointestinal disorders: very common: diarrhoea and vomiting. General disorders and administration site conditions: very common: Fatigue. Injury, poisoning and procedural complications: very common: infusion reaction. Immune system disorders: uncommon: anaphylactic reaction. Reported in transplant ineligible patients with multiple myeloma treated with isatuximab in combination with bortezomib, lenalidomide, and dexamethasone: Infections/infestations: very common: pneumonia, bronchitis, Covid-19. Neoplasms benign, malignant and unspecified: common: skin cancer, solid tumor, uncommon: hematology malignancy. Blood and lymphatic system disorders: very common: neutropenia, thrombocytopenia, common: anaemia, not known: lymphopenia. Immune system disorders: uncommon: anaphylactic reaction. Eye disorders: very common: cataract. Gastrointestinal disorders: very common: diarrhoea, common: vomiting. General disorders and administration site conditions: very common: fatigue. Injury, poisoning and procedural complications: very common: infusion reaction.
Pharmacotherapeutic group: Antineoplastic agents, monoclonal antibodies, ATC code: L01FC02. **List of excipients:** Sucrose, Histidine hydrochloride monohydrate, Histidine, Polysorbate 80 and Water for injections. **Legal classification:** Prescription Only Medicine. **Marketing authorization holder:** Sanofi Winthrop Industrie, 82, avenue Raspail, 94250 Gentilly, France. **Date of last revised:** November 2024.

To report an adverse event or in case of any medical enquiry, please call email at:
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