▼ This medicinal product is subject to additional monitoring.

Compulsary information: SARCLISA (isatuximab) 20mg/mL concentrate for solution for infusion
Please refer to the Summary of Product Characteristics (SPC) before prescribing.

Presentations: Each vial contains 100 mg of isatuximab in 5 mL of concentrate or contains 500 mg of isatuximab in 25 mL of concentrate.
Indication: 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 therapies including lenalidomide and a proteasome inhibitor (PI) and have demonstrated disease progression on the last therapy. Sarclisa is indicated in combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy.
Dosage and Administration*: SARCLISA should be administered by a healthcare professional, in an environment where resuscitation facilities are available. *Premedication, with the following medicinal products, should be administered 15-60 minutes prior to starting a SARCLISA infusion:* Dexamethasone 40 mg oral or intravenous (IV) (or 20 mg oral or IV for patients ≥75 years of age) when administered in combination with isatuximab and pomalidomide; Dexamethasone 20 mg (IV on the days of isatuximab and/or carfilzomib infusions, and oral on the other days): when administered in combination with isatuximab and carfilzomib; Acetaminophen 650 mg to 1000 mg oral (or equivalent); Diphenhydramine 25 mg to 50 mg IV or oral (or equivalent [e.g., cetirizine, promethazine, dexchlorpheniramine]). The IV route is preferred for diphenhydramine for at least the first 4 infusions. The above recommended dose of dexamethasone (oral or IV) 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 and before isatuximab and carfilzomib administration. Patients who do not experience an infusion reaction upon their first 4 administrations of SARCLISA may have their need for subsequent premedication reconsidered. *Managing neutropenia:* The use of colony-stimulating factors (e.g., G-CSF) should be considered to mitigate the risk of neutropenia. In the event of grade 4 neutropenia, SARCLISA administration should be delayed until neutrophil count improves to at least 1.0 x 10^9/L. *Posology:* The recommended dose of SARCLISA is 10 mg/kg body weight administered as an IV infusion in combination with pomalidomide and dexamethasone (Isa-Pd regimen) or in combination with carfilzomib and dexamethasone (Isa-Kd regimen). *Cycle 1:* Dosing on days 1, 8, 15 and 22 (weekly). *Cycle 2 and beyond:* Dosing on days 1, 15 (every 2 weeks). Each treatment cycle consists of a 28-day period. Treatment is repeated until disease progression or unacceptable toxicity. For other medicinal products that are administered with SARCLISA, refer to the respective current summary of product characteristics. The administration schedule must be carefully followed. *Missed dose:* If a dose of SARCLISA is missed, administer the dose as soon as possible and adjust the treatment schedule, accordingly, maintaining the treatment interval. *Dose adjustments:* No dose reduction of SARCLISA is recommended. Administration adjustments should be made if patients experience infusion reactions. *Infusion rates:* please refer to full SmPC.
Special Populations: *Elderly:* no dose adjustment is recommended. *Patients with mild to severe renal impairment:* no dose adjustment is recommended. *Patients with mild hepatic impairment:* no dose adjustment is recommended. Data in patients with moderate and severe hepatic impairment are limited, but there is no evidence to suggest that dose adjustment is required in these patients. *Paediatric population (<18 years old):* No data available.
Contraindications: Hypersensitivity to the active substance or to any of its excipients.
Precautions and Warnings*: *Traceability:* In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded. *Infusion reactions:* Infusion reactions, mostly mild or moderate, have been observed in 38.2% of patients treated with SARCLISA in ICARIA-MM (Isa-Pd regimen), and in 45.8% of patients in the IKEMA trial (Isa-Kd regimen). In ICARIA-MM, all infusion reactions started during the first SARCLISA infusion and resolved on the same day in 98% of the infusions. The most common symptoms of an infusion reaction included dyspnoea, cough, chills, and nausea. The most common severe signs and symptoms included hypertension, dyspnoea, and bronchospasm. In IKEMA, the infusion reactions occurred on the infusion day in 99.2% of episodes. In 94.4% of those experiencing an infusion reaction experienced it during the first cycle of treatment. All infusion reactions resolved. The most common symptoms of an infusion reaction included cough, dyspnoea, nasal congestion, vomiting and nausea. The most common severe signs and symptoms included hypertension and dyspnoea. Serious infusion reactions including severe anaphylactic reactions have been observed after SARCLISA administration. Vital signs should be frequently monitored during the entire SARCLISA infusion. When required, interrupt SARCLISA infusion and provide appropriate medical and supportive measures. In case symptoms do not improve after interruption of SARCLISA infusion, persist or worsen despite appropriate treatment with medicinal products, require hospitalization or are life-threatening, permanently discontinue SARCLISA and institute appropriate management. *Neutropenia:* In patients receiving Isa-Pd, neutropenia occurred as a laboratory abnormality in 96.1% of patients and as an adverse reaction in 46.7% of patients, with Grade 3-4 neutropenia reported as a laboratory abnormality in 84.9% of patients and as an adverse reaction in 45.4% of patients. Neutropenic complications have been observed in 30.3% of patients, including 11.8% of febrile neutropenia and 25.0% of neutropenic infections. In patients treated with Isa-Kd, neutropenia occurred as a laboratory abnormality in 54.8% of patients and as an adverse reaction in 4.5% of patients, with Grade 3-4 neutropenia reported as a laboratory abnormality in 19.2% of patients (with 17.5% Grade 3 and 1.7% Grade 4) and as an adverse reaction in 4.0% of patients. Neutropenic complications have been observed in 2.8% of patients, including 1.1% of febrile neutropenia and 1.7% of neutropenic infections. Complete blood cell counts should be monitored periodically during treatment. Patients with neutropenia should be monitored for signs of infection. *Infection:* A higher incidence of infections including grade ≥3 infections, mainly pneumonia, upper respiratory tract

infection and bronchitis, occurred with SARCLISA. Patients receiving SARCLISA should be closely monitored for signs of infection and appropriate standard therapy instituted. Antibiotics and antiviral prophylaxis can be considered during treatment. *Second primary malignancies (SPMs):* In ICARIA-MM, SPMs were reported at a median follow-up time of 52.44 months in 10 patients (6.6%) treated with Isa-Pd and in 3 patient (2%) treated with Pd. SPM were skin cancer in 6 patients treated with Isa-Pd and in 3 patients treated with Pd, solid tumours other than skin cancer in 3 patients treated with Isa-Pd (one patient also had a skin cancer), and haematological malignancy (myelodysplastic syndrome) in 1 patient treated with Isa- Pd. Patients continued treatment after resection of the new malignancy, except two patients treated with Isa-Pd. One patient developed metastatic melanoma and the other developed myelodysplastic syndrome. The overall benefit of Isa-Pd remains favourable (see section 5.1). In ongoing IKEMA study, at a median follow – up time of 20.73 months, SPMs were reported in 13 patients (7.3%) treated with Isa-Kd and in 6 patients (4.9%) treated with Kd. SPMs were skin cancers in 9 patients (5.1%) treated with Isa-Kd and in 3 patients (2.5%) treated with Kd and were solid tumours other than skin cancer in 5 patients (2.8%) treated with Isa-Kd and in 4 patients (3.3%) treated with Kd. One patient (0.6%) in the Isa-Kd group and one patient (0.8%) in the Kd group had both skin cancer and solid tumours other than skin cancer. Patients with skin cancer continued treatment after resection of the skin cancer. Solid tumours other than skin cancer were diagnosed within 3 months after treatment initiation in 3 patients (1.7%) treated with Isa-Kd and in 2 patients (1.6%) treated with Kd. The overall incidence of SPMs in all the SARCLISA-exposed patients is 4.1%. Physicians should carefully evaluate patients before and during treatment as per IMWG guidelines for occurrence of SPM and initiate treatment as indicated. *Tumour lysis syndrome:* Cases of tumour lysis syndrome (TLS) have been reported in patients who received isatuximab. Patients should be monitored closely, and appropriate precautions taken. *Interference with Serological Testing (indirect antiglobulin test):* SARCLISA administration may result in a false positive indirect antiglobulin test (indirect Coombs test). To avoid potential problems with Red Blood Cell transfusion, patients being treated with SARCLISA should have blood type and screen tests performed prior to the first SARCLISA infusion. Phenotyping may be considered prior to starting SARCLISA treatment as per local practice. If treatment with SARCLISA has already started, the blood bank should be informed that the patient is receiving SARCLISA and SARCLISA interference with blood compatibility testing can be resolved using dithiothreitol (DTT)-treated RBCs. If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices. *Interference with determination of complete response:* SARCLISA can interfere with both serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the clinical monitoring of endogenous M-protein. Interference can impact the accuracy of the determination of complete response in some patients with IgG kappa myeloma protein. ***Interactions*:*** *Interference with serological testing:* Because CD38 protein is expressed on the surface of red blood cells, SARCLISA, an anti-CD38 antibody, may interfere with blood bank serologic tests with potential false positive reactions in indirect antiglobulin tests (indirect Coombs tests), antibody detection (screening) tests, antibody identification panels, and antihuman globulin (AHG) crossmatches in patients treated with SARCLISA. *Interference with Serum Protein Electrophoresis and Immunofixation Tests:* SARCLISA may be incidentally detected by serum protein electrophoresis (SPE) and immunofixation (IFE) assays used for the monitoring of M-protein and could interfere with accurate response classification based on International Myeloma Working Group (IMWG) criteria. ***Fertility, pregnancy and lactation*:*** Women of childbearing potential treated with SARCLISA should use effective contraception during treatment and for at least 5 months after cessation of treatment. There are no available data on isatuximab use in pregnant women. Immunoglobulin G1 monoclonal antibodies are known to cross the placenta after the first trimester of pregnancy. The use of SARCLISA in pregnant women is not recommended. It is unknown whether isatuximab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which is decreasing to low concentrations soon afterwards; however, a risk to the breast-fed infant cannot be excluded during this short period just after birth. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from isatuximab therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman. No human and animal data are available to determine potential effects of isatuximab on fertility in males and females.

Adverse Reactions: In ICARIA-MM (Isa-Pd): *Very common:* Neutropenia, infusion reactions, pneumonia*, upper respiratory tract infection, diarrhoea, bronchitis, dyspnoea, nausea, febrile neutropenia**, vomiting. *Common:* Decreased appetite, weight decreased, atrial fibrillation, skin cancer, Solid tumour (non-skin cancer), herpes zoster. *Uncommon:* Anaphylactic reaction, haematology malignancy. In IKEMA (Isa-Kd): *Very common:* Infusion reactions, hypertension, diarrhoea, upper respiratory tract infection, pneumonia*, fatigue, dyspnoea, bronchitis, cough, vomiting. *Common:* Skin cancers, neutropenia, solid tumours other than skin cancers, herpes zoster. Uncommon*:* Anaphylactic reaction**. **These adverse events also occurred as serious adverse events. ***Prescribers should consult the SPC in relation to other adverse reactions.***

Marketing Authorisation Holder: Sanofi Winthrop Industries, 82 avenue Raspail, 94250 Gentilly, France.

Date of last revision of SmPC: March 2023

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu. Before prescribing the product always refer to your full local prescribing information as this information may vary from country to country.

Belgium:
Prescription medication. Reimbursed. The SmPC is available on https://www.afmps.be/. In Belgium Sarclisa is provided by Sanofi Belgium NV, Leonardo Da Vincilaan 19 1831 Diegem, tel +32 27 10 54 00. For questions on our medicinal products, please contact: medical_info.belgium@sanofi.com.

Netherlands:
L01XC38. U.R. Sarclisa wordt vergoed via add-on. Voor prijzen zie de Z-index taxe. Voor meer informatie zie de SmPC op http://www.geneesmiddeleninformatiebank.nl. Lokale vertegenwoordiger: Genzyme Europe B.V. Paasheuvelweg 25, 1105 BP Amsterdam. Tel: +31 (0)20 2454000.

Denmark:
Pakningsstørrelser: 1 htgl. koncentrat (5 ml) til infusionsvæske, opløsning (Vnr. 45 89 04). 1 htgl. koncentrat (25 ml) til infusionsvæske, opløsning (Vnr. 13 30 49). **For dagsaktuel pris** se www.medicinpriser.dk **Udlevering:** BEGR. **Tilskud:** Ikke tilskudsberettiget. **Indehaver af markedsføringstilladelsen**: Sanofi Winthrop Industrie, 82 avenue Raspail, 94250 Gentilly, France. De med * markerede afsnit er omskrevet/forkortet i forhold til det godkendte produktresumé. Produktresuméet kan vederlagsfrit rekvireres hos Sanofi A/S, Lyngbyvej 2, 2100 København Ø.
Dato for reklamematerialet:

Finland
Pakkaukset ja hinnat: Sarclisa TMH 100 mg 558,04 €, 500 mg 2790,18 € Reseptilääke, sairaalalääke. Huom. Tutustu valmisteyhteenvetoon ennen lääkkeen määräämistä. **Lisätiedot:** www.sanofi.fi

Norway:
Reseptstatus: C Pakninger og priser: Hetteglass 5 ml, vnr 458904, **Pris** 7 908,50/ Hetteglass 25 ml, vnr 133049, Pris 39 397,30. **Refusjon:** Beslutning fra Beslutningsforum avventes.
Lokal representant: sanofi-aventis Norge AS, Prof. Kohts vei 5-17, 1325 Lysaker.
Fullstendig preparatomtale finnes på www.legemiddelsok.no/

Sweden:
Prescription medication. Not reimbursed. L01XC38. The SmPC is available on www.fass.se. In Sweden Sarclisa is provided by Sanofi AB, Box 300 52, 104 25 Stockholm, tel +46 8 634 50 00. For questions on our medicinal products, please contact infoavd@sanofi.com.

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