

Prescribing Information: Sarclisa (isatuximab) 20 mg/mL concentrate for solution for infusion and Sarclisa 1400 mg solution for injection

Please refer to the Summary of Product Characteristics (SmPC) before prescribing

Presentations

Sarclisa IV: Each vial contains 100 mg of isatuximab in 5 mL of concentrate or contains 500 mg of isatuximab in 25 mL of concentrate.

Sarclisa SC: Each vial contains 1400 mg of isatuximab in 10 mL solution.

Indications

Isatuximab 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
- 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

Treatment with isatuximab should be prescribed by a specialist in the treatment of malignancies. Patients may start treatment using intravenous or subcutaneous isatuximab. Patients currently receiving intravenous isatuximab may switch to subcutaneous isatuximab, at any time during their treatment, once cycle 1 is completed.

Sarclisa IV: should be administered intravenously (IV) by a healthcare professional, in an environment where resuscitation facilities are available.

Sarclisa SC: should be administered by a healthcare professional as a subcutaneous (SC) injection only. For the first dose only, immediate access to medical support should be available to manage systemic administration reactions (SARs) if they occur. Once the cycle 1 is completed, subsequent SC injections may be administered at the patient's home by a healthcare professional, as deemed appropriate, provided there were no SARs in the previous cycle.

Method of Administration

Sarclisa IV: Administered as an IV infusion. Please refer to the SmPC for full details on infusion rates, preparation, and administration.

Sarclisa SC: For abdominal subcutaneous administration only, using the CirCLIQ On-Body Delivery System (OBDS) or with a syringe and infusion set for manual administration. Rotate the site of each SC administration. Do not inject other medications in the area where isatuximab SC is injected. Do not inject into areas where the skin is injured, tender, red, hot, has scars, or is excessively hairy. Please refer to the SmPC for full details.

Pre-medication:

Pre-medication should be administered 15 – 60 minutes prior to starting isatuximab to reduce the risk and severity of infusion/SARs.

Sarclisa IV:

- Dexamethasone 40 mg oral or IV (or 20 mg oral or IV for patients ≥ 75 years of age) when administered in combination with isatuximab and pomalidomide; 20 mg when administered with isatuximab, bortezomib, and lenalidomide.
- Montelukast 10 mg oral (or equivalent), at least at cycle 1
- Paracetamol 650 mg to 1000 mg oral (or equivalent)
- H2 antagonists (ranitidine 50 mg IV or equivalent [e.g. cimetidine]), or oral proton pump inhibitors (e.g. omeprazole, esomeprazole).
- Diphenhydramine 25 mg to 50 mg IV or oral (or equivalent [e.g., cetirizine, promethazine, dexchlorpheniramine]) - IV use of diphenhydramine is preferred for at least the first 4 infusions.

Sarclisa SC:

- Dexamethasone 40 mg (or 20 mg for patients ≥ 75 years) when administered with isatuximab and pomalidomide; 20 mg when administered with isatuximab, bortezomib, and lenalidomide
- Montelukast 10 mg oral (or equivalent), at cycle 1 only
- Paracetamol 650 mg to 1000 mg oral (or equivalent)

- Diphenhydramine 25 mg to 50 mg IV or oral (or equivalent [e.g., cetirizine, promethazine, dexchlorpheniramine]) - IV use of diphenhydramine is preferred for at least the first 4 administrations

The above recommended dose of dexamethasone corresponds to the total dose to be administered only once before isatuximab administration, as part of the premedication and of the backbone treatment. Patients who do not experience an infusion/SAR upon their first 4 administrations of isatuximab may have their need for subsequent premedication reconsidered.

Management of neutropenia: The use of colony-stimulating factors (e.g. G-CSF) should be considered to mitigate the risk of neutropenia, and in the event of Grades 3/4 haematological toxicity, Sarclisa administration should be delayed or omitted according to local guidelines.

Prevention of infection: Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) according to treatment guidelines should be considered during treatment.

Posology

Sarclisa IV Recommended dose: 10 mg/kg body weight IV infusion in combination with pomalidomide and dexamethasone (Isa-Pd):

- Each treatment cycle consists of a 28-day period
- Cycle 1: 10 mg/kg IV weekly; days 1, 8, 15 and 22
- Cycle 2 and beyond: 10 mg/kg IV every 2 weeks; days 1 and 15

In combination with bortezomib, lenalidomide, and dexamethasone (Isa-VRd):

- Each treatment cycle consists of a 42-day period from cycles 1 to 4, and of a 28-day period from cycle 5
- Cycle 1 (42-day cycle): 10 mg/kg IV; days 1, 8, 15, 22 and 29
- Cycles 2 to 4 (42-day cycles): 10 mg/kg IV every 2 weeks; days 1, 15 and 29
- Cycles 5 to 17 (28-day cycles): 10 mg/kg IV every 2 weeks; days 1 and 15
- Cycle 18 and beyond (28-day cycles): 10 mg/kg IV every 4 weeks; day 1

Treatment is repeated until disease progression or unacceptable toxicity.

Sarclisa SC Recommended dose: 1400 mg fixed dose SC injection in combination with pomalidomide and dexamethasone (Isa-SC + Pd):

- Each treatment cycle consists of a 28-day period
 - Cycle 1: 1400 mg SC weekly; Days 1, 8, 15 and 22
 - Cycle 2 and beyond: 1400 mg SC every 2 weeks; days 1 and 15
- In combination with bortezomib, lenalidomide, and dexamethasone (Isa-SC + VRd):
- Each treatment cycle consists of a 42-day period from cycles 1 to 4, and a 28-day period from cycle 5 onwards
 - Cycle 1 (42-day cycle): 1400 mg SC; days 1, 8, 15, 22 and 29
 - Cycles 2 to 4 (42-day cycles): 1400 mg SC every 2 weeks; days 1, 15 and 29
 - Cycles 5 to 17 (28-day cycles): 1400 mg SC every 2 weeks; days 1 and 15
 - Cycle 18 and beyond (28-day cycles): 1400 mg SC every 4 weeks; day 1

Treatment is repeated until disease progression or unacceptable toxicity.

Body weight > 120 kg (**SC formulation only**): There is a potential for reduced efficacy with isatuximab SC in patients with a body weight > 120 kg, due to the effect of body weight on exposure.

Missed dose

The administration schedule must be carefully followed. If a planned dose of isatuximab is missed, administer the dose as soon as

possible and adjust the treatment schedule accordingly, maintaining the treatment interval.

Dose adjustments:

Sarclisa IV: No dose reduction of isatuximab is recommended. Administration adjustments should be made if patients experience IRs or in case of Grade 3 or 4 neutropenia, or febrile neutropenia and/or neutropenic infection. Please refer to the SmPC for full details on infusion rates and administration adjustments.

Sarclisa SC: Dose reduction of isatuximab SC is not permitted. Dose delay or omission may be required. In case of Grade 3 or 4 neutropenia, or febrile neutropenia and/or neutropenic infection, or if patients experience systemic administration reactions or injection site reactions, please refer to the SmPC for full details and administration adjustments.

Contraindications: Hypersensitivity to the active substance or to any of its excipients.

Warnings and Precautions

Infusion reactions (IRs) - IV formulation: IRs, mostly mild or moderate, have been observed in 38.2% of patients treated with isatuximab in ICARIA-MM (Isa-Pd regimen), and in 24.0% of patients treated with Isa-VRd in IMROZ. In ICARIA-MM, all IRs started during the first isatuximab infusion and resolved on the same day in 98% of the infusions. The most common symptoms of an IR included dyspnoea, cough, chills and nausea and the most common severe signs and symptoms included hypertension, dyspnoea and bronchospasm. In IMROZ, the IRs started on the infusion day in all patients, mostly during the first isatuximab infusion, and resolved the same day in 97.3% of patients. All IRs resolved. The most common symptoms included dyspnoea and chills and the most common severe sign and symptom was hypertension. Serious IRs including severe anaphylactic reactions have been observed after isatuximab administration. Anaphylactic reactions with a fatal outcome have been reported. To decrease the risk and severity of IRs, patients should be appropriately pre-medicated prior to isatuximab infusion and vital signs should be frequently monitored during the entire infusion. When required, interrupt isatuximab infusion and provide appropriate medical and supportive measures. In case symptoms do not improve to Grade ≤ 1 after interruption of isatuximab infusion, persist or worsen despite appropriate treatment with medicinal products, require hospitalisation or are life-threatening, permanently discontinue Sarclisa and institute appropriate management. In case of anaphylactic reaction or life-threatening (Grade 4) infusion reaction, permanently discontinue Sarclisa and institute appropriate management.

Systemic Administration Reactions (SARs) — SC formulation: In clinical trials with subcutaneous isatuximab (N = 522), SARs occurred in 16 patients (3.1%); 14 patients (2.7%) experienced only one episode. An SAR occurred at first administration in 10 patients (1.9%). They were mostly low grades (Grade 1 or 2) and resolved at the most within 3 days. The reported symptoms of SARs (all below 1%) were mainly pyrexia, dyspnoea, and sinus tachycardia. There was one Grade 3 episode of SAR in one patient that experienced hypertension and dyspnoea. In case of Grade ≥ 2 SARs, administration adjustments should be considered (see SmPC). To decrease the risk and severity of SARs, patients should be pre-medicated prior to isatuximab SC administration with montelukast (at cycle 1 only), acetaminophen, diphenhydramine or equivalent; dexamethasone is to be used as both premedication and anti-myeloma treatment (see SmPC).

Neutropenia: Neutropenia was reported in clinical trials with isatuximab SC or IV in combination therapies. With isatuximab SC combination therapies, a higher incidence of Grade 3 - 4 neutropenia reported as laboratory abnormality was observed in patients with body weight ≤ 50 kg compared to patients with a higher body weight, with however similar incidences of neutropenic complications (see SmPC). Complete blood cell counts should be monitored periodically during treatment. Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) can be considered during treatment (see SmPC). Patients with neutropenia should be monitored for signs of infection. No dose reductions of isatuximab are recommended. Isatuximab dose delays and the use of colony-stimulating factors (e.g. G-CSF) should be considered to mitigate the risk of neutropenia (see SmPC).

Infection: Infections were reported in clinical trials with isatuximab SC or IV in combination therapies, with an incidence of 66.4% of patients, including Grade ≥ 3 infections reported in 29.9% of patients. Upper respiratory tract infection, pneumonia, and bronchitis were the most frequently reported infections (see SmPC). Patients receiving isatuximab subcutaneous should be closely monitored for signs of infection and appropriate standard therapy instituted. Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) should be considered during treatment (see SmPC).

Second primary malignancies (SPMs): SPMs were reported in clinical trials with isatuximab SC or IV in combination therapies (see SmPC). The overall incidence of SPMs in isatuximab-exposed patients (SC and IV formulations) is 5.4%. Monitor patients for the development of SPMs and initiate treatment as indicated.

Tumour lysis syndrome (TLS): Cases of TLS have been reported in patients who received isatuximab. Patients should be monitored closely and appropriate precautions taken.

Interference with serological testing: Because CD38 protein is expressed on the surface of red blood cells (RBCs), isatuximab, 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 isatuximab. This interference may persist for at least 6 months after the last administration of isatuximab. To avoid potential problems with RBC transfusion, patients being treated with isatuximab should have blood type and screen tests performed prior to the first administration. Phenotyping may be considered prior to starting isatuximab treatment as per local practice. If treatment with isatuximab has already started, the blood bank should be informed that the patient is receiving isatuximab and isatuximab interference with blood compatibility testing can be resolved using dithiothreitol (DTT)-treated RBCs. Patients should be monitored for theoretical risk of haemolysis. If an emergency transfusion is required, non-cross-matched ABO/RhD-compatible RBCs can be given as per local blood bank practices.

Educational materials: Please see SmPC for more details in relation to the materials available for HCPs at blood banks/transfusion centres, and patients in relation to interference with serological testing.

Fertility, pregnancy and lactation

Women of childbearing potential treated with isatuximab should use effective contraception during treatment and for 7 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 isatuximab 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

Isa-Pd: **Very common:** Pneumonia*, upper respiratory tract infection, neutropenic infection (SC only), bronchitis, Covid-19 (SC only), neutropenia, thrombocytopenia (IV only), decreased appetite (IV only), insomnia (SC only), peripheral sensory neuropathy (SC only), dyspnoea, cough (SC only), diarrhoea, constipation (SC only), nausea, vomiting (IV only), back pain (SC only), arthralgia (SC only), muscle spasms (SC only), fatigue (SC only), oedema peripheral (SC only), pyrexia (SC only), systemic administration reactions/infusion reactions (IV only). **Common:** Herpes zoster, skin cancer, solid tumour (non-skin cancer), thrombocytopenia (SC only), anaemia, febrile neutropenia, decreased appetite (SC only), dizziness (SC only), atrial fibrillation, vomiting (SC only), weight decreased, systemic administration reactions (SC only), injection site reactions (SC only). **Other Serious Adverse Drug Reactions (Uncommon):** haematology malignancy and anaphylactic reaction (based on post-marketing experience, anaphylactic reactions including fatal cases have been reported).

Isa-VRd: Very Common: Pneumonia*, upper respiratory tract infection (SC only), bronchitis, Covid-19, neutropenia, thrombocytopenia, lymphopenia (SC only), insomnia (SC only), peripheral sensory neuropathy (SC only), polyneuropathy (SC only), cataract, diarrhoea, constipation (SC only), rash (SC only), back pain (SC only), oedema peripheral (SC only), asthenia (SC only), fatigue, pyrexia (SC only), systemic administration reactions/infusion reactions (IV only), injection site reactions (SC only). Common: Neutropenic infection (SC only), skin cancer, solid tumour (non-skin cancer), anaemia, febrile neutropenia (SC only), dizziness (SC only), vomiting, weight decreased (SC only), systemic administration reactions (SC only). Other Serious Adverse Drug Reactions (Uncommon): haematology malignancy and anaphylactic reaction (based on post-marketing experience, anaphylactic reactions including fatal cases have been reported). *These adverse events also occurred as serious adverse events. *Prescribers should consult the SmPC in relation to other adverse reactions.*

Legal Category: POM

List price:

Sarclisa IV: 100 mg x 1 vial: £506.94; SARCLISA 500 mg x 1 vial: £2,534.69

Sarclisa SC: £3,983.53

Marketing Authorisation Number:

Sarclisa IV: PLGB 04425/0887

Sarclisa SC: PL 04425/0915

Marketing Authorisation Holder: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK

Further information is available from: Sanofi, 410 Thames Valley Park Drive, Reading, Berkshire, RG6 1PT, UK. uk-medicalinformation@sanofi.com

Date of preparation: June 2026

Document no: MAT-XU-2503407 (v2.0)

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to the Sanofi drug safety department on Tel: 0800 0902 314. Alternatively, send via email to UK-drugsafety@sanofi.com