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on multiple myeloma

EHA-EMN evidence-based guidelines for diagnosis, treatment and follow-up of patients with multiple myeloma

Nature Reviews Clinical Oncology, 2025 September; 22(9):680–700

Minimal residual disease-based end point for accelerated assessment of clinical trials in multiple myeloma: a pooled analysis of individual patient data from multiple randomized trials

Journal of Clinical Oncology, 2025 April 10; 43(11):1289–301

Isatuximab, bortezomib, lenalidomide, and limited dexamethasone in patients with transplant-ineligible multiple myeloma (REST): a multicentre, single-arm, phase 2 trial

The Lancet Haematology, 2025 February; 12(2):e120–7

International Myeloma Society/International Myeloma Working Group consensus recommendations on the definition of high-risk multiple myeloma

Journal of Clinical Oncology, 2025 August 20; 43(24):2739–51

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Editor
Catherine Harris Booth

Consulting Editor
Niels van de Donk, MD PhD
Professor of Haematology,
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Amsterdam UMC,
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Medical Writers (this issue)
Milena Braga-Basaria
Kathy Croom
Lorraine Law
Kathy Longley

Art Design
Jan van Halm

Layout and Printing
Drukmeesters,
Zwijndrecht, the Netherlands

Publishing Director
Evelien Enter

Publisher
Waldemar H.G. Dobrowolski

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EHA-EMN EVIDENCE-BASED GUIDELINES FOR DIAGNOSIS, TREATMENT AND FOLLOW-UP OF PATIENTS WITH MULTIPLE MYELOMA

Nature Reviews Clinical Oncology, 2025 September; 22(9):680–700

AUTHORS: Dimopoulos MA, Terpos E, Boccadoro M, et al.
CENTRE FOR CORRESPONDENCE: Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece

BACKGROUND & AIMS: Clinical practice guidelines for multiple myeloma (MM) were co-developed in 2021 by the European Hematology Association (EHA) and the European Society for Medical Oncology. Since then, a new staging system for high-risk MM has been published, new methods have been developed for prognosis, and novel treatment regimens have been approved for both newly diagnosed and relapsed or refractory disease. The aims of this article were to provide up-to-date recommendations on the management of MM and to propose practical treatment algorithms.

TYPE OF ARTICLE: Evidence-based guidelines.

FINDINGS: An expert panel convened by the EHA and the European Myeloma Network (EMN) reviewed the scientific literature on the diagnosis and management of MM published during 2021–2025. They made no new recommendations on diagnostic criteria for MM. The consensus definition of high-risk MM was updated in 2024 by the International Myeloma Society and the International Myeloma Working Group, which will influence disease staging and patient prognosis in the future.

Recommendations on assessment include: (a) evaluating patients with smouldering MM every 6 months (low-risk patients) or 3–6 months (intermediate-risk patients) to monitor progression; and (b) using positron-emission tomography–computed tomography and diffusion-weighted magnetic resonance imaging to detect the presence of minimal residual disease as a complement to bone marrow evaluations.

Treatment recommendations are given for different clinical scenarios, including: (a) high-risk smouldering MM; (b) patients with newly diagnosed MM either eligible or ineligible for autologous stem cell transplantation and those with frailty; and (c) patients with relapsed or refractory MM who previously received either one or two or more lines of treatment. For example, for patients who have received one prior line of treatment comprising a bortezomib-based regimen upfront without lenalidomide or an anti-CD38 antibody and who have bortezomib-refractory disease, recommendations include daratumumab with lenalidomide and dexamethasone, and daratumumab or isatuximab with carfilzomib and dexamethasone.

Recommendations are also given for managing common complications and adverse events, including bone disease, anaemia, infection and impaired renal function; and common adverse events resulting from novel T-cell-mobilizing therapeutic agents, including ocular toxicities, cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome.

CONCLUSION: Comprehensive evidence-based recommendations are provided for treating patients with MM in routine clinical practice.

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MINIMAL RESIDUAL DISEASE-BASED END POINT FOR ACCELERATED ASSESSMENT OF CLINICAL TRIALS IN MULTIPLE MYELOMA:

A POOLED ANALYSIS OF INDIVIDUAL PATIENT DATA FROM MULTIPLE RANDOMIZED TRIALS

Journal of Clinical Oncology, 2025 April 10; 43(11):1289–301

AUTHORS: Shi Q, Paiva B, Pederson LD, et al., for the International Independent Team for Endpoint Approval of Myeloma Minimal Residual Disease (i2TEAMM) Group
CENTRE FOR CORRESPONDENCE: Department of Quantitative Health Sciences, Mayo Clinic, Rochester, Minnesota, USA

BACKGROUND & AIM: As drug combinations have extended the lives of patients with multiple myeloma (MM), future trials that rely on survival endpoints will need large sample sizes and long follow-ups to observe statistically or clinically meaningful treatment effects. It is therefore important to identify surrogate endpoints that can predict long-term benefit at an earlier timepoint and thus expedite drug development. The aim of this study was to investigate whether minimal residual disease-negative complete response (MRD-CR) can be used as an intermediate surrogate endpoint for progression-free survival (PFS) and overall survival (OS) in patients with various types of MM.

STUDY DESIGN: Pooled analysis of individual patient data.

ENDPOINT: Rate of MRD-CR at 9 and 12 months.

METHOD: Individual patient data were collected from 20 randomized controlled trials that enrolled at least 100 patients with MM. Of these, 11 trials (n=4773) had sufficient data to calculate the global odds ratio, which was used to evaluate whether MRD-CR (10^{-5} threshold) is likely to predict a PFS or OS benefit of new therapies (where a global OR of ≤1.5 indicates a weak correlation and ≥3.0 indicates a strong correlation between the surrogate endpoint and survival). Landmark analyses comparing PFS or OS in patients with or without 9- or 12-month MRD-CR were also performed.

RESULTS: The global OR for 9-month MRD-CR in predicting PFS was consistently high across transplant-eligible patients with newly diagnosed MM (OR 3.1, 95% confidence interval 2.1–4.0), transplant-ineligible patients with newly diagnosed MM (OR 9.8, 95% CI 5.1–14.5) and patients with relapsed or refractory MM (OR 8.2, 95% CI 4.4–12.1). Corresponding global ORs for 12-month MRD-CR were 4.5 (95% CI 3.2–5.7), 12.0 (95% CI 7.3–16.6) and 16.2 (95% CI 5.8–26.7). High global OR estimates were similarly seen with OS for both 9- and 12-month MRD-CR. In the landmark analyses, 12-month MRD-CR was found to have significant prognostic value for PFS and OS in all three populations (hazard ratios 0.22–0.37, stratified log-rank p<0.0001), while 9-month MRD-CR exhibited moderate trial-level correlations after pooling comparisons from the three populations (R^2 0.61–0.72 and R^2 0.54–0.69 for PFS and OS, respectively).

CONCLUSION: These results support 9- and 12-month MRD-CR (10^{-5} threshold) as intermediate surrogate endpoints for PFS and OS in patients with MM.

https://doi.org/10.1200/JCO-24-02020

ISATUXIMAB, BORTEZOMIB, LENALIDOMIDE, AND LIMITED DEXAMETHASONE IN PATIENTS WITH TRANSPLANT-INELIGIBLE MULTIPLE MYELOMA (REST):

A MULTICENTRE, SINGLE-ARM, PHASE 2 TRIAL

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AUTHORS: Askeland FB, Haukås E, Slørdahl TS, Klostergaard A, Alexandersen T, Lysén A, Abdollahi P, Nielsen LK, Hermansen E, Schjesvold F
CENTRE FOR CORRESPONDENCE: Oslo Myeloma Center, Department of Hematology, Oslo University Hospital, Oslo, Norway

BACKGROUND & AIM: Studies have shown that adding an anti-CD38 monoclonal antibody to standard therapies can improve outcomes in patients with newly diagnosed multiple myeloma (NDMM) who are ineligible for autologous haematopoietic stem-cell transplantation. However, most regimens use long-term corticosteroids, which increases the infection risk, especially in older patients. The aim of this study was to evaluate the safety and activity of isatuximab, bortezomib and lenalidomide, with limited use of dexamethasone, in patients with transplant-ineligible NDMM, including those older than 79 years.

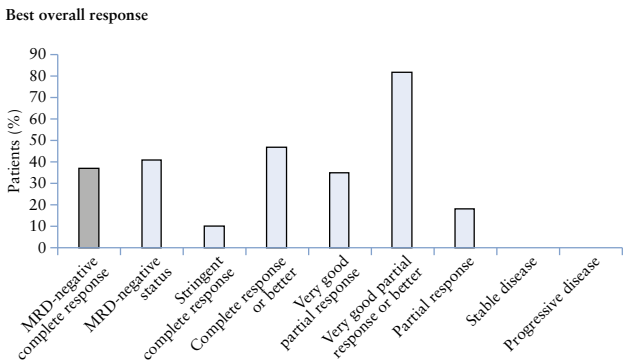
STUDY DESIGN: Investigator-initiated, multicentre, open-label, phase 2 trial.

ENDPOINTS: Primary: measurable residual disease-negative complete response (10^{-5} threshold) at or after 18 cycles of treatment. Secondary endpoints included 18-month progression-free and overall survival, and safety.

METHOD: Adults with transplant-ineligible NDMM (*n*=51) received isatuximab, weekly bortezomib and lenalidomide in 28-day cycles. Oral dexamethasone (20 mg) was given on days 1, 8, 15 and 22 during the first two cycles only.

RESULTS: Patients had a median age of 77 years (interquartile range 73.5–80 years) and 31% were 80 years or older. Median follow-up was 27.0 months (IQR 23.0–33.7 months) and the median treatment duration was 22 months (IQR 15.2–28.8 months). Measurable residual disease-negative complete response was seen in 19 patients (37%; Figure). At 18 months, the progression-free survival rate was 78% and the overall survival rate was 88%. The most common grade 3/4 adverse events were neutropenia (55%), infections (41%) and thrombocytopenia (22%). A total of 48 serious grade 3 or worse adverse events were reported in 27 patients (53%), and two deaths (one pneumonia, one sepsis) were considered possibly related to treatment.

CONCLUSIONS: In this cohort of older transplant-ineligible patients with NDMM, treatment with isatuximab, bortezomib, lenalidomide and limited dexamethasone was active and safe. The incidence of infection was similar to that reported in previous studies of similar combination therapies, despite the considerably older population.



https://doi.org/10.1016/S2352-3026(24)00347-8

INTERNATIONAL MYELOMA SOCIETY/ INTERNATIONAL MYELOMA WORKING GROUP CONSENSUS RECOMMENDATIONS ON THE DEFINITION OF HIGH-RISK MULTIPLE MYELOMA

Journal of Clinical Oncology, 2025 August 20; 43(24):2739–51

AUTHORS: Avet-Loiseau H, Davies FE, Samur MK, et al.
CENTRE FOR CORRESPONDENCE: Department of Medical Oncology, Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA

BACKGROUND & AIM: High-risk multiple myeloma is difficult to identify and manage, partly because there is a lack of uniformity in either criteria or thresholds for specific markers of the condition. Moreover, traditional prognostic factors for multiple myeloma are not suitable in the current era of triplet and quadruplet therapies and new molecular and genomic risk factors are emerging. Consequently, the International Myeloma Society and the International Myeloma Working Group convened an expert panel to develop a practical consensus definition of high-risk multiple myeloma that takes into account new evidence from molecular and genomic assays, updated clinical data and contemporary approaches to risk stratification. The aim of this paper was to report on this consensus definition and its implications.

TYPE OF ARTICLE: Consensus recommendations.

FINDINGS: The expert panel set out to develop a definition of high-risk multiple myeloma that could identify a subset of approximately 20% of patients with the poorest prognosis despite receiving treatment with current therapies, including triplet or quadruplet combinations and posttransplantation maintenance therapy. The following considerations were taken into account: (a) whole-genome sequencing or next-generation sequencing (NGS) should be used for broad molecular profiling; (b) interphase fluorescence in situ hybridization is not considered sufficient for risk stratification in patients with multiple myeloma; (c) bone marrow samples should be used for evaluating the molecular profile; and (d) risk assessment should be performed at diagnosis and relapse.

The Consensus Genomic Staging definition of high-risk multiple myeloma developed by the panel requires the presence of at least one of the following abnormalities: (a) del(17p) with a cut-off clonal fraction of ≥20% or *TP53* mutation (both assessed on CD138-positive/purified cells); (b) one of the *IgH* translocations t(4;14), t(14;16) or t(14;20), provided they co-occur with a chromosome 1q+ abnormality or del(1p32); (c) monoallelic del(1p32) co-occurring with a chromosome 1q+ abnormality or biallelic del(1p32), as detected by the loss of *FAF1* or *CDKN2C*; or (d) a high β_2 microglobulin level (≥5.5 mg/L) with a normal creatinine level (<1.2 mg/dL) – however, the panel noted that this clinical definition is not a substitute for detailed genomic profiling.

CONCLUSIONS: An expert panel developed the first consensus definition of high-risk multiple myeloma based on genomic high-risk features in the setting of contemporary therapies. Use of a consistent definition will enable patients to be given more realistic prognostic information, facilitate the comparison of outcome data from clinical trials and could be incorporated into a risk-stratified approach to treatment.

https://doi.org/10.1200/JCO-24-01893

Compulsory 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. *Excipient with known effect:* This medicine contains 0.2 mg of polysorbate 80 in each mL of isatuximab concentrate for solution for infusion, which is equivalent to 0.1 mg/kg of body weight. Polysorbates may cause allergic reactions. **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, in combination with carfilzomib and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least one prior therapy and 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 transplantation, and in combination with bortezomib, lenalidomide, and dexamethasone, for the induction treatment of adult patients with newly diagnosed multiple myeloma who are eligible 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, 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. Dexamethasone 20 mg (intravenous on the days of isatuximab infusion, and oral on the other days): when administered in combination with isatuximab, bortezomib, and lenalidomide. Montelukast 10 mg oral (or equivalent), at least at cycle 1. Acetaminophen 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]). The IV use 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, before isatuximab and carfilzomib administration, and before isatuximab, bortezomib, and lenalidomide administration. Patients who do not experience an infusion reaction upon their first 4 administrations of SARCLISA 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. In the event of grade 3 or grade 4 neutropenia or febrile neutropenia and/or neutropenic infection, SARCLISA administration should be delayed or omitted until recovery. *Prevention of infection:* Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) can be considered during treatment. *Posology:* The recommended dose of SARCLISA is 10 mg/kg body weight administered as an intravenous infusion in combination with pomalidomide and dexamethasone (Isa-Pd) or in combination with carfilzomib and dexamethasone (Isa-Kd), or in combination with bortezomib, lenalidomide, and dexamethasone (Isa-VRd). SARCLISA dosing schedule for Isa-Pd or Isa-Kd: *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. SARCLISA dosing schedule for Isa-VRd in patients who are ineligible for autologous stem cell transplant (ASCT) (IMROZ) *Cycle 1:* Dosing on days 1, 8, 15, 22 and 29 (weekly). *Cycles 2 to 4:* Dosing on days 1, 15, and 29 (every 2 weeks). *Cycles 5 to 17: Dosing on days 1 and 15 (every 2 weeks). Cycle 18 and beyond: Dosing on day 1 (every 4 weeks).* 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. SARCLISA dosing schedule for Isa-VRd in patients who are eligible for ASCT (GMMG-HD7) *Induction treatment: Cycle 1:* Dosing on days 1, 8, 15, 22 and 29 (weekly). *Cycles 2 to 3:* Dosing on days 1, 15, and 29 (every 2 weeks). Stop for intensification treatment (high dose chemotherapy and ASCT) followed by SOC maintenance treatment. *Missed dose:* The administration schedule must be carefully followed. If a planned 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 or in case of Grade 3 or 4 neutropenia, or febrile neutropenia and/or neutropenic infection. *Infusion rates:* please refer to full SmPC. **Special Populations:** *Elderly:* no dose adjustment is recommended. *Patients with renal impairment:* No dose adjustment is recommended in patients with mild to severe renal impairment including end-stage renal disease. *Patients with hepatic impairment:* No dose adjustment is recommended in patients with mild hepatic impairment. 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):* Outside its authorized indications, SARCLISA has been studied in children aged 28 days to less than 18 years of age with relapsed or refractory acute lymphoblastic or myeloid leukaemia but efficacy has not been established. **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 (IRs):* Infusion reactions, mostly mild or moderate, have been observed in 38.2% of patients treated with SARCLISA in ICARIA-MM, in 45.8% of patients treated with Isa-Kd in IKEMA, and in 24.0% of patients treated with Isa-VRd in IMROZ. 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 patients treated with Isa-Kd, 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. In IMROZ, the infusion reactions started on the infusion day in all patients, mostly during the first SARCLISA infusion, and resolved the same day in 97.3% of patients. All infusion reactions resolved. The most common symptoms of an infusion reaction included dyspnoea and chills. The most common severe sign and symptom was hypertension. However, serious infusion reactions including severe anaphylactic reactions have also been observed after SARCLISA administration. To decrease the risk and severity of infusion reactions, patients should be pre-medicated prior to SARCLISA infusion with acetaminophen, diphenhydramine or equivalent; dexamethasone is to be used as both premedication and anti-myeloma treatment. 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 to grade ≤1 after interruption of SARCLISA infusion, persist or worsen despite appropriate medicinal products, require hospitalization or are life-threatening, permanently discontinue SARCLISA and institute appropriate management. *Neutropenia*: Neutropenia was reported as a laboratory abnormality in: 96.1 % of Isa-Pd patients; 54.8% of Isa-Kd patients; and 87.5% of Isa-VRd patients. Neutropenia was reported as an adverse reaction in: 46.7 % of Isa-Pd patients; 4.5 % of Isa-Kd patients; and 30% of Isa-VRd patients. Grade 3-4 neutropenia reported as a laboratory abnormality in: 84.9 % of Isa-Pd patients and as an adverse reaction in 45.4 % of Isa-Pd patients; as a laboratory abnormality in 19.2 % of Isa-Kd patients (with 17.5 % Grade 3 and 1.7 % Grade 4) and as an adverse reaction in 4.0 % of Isa-Kd patients; and as a laboratory abnormality in 54.4% of Isa-VRd patients (with 35.7% Grade 3 and 18.6% Grade 4) and as an adverse reaction in 30% of Isa-VRd patients. Neutropenic complications have been observed in: 30.3 % of Isa-Pd patients (including 11.8 % of febrile neutropenia and 25.0 % of neutropenic infections); 2.8 % of Isa-Kd patients (including 1.1 % of febrile neutropenia and 1.7 % of neutropenic infections); and 12.5% of patients (including 2.3% of febrile neutropenia and 10.6% of neutropenic infection). Complete blood cell counts should be monitored periodically during treatment. Patients with neutropenia should be monitored for signs of infection. No dose reductions of SARCLISA are recommended. SARCLISA dose delays and the use of colony-stimulating factors (e.g. G-CSF) should be considered to mitigate the risk of neutropenia. *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. Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) according to treatment guidelines should be considered during treatment. *Second primary malignancies (SPMs)*: In ICARIA-MM, second primary malignancies (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 patients (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. In IKEMA study, at a median follow-up time of 56.61 months, SPMs were reported in 18 patients (10.2%) treated with Isa-Kd and in 10 patients (8.2%) treated with Kd. SPMs were skin cancers in 13 patients (7.3%) treated with Isa-Kd and in 4 patients (3.3%) treated with Kd, were solid tumours other than skin cancer in 7 patients (4.0%) treated with Isa-Kd and in 6 patients (4.9%) treated with Kd, and haematological malignancy (acute myeloid leukaemia) in 1 patient (0.8%) in the Kd group. For 1 patient (0.6%) in the Isa-Kd group, the aetiology of the SPM was unknown. Two patients (1.1%) 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. In IMROZ study, at a median follow-up time of 59.73 months, SPMs were reported in 42 patients (16.0%) treated with Isa-VRd (0.041 events per patient-year) and in 16 patients (8.8%) treated with VRd (0.026 events per patient-year). SPMs were skin cancers in 22 patients (8.4%) treated with Isa-VRd and in 7 patients (3.9%) treated with VRd, were solid tumours other than skin cancer in 17 patients (6.5%) treated with Isa-VRd and in 7 patients (3.9%) treated with VRd, and haematological malignancy in 3 patients (1.1%) treated with Isa-VRd and in 2 patients (1.1%) treated with VRd. Patients with SPM of skin cancer continued treatment after resection of the skin cancer, except one patient in each treatment group. SPMs with fatal outcome were reported in 6 patients (2.3%) treated with Isa-VRd (neuroendocrine carcinoma of the skin, malignant melanoma, squamous cell carcinoma of skin, squamous cell carcinoma of lung, colorectal cancer, and rectal adenocarcinoma) and in 2 patients (1.1%) treated with VRd (metastases to peritoneum and adenocarcinoma of colon). The overall incidence of SPMs in all the SARCLISA-exposed patients is 4,3%. 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). This interference with the indirect Coombs test may persist for at least 6 months after the last infusion of SARCLISA. 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 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:* Decreased appetite, neutropenia, thrombocytopenia, infusion reactions, pneumonia*, upper respiratory tract infection, diarrhoea, bronchitis, dyspnoea, nausea, vomiting. *Common:* Weight decreased, atrial fibrillation, skin cancers, Solid tumour (non-skin cancer), herpes zoster, febrile neutropenia, anaemia. *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:* anaemia, neutropenia, thrombocytopenia, skin cancers, solid tumours other than skin cancers, herpes zoster. Uncommon: Anaphylactic reaction**. Not known: Lymphopenia. In IMROZ (Isa-VRd): Very common: pneumonia, upper respiratory tract infection, bronchitis, COVID-19, neutropenia, thrombocytopenia, dyspnoea, diarrhoea, nausea, vomiting, infusion reaction, decreased appetite, Common: febrile neutropenia, anaemia, herpes zoster, skin cancer, solid tumour (non-skin cancer), atrial fibrillation, weight decreased. Uncommon: haematology malignancy, anaphylactic reaction**. Not known lymphopenia. In GMMG-HD7 (Isa-VRd): Very common: Neutropenia, infusion reactions. Common: Pneumonia, anaemia, thrombocytopenia, lymphopenia, neutrophil count decreased. Uncommon: Anaphylactic reaction**, solid tumours (non-skin cancers). **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: 18.07.2025 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.

Netherlands:
L01FC02. 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: Sanofi B.V. Paasheuvelweg 25, 1105 BP Amsterdam. Tel: +31 (0)20 2454000.

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.

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.

Norway:
Refusjon: H-resept: L01F C02. Refusjonsberettiget bruk: Isatuxsimab (Sarclisa) som kombinasjonsbehandling med karfilzomib og deksametason ved myelomatose, etter minst en tidligere behandling. Som kombinasjon med bortezomib og deksametason som førstelinjebehandling av voksne pasienter med nydiagnostisert myelomatose hvor autolog stamcelletransplantasjon ikke er aktuelt **Pakninger og priser:** 5 ml (hettegl.) kr 7908,50. 25 ml (hettegl.) kr 39397,30. **Reseptstatus: C Lokal representant:** sanofi-aventis Norge AS, Prof. Kohts vei 5-17, 1325 Lysaker. Tlf: +47 67 10 71 00. Fullstendig preparatomtale finnes på www.legemiddelsok.no/.

Sweden:
Prescription medication. Not reimbursed. L01FC02. 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.

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.