Report SARCLISA® - Isatuximab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Isatuximab **Brand Name:** Sarclisa **Originator/licensee:** Sanofi Winthrop Industrie **Classification:** NI **ATC code:** L01XC38 **Orphan Status:** **Eu:** / **Us:** Yes **Mechanism of action:** Isatuximab is a monoclonal antibody that has been designed to attach to the protein CD38, which is found in high amounts on multiple myeloma cells. By attaching to CD38 on the multiple myeloma cells, isatuximab activates the immune system to kill the cancer cells [1].	**Authorized Indication:** **EMA**: Isatuximab is indicated in combination with bortezomib, lenalidomide, and dexamethasone, for the induction treatment of adults with NDMM who are eligible for ASCT [1]. **FDA:** Isatuximab is indicated in combination with bortezomib, lenalidomide, and dexamethasone, for the treatment of adults with NDMM who are not eligible for ASCT [2]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 19/06/2025 **FDA M.A. date:** 25/10/2024 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS:** **AE**: Adverse Event **ASCT**: autologous stem cell transplant **CHMP**: Committee for Medicinal Products for Human Use **CI**: Confidential Interval **ECOG**: Eastern Cooperative Oncology Group **HR**: Hazard Ratio **IV**: Intravenously **IMWG**: International Myeloma Working Group **M.A.:** Marketing Authorization **MM:** Multiple myeloma **MRD:** Minimal residual disease **NDMM**: Newly diagnosed multiple myeloma **OS**: Oral administration **PFS**: Progression-Free Survival **P.O.**: Positive Opinion **PS**: Performance Status **Pts**: Patients **R-ISS**: Revised International Staging System **SAE**: Serious adverse events **VRd**: lenalidomide, bortezomib, and dexamethasone **WHO**: World Health Organization	**Summary of clinical EFFICACY:** **GMMG-HD7 (NCT03617731)** was an open-label, multicentre, randomised, active-controlled, phase III trial designed to assess the efficacy and safety of isatuximab for the induction and maintenance treatment of NDMM. The trial is divided in two parts: in part one pts. received induction therapy (three 42-days cycles); in part two pts. received maintenance therapy (isatuximab in combination with lenalidomide or lenalidomide alone) after high-dose melphalan and autologous HSCT. Part two in ongoing. Eligible pts. were aged 18-70 years of age, with a confirmed diagnosis of untreated MM, according to IMWG criteria, requiring systemic treatment and a WHO PS of 0-2. Pts. had to be eligible for induction therapy, high-dose melphalan and autologous ASCT. In part one, pts. (n= 662) were randomly assigned in a 1:1 ration to receive three cycles of induction therapy either with isatuximab plus VRd (isatuximab group; n= 331)) or VRd alone (control group; n= 329). Isatuximab was administered 10 mg/Kg IV on days 1, 8, 15, 22 and 29 of cycle 1 and on days 1, 15 and 29 of cycles 2 and 3. Pts. were stratified according to the R-ISS. In part one, the primary endpoint was MRD negativity assessed by flow cytometry, after induction therapy, in the ITT population. MRD negativity after induction therapy was reached in 166 (50%) pts. in the isatuximab group and 117 (36%) in the control group (OR 1.82 [95% CI 1.33–2.48]; p=0.00017). At the final analysis (data cut off: January 31, 2024), MRD negativity rates were 66% for isatuximab group and 48% for control group [3,4]. **Summary of clinical SAFETY:** Safety analyses were carried out for all pts. in the ITT population who received at least one dose of trial medications. Grade 3-4 AEs occurred in 63% of pts. in the isatuximab group (n=208) and in 61% of pts. in control group (n= 199). Grade 3-4 neutropenia 4 occurred in 77 (23%) vs 23 (7%) pts. and infections of grade 3 or 4 occurred in 40 (12%) versus 32 (10%) pts. At least one SAE of grade 3 or 4 was reported during induction therapy for 92 (28%) pts. in the isatuximab group versus 93 (28%) in the control group. 12 deaths occurred during or after induction therapy (four [1%] in the isatuximab group vs eight [2%] in the control group. Among those, one death due to septic shock in the isatuximab group and four deaths were considered treatment related. **Ongoing studies:** ● ***For the same indication:*** Yes ● ***For other indications:*** No **Discontinued studies (for the same indication):** No --- **References:** [1] https://www.ema.europa.eu/en/medicines/human/EPAR/sarclisa [2] https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761113s011lbl.pdf [3] https://www.sciencedirect.com/science/article/abs/pii/S2352302622002630?via%3Dihub [4] https://ascopubs.org/doi/pdf/10.1200/JCO-24-02266 [5] https://gallery.farmadati.it/Home.aspx [6] http://www.sefap.it/web/upload/GIFF2018-2_23_30.pdf [7] https://www.osservatoriomalattierare.it/i-tumori-rari/mieloma-multiplo/16849-mieloma-multiplo-in-italia-si-stimano-circa-6-000-nuovi-casi-all-anno [8] https://gecoopendata.registrotumoriveneto.it/incidenza.php?sede=mieloma&codSede=C88-C90.9 [9] https://www.iss.it/documents/20126/8404001/LG92_SIE_MM_v3.5.pdf/e60ca973-8456-16c0-0dda-5f7103b8d11e?t=1678805774591	**Cost of therapy:** In Italy 100mg of Isatuximab concentrate for infusion cost 630.11 € (ex-factory price) [5]. **Epidemiology:** NDMM accounts for 10% of all hematologic malignancies worldwide [6]. In Italy, 6,000 new cases are estimated per year [7]. In the Veneto Region, in 2021, 576 new cases were diagnosed [8]. --- **POSSIBLE PLACE IN THERAPY**: For newly diagnosed multiple myeloma pts, who are eligible for stem cell transplantation, the standards of care are represented by the combinations bortezomib-lenalodomide-dexamethasone and bortezomib-thalidomide-dexamethasone [9]. The addition of isatuximab at the regimens could improve the benefits for these pts. **OTHER INDICATIONS IN DEVELOPMENT:** Acute Lymphoblastic Leukaemia (NCT06648889); Amyloidosis (NCT05066607) **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT**: - **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Ixazomib + Lenalidomide (NCT04217967) *Service reorganization: No *Possible off label use: Yes

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