Report SARCLISA® - Isatuximab

Product Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: Isatuximab **Brand Name:** Sarclisa® **Originator/licensee:**Sanofi Aventis US LLC **Classification :** NI **ATC code:** L01XC38 **Orphan Status:** **EU:** No **USA:** Yes **Mechanism of action:**Isa is an IgG1-derived monoclonal antibody that binds to a specific extracellular epitope of CD38 receptor. CD38 is a transmembrane glycoprotein that is highly expressed on multiple myeloma cells[1].	**Authorized Indication** **FDA:** in combination with K and d, for the treatment of adult pts with relapsed or refractory MM who havereceived one to three prior lines of therapy[2]. **EMA:** in combination with K and d, for the treatment of adult pts with MM who have received at least one prior therapy [3]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 25/02/2021 **FDA M.A. date:** 02/03/2020 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No ----- **ABBREVIATIONS:** **CHMP**: Committee for Medicinal Products for Human Use; **d:** dexamethasone; **DaraKd:**daratumumab/carlfizomib/dexamethasone; **EloPd:**elotuzumab/pomalidomide/dexamethasone; **HR:** hazard ratio; **Isa:** isatuximab; **Isa-Kd:** isatuximab/carlfizomib/dexamethasone; **IsaPd:**isatuximab/pomalidomide/dexamethasone; **IV:** intravenous; **K:**carlfizomib; **Kd:**carlfizomib and dexamethasone;**M.A.**: Marketing Authorization; **MM**: multiple myeloma; **OS:** oral administration; **PFS:** progression free survival; **P.O:** Positive Opinion **PomVd:** pomalidomide/bortezomib/dexamethasone **pts:** patients.	**Summary of clinical EFFICACY:** ***Pivotal:*** **IKEMA (NCT03275285):**ongoing, prospective, multicentre, multinational, randomized, open-label, parallel-group, two-arm, Phase III study, evaluating the efficacy and safety of Isa in combination with K+d. 302 adult pts with relapsed and/or refractory MM, who have received one to three prior lines of therapy and withmeasurable serum M-protein (≥0.5 g/dl) and/or urine M-protein (≥200 mg/24 h) have been randomized in a 3:2 ratio to receiveeither: • **Isa-Kd (n = 179):** - **Isa (IV):** 10 mg/kgon day 1, 8, 15, 22 of 1st cycle, then on day 1 and 15 of subsequent cycles; - **K (IV):** 20 mg/m²on day 1 and 2; 56 mg/m² 8, 9, 15 and 16 of 1stcycle; 56mg/m²on day 1, 2, 8, 9, 15 and 16 for all subsequent cycles of each 28-day cycle; - **D (IV or OS):** 20 mg on day 1, 2, 8, 9, 15, 16, 22 and 23 of each28-day cycle; • **Kd (n = 123):** - **K (IV):** 20 mg/m2 on day 1 and 2; 56 mg/m² 8, 9, 15 and 16 of 1stcycle; 56 mg/m2 on day 1, 2, 8, 9, 15 and 16 for all subsequent cycles of each 28-day cycle; - **D (IV or OS):** 20 mg on day 1, 2, 8, 9, 15, 16, 22 and 23 of each 28-day cycle The primary endpoint was PFS. At a median follow-up of 20.7 months, median PFS was not reached for IsaKd whereas it was 19.1 months for Kd (HR 0.53; P = 0.0007); The addition of Isa to Kd demonstrated statistically significant improvement in PFSbenefit with a 47% reduction in the risk of progression or death[2][4][5]. **Summary of clinical SAFETY:** **IKEMA (NCT03275285):**The most common adverse reactions (≥20%) were upper respiratory tract infection, infusionrelated reactions, fatigue, hypertension, diarrhoea, pneumonia, dyspnoea, insomnia, bronchitis, cough and back pain**.** The most common haematology laboratory abnormalities (≥80%) were decreased haemoglobin, decreased lymphocytes, and decreased platelets[2]. **Ongoing studies:** • ***For the same indication:*** Yes • ***For other indications:*** Yes **Discontinued studies (for the same indication):**No **References:** **[1].**https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/761113Orig1s000MultidisciplineR.pdf **[2].** https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761113s003lbl.pdf **[3].** https://www.ema.europa.eu/en/medicines/human/summaries-opinion/sarclisa-0 **[4].**Moreau P, Dimopoulos M, Mikhael J, et al. Isatuximab plus carfilzomiband dexamethasone vs carfilzomib and dexamethasone in relapsed/refractory multiple myeloma (IKEMA): interim analysis of a phase 3,randomized, open-label study. Presented at: The European HematologyAssociation 25th Annual Congress; June 11-21, 2020: Virtual Congress.Abstract LBA2603. **[5].**https://clinicaltrials.gov/ct2/show/record/NCT03275285?term=NCT03275285&draw=2&rank=1&view=record **[6].** https://gallery.farmadati.it/Home.aspx **[7].** Usmani S.Z. Hoering A. Cavo M. et al. Clinical predictors of long-term survival in newly diagnosed transplant eligible multiple myeloma - an IMWG Research Project. Blood Cancer J. 2018; 8: 123 **[8].**M.A. Dimopoulos, P. Moreau, E. Terpos et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†, Annals of Oncology, Volume 32, Issue 3, 2021, Pages 309-322 **[9].**https://www.clinicaltrials.gov/	**Economic impact:**1,459.19 €* for 1 IV vial 100mg/5mL (20 mg/mL**)** of Isa[6]. Price for 1st cycle: 5,836.76 € Price for subsequent cycles: 2,918.38 € **retail price including VAT* *The costs were calculated considering the dosage for a man weighing 70 kg.* **Epidemiology:**MM is a plasma cell neoplasm that accounts for 1%-1.8% of all cancers and is the second most common haematological malignancy with an estimated incidence in Europe of 4.5-6.0/100,000/year. Despite the significant improvement in pts' survival over the past 20 years, only 10%-15% of pts achieve or exceed expected survival compared with the matched general population[7]. ----- **POSSIBLE PLACE IN THERAPY:** **Patients who have received one prior line of therapy:** PomVd, DaraKdorIsaKd are recommended therapies for pts who were previously exposed or arerefractory to lenalidomide, while DaraKd or IsaKd can also be given in pts who are refractory to bortezomib. **Pts at third and subsequent lines of treatment:**for pts who have been exposed or are refractory to both bortezomib and lenalidomide, DaraKd, IsaPd, IsaKd or EloPd are recommended. [8] **OTHER INDICATIONS IN DEVELOPMENT:** Monoclonal Gammopathy; Smoldering Plasma Cell Myeloma; Natural Killer/T-cell Lymphoma; Plasma Cell Myeloma; T-cell Type Acute Leukemia-Precursor; Acute Lymphoblastic Leukemia; other [9]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** **IMROZ (NCT03319667):** aphase 3 study assessing the clinical benefit ofIsa in combination with bortezomib, lenalidomide and dexamethasone versus bortezomib, lenalidomide and dexamethasone in pts with newly diagnosed MM not eligible for transplant[9]. **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:**Vorinostat (in combination with bortezomib),AT9283, TJ202 (in combination with lenalidomide and d) [9]. *Service reorganization: Yes *Possible off label use: Yes

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