SARCLISA

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
II/0035	Extension of indication to include, in combination with bortezomib, lenalidomide and dexamethasone, the induction treatment of adult patients with newly diagnosed multiple myeloma (NDMM) who are eligible for autologous stem cell transplant (ASCT) for SARCLISA, based on the results from study	19/06/2025	18/07/2025	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Sarclisa-H-C-004977-II-0035'

[1] Notifications are issued for type I variations and Article 61(3) notifications (unless part of a group including a type II variation or extension application or a worksharing application). Opinions are issued for all other procedures.
[2] A Commission decision (CD) is issued for procedures that affect the terms of the marketing authorisation (e.g. summary of product characteristics, annex II, labelling, package leaflet). The CD is issued within two months of the opinion for variations falling under the scope of Article 23.1a(a) of Regulation (EU) No. 712/2012, or within one year for other procedures.
[3] SmPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

	IIT15403 (GMMG-HD7); this is a randomised phase III study designed to assess the efficacy and safety of Sarclisa for the induction and maintenance treatment of NDMM. As a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the PI. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
R/0033	Renewal of the marketing authorisation.	12/12/2024	20/02/2025	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Sarclisa in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0030	Extension of indication to include in combination with bortezomib, lenalidomide, and dexamethasone the treatment of adult patients with newly diagnosed active multiple myeloma who are not eligible for autologous stem cell transplant (ASCT) for Sarclisa, based on results from EFC12522 (IMROZ) pivotal phase III study and the supportive TCD13983 phase 1b/2 study. EFC12522 is an ongoing prospective, multicenter, international, randomized, open-label, 2-arm parallel group study to assess the clinical benefit of VRd (control group) versus IVRd (active group) for the treatment of participants with NDMM who are not eligible for ASCT. As a consequence,	14/11/2024	20/01/2025	SmPC and PL	Please refer to Scientific Discussion 'Sarclisa-EMEA/H/C/004977/II/30'.

	sections 4.1, 4.2, 4.4, 4.5, 4.7, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 2.1 of the RMP has also been submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IB/0034/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.z - Quality change - Finished product - Other variation	17/12/2024	n/a		
N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/07/2024	20/01/2025	PL	
IB/0031/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.I.b.2.e - Change in test procedure for AS or	16/05/2024	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised				

IB/0029	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	11/04/2024	n/a		
II/0027	Update of section 4.8 of the SmPC in order to add 'Thrombocytopenia' and 'Anaemia' to the list of adverse drug reactions (ADRs) and to amend the frequency of all remaining ADRs with their appropriate frequencies, following PRAC request in the outcome of the PSUSA procedure PSUSA/00010851/202303. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	11/04/2024	20/01/2025	SmPC and PL	Not applicable. For more information, please refer to the Summary of Product Characteristics.
II/0025	Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to amend an existing warning on second primary malignancies and to update efficacy and safety information based on Overall Survival analysis from study EFC15246 (IKEMA - Randomized, open label, multicenter study assessing the clinical benefit of isatuximab combined with carfilzomib (Kyprolis) and dexamethasone versus carfilzomib with dexamethasone in patients with relapsed and/or refractory multiple myeloma previously treated with 1 to 3 prior lines). In addition, the MAH took this opportunity to introduce editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to	11/04/2024	20/01/2025	SmPC and PL	Not applicable.

	new quality, preclinical, clinical or pharmacovigilance data				
II/0028	Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to update information on paediatric population based on final results from study ACT15378 (ISAKIDS). This was a Phase 2, single-arm, multicenter, open-label study evaluating the antitumor activity, safety, and PK of isatuximab in combination with standard salvage chemotherapies in paediatric participants with R/R ALL (including both T-ALL and B-ALL) and AML conducted in 3 separate cohorts. Male and female children from 28 days to less than 18 years of age with R/R T-ALL, B-ALL, or AML in first or second relapse were eligible. Participants under 2 years of age could only be enrolled after the dose reassessment is completed on the first 20 participants who were 2 to less than 18 years of age. The Package Leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	04/04/2024	20/01/2025	SmPC and PL	SmPC new text Outside its authorised indications, isatuximab 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. For more information, please refer to the Summary of Product Characteristics.
II/0026	Update of sections 4.2, 4.4 and 5.2 of the SmPC based on final results from study TED16414, listed as a category 3 study in the RMP; this is a phase 1b/2 open label, non-randomized, multi center study to evaluate the safety, pharmacokinetics, and preliminary efficacy of isatuximab (SAR650984) in patients awaiting kidney transplantation. The	22/02/2024	20/01/2025	SmPC and PL	Based on population pharmacokinetic analysis and on clinical data no dose adjustment of isatuximab is needed in patients with mild, moderate, severe or end-stage renal impaired function. For more information, please refer to the Summary of Product Characteristics.

	Package Leaflet is updated accordingly. The RMP version 1.6 has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0024	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	11/01/2024	n/a		
IB/0023	B.I.d.1.a.4 - Stability of AS - Change in the re-test period/storage period - Extension or introduction of a re-test period/storage period supported by real time data	17/10/2023	n/a		
PSUSA/10851 /202303	Periodic Safety Update EU Single assessment - isatuximab	28/09/2023	n/a		PRAC Recommendation - maintenance
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/06/2023	16/02/2024	PL	
II/0020	Update of sections 4.4, 4.8 and 5.1 of the SmPC in order to update an existing warning on 'second primary malignancies', update the list of adverse drug reactions (ADRs) and update the efficacy and safety information based on final OS analysis from ICARIA study (EFC14335), following a recommendation by the CHMP during the initial MAA. This is a phase 3 randomized, open-label,	30/03/2023	16/02/2024	SmPC	

	multicenter study designed to assess the efficacy, safety, and pharmacokinetics (PK) of isatuximab in combination with pomalidomide and low-dose dexamethasone (IPd) compared with pomalidomide and low-dose dexamethasone (Pd) in patients with refractory or relapsed and refractory multiple myeloma. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
T/0019	Transfer of Marketing Authorisation	28/10/2022	20/12/2022	SmPC, Labelling and PL	
PSUSA/10851 /202203	Periodic Safety Update EU Single assessment - isatuximab	13/10/2022	16/12/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10851/202203.
II/0018/G	This was an application for a group of variations. C.I.4: Update of sections 4.5, 5.1 and 5.2 of the SmPC in order to update the efficacy and pharmacokinetic data based on final progression-free survival (PFS) efficacy results from IKEMA study (EFC15246) and to introduce the Sebia Hydrashift assay, a validated assay to determine the complete response rate. IKEMA study (EFC15246) is a phase 3 randomized, open label, multicenter study assessing the clinical benefit of isatuximab combined with carfilzomib (Kyprolis) and dexamethasone versus carfilzomib with dexamethasone in patients with	15/12/2022	16/02/2024	SmPC	In patients with persistent very good partial response, where isatuximab interference is suspected, consideration should be given to the use of a validated isatuximab-specific immunofixation (IFE) assay to distinguish isatuximab from any remaining endogenous M protein in the patient's serum, in order to facilitate determination of a complete response. For more information, please refer to the Summary of Product Characteristics.

	relapsed and/or refractory multiple myeloma previously treated with 1 to 3 prior lines. A.6: Update of section 5.1 of the SmPC in order to update ATC code following amendment by WHO. A.6 - Administrative change - Change in ATC Code/ATC Vet Code C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0017/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method B.I.a.1.k - Change in the manufacturer of AS or of a	15/12/2022	16/02/2024	Annex II	

	starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
II/0015	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	14/07/2022	n/a		

	Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
II/0014	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to amend an existing warning on Infections by adding herpes zoster prophylaxis as antiviral prophylaxis, following FDA post-market survey and request to update the US PI based on a cumulative assessment of Sanofi global PV database and scientific literature. The Package Leaflet is updated accordingly. is recommended for approval. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/06/2022	16/12/2022	SmPC and PL	SmPC new text Section 4.2: Prevention of infection Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) can be considered during treatment (see section 4.4). Section 4.2 For more information, please refer to the Summary of Product Characteristics. Section 4.4 Antibacterial and antiviral prophylaxis (such as herpes zoster prophylaxis) can be considered during treatment (see sections 4.2 and 4.8). Section 4.8 Tables 3 and 4 are updated to include ADR Herpes zoster infection under SOC "Infections and infestations" with frequency common
PSUSA/10851 /202109	Periodic Safety Update EU Single assessment - isatuximab	07/04/2022	n/a		PRAC Recommendation - maintenance
IB/0013/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or	17/12/2021	n/a		

	manufacturer of a novel excipient B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
PSUSA/10851 /202103	Periodic Safety Update EU Single assessment - isatuximab	14/10/2021	16/12/2021		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10851/202103.
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/11/2021	16/12/2022	PL	
II/0009/G	This was an application for a group of variations. Type II variation B.I.a.4.d Change to in-process tests or limits applied during the manufacture of the active substance - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the active substance - To change the non-critical process parameter limits for viability, viable cell density and step duration for the shake flask and 2L wave bag step of the manufacturing process for isatuximab active	22/07/2021	n/a		

	substance. The proposed limits will remain within the generation number limit and total cell culture durations established per LIVCA (3.2.S.2.3 Limit of In Vitro Cell Age (LIVCA)). Type IB variation B.I.a.2.a: Change in the manufacturing process of the active substance - Minor change in the manufacturing process of the active substance - To introduce a change to the method of preparation for the Working Cell Bank (WCB) used in the manufacture of Sarclisa (isatuximab). Type IB variation - B.I.b.2.z Change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance - other change - To introduce a change to the Master Cell Bank (MCB) stability testing assessment from a direct or indirect study to an indirect study only. The Applicant took the opportunity to make the following editorial changes: - Section 3.2.S.4.1 - Table 1 - Specifications for isatuximab active substance will be updated to correct the Microbiological examination (membrane filtration) with the footnote "(a) Tested only at release". This is an editorial change since section 3.2.S.7 already lists the correct shelf life test. - Section 3.2.S.4.4 - this section has been updated to correct the table numbers and to include post-PPQ				

	results and alignment with acceptance criteria submitted with EMEA/H/C/004977/IB/0004. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation				
PSUSA/10851 /202009	Periodic Safety Update EU Single assessment - isatuximab	22/04/2021	17/06/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10851/202009.
IB/0008	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/06/2021	n/a		
IA/0007/G	This was an application for a group of variations. A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition	22/04/2021	n/a		

	of a new in-process test and limits				
II/0003	An Extension of indication for Sarclisa to add combination with carfilzomib and dexamethasone, for the treatment of patients with multiple myeloma who have received at least one prior therapy. As a consequence the sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 have been updated. The PL is updated accordingly. The MAH took the opportunity to introduce minor changes in the SmPC sections 4.9, 6.3 and 6.6 and update the details of local representatives. Editorial changes have been also introduced to the Annex II key elements of the RMMs. The RMP version 1.2 has been updated. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	25/02/2021	15/04/2021	SmPC and PL	Please refer to Scientific Discussion 'Sarclisa-H-C-004977-II-0003'
IB/0005	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	26/01/2021	n/a		
IB/0004	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	25/11/2020	n/a		
IB/0002	B.I.a.3.e - Change in batch size (including batch size ranges) of AS or intermediate - The scale for a biological/immunological AS is increased/decreased without process change (e.g. duplication of line)	02/07/2020	n/a		

IB/0001	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	29/06/2020	n/a		