Ultomiris

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/0039	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	31/08/2023	n/a		
PSUSA/10787 /202212	Periodic Safety Update EU Single assessment - ravulizumab	31/08/2023	n/a		PRAC Recommendation - maintenance

[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).

II/0034	Update of sections 4.8 and 5.1 of the SmPC in order to update efficacy and safety information based on final results from study ALXN1210-PNH-302, a Phase III, randomised, open-label, active controlled study of ALXN1210 versus eculizumab in adult patients with paroxysmal nocturnal hemoglobinuria (PNH) currently treated with eculizumab, listed as a category 3 study in the RMP. 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	13/07/2023		SmPC and PL	SmPC new text Section 4.8 The frequency of the most common AE has been updated and the following AE are also switched from common to very common: pyrexia, nausea, arthralgia, fatigue, back pain, and abdominal pain. Section 5.1 It was added that "The final efficacy analysis for the study included all patients ever treated with ravulizumab (n=192) and had a median treatment duration of 968 days".
IB/0038/G	This was an application for a group of variations. B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.II.g.3 - Deletion of an approved change management protocol related to the finished product	23/06/2023	n/a		
X/0027/G	This was an application for a group of variations. Extension application to introduce a new pharmaceutical form (solution for injection) associated with new strength (245 mg) and route of administration (subcutaneous use), grouped with a type II variation (C.I.4) to align the Summary of product characteristics and Labelling of Ultomiris intravenous formulation (IV) with the proposed	30/03/2023	31/05/2023	SmPC, Labelling and PL	Not applicable

	Ultomiris subcutaneous formulation (SC). The RMP (version 7.0) is updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10.3. Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form Annex I_2.(e) Change or addition of a new route of administration C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0037/G	This was an application for a group of variations. B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.II.g.3 - Deletion of an approved change management protocol related to the finished product	25/05/2023	n/a		
II/0032	Extension of indication to include the treatment of adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin 4 (AQP4) antibody-positive, based on interim results from study ALXN1210-NMO-307; this is a phase 3, external placebo-controlled, open-label, multicenter study to evaluate the efficacy and safety of ravulizumab in adult patients with NMOSD. As a	30/03/2023	05/05/2023	SmPC and PL	Please refer to Scientific Discussion 'Product Name-H-C-Product Number-II-0032

	consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6.0 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial 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				
IAIN/0035/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible 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 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)	17/03/2023	05/05/2023	Annex II and PL	
II/0033/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch	24/11/2022	n/a		

	control/testing takes place B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes				
II/0030	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	06/10/2022	05/05/2023	Annex II	
II/0026	Extension of indication to include treatment of adult patients with generalized myasthenia gravis (gMG). As a consequence, Sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 and 6.6 of the SmPC and corresponding sections in the Package Leaflet are updated accordingly. The RMP has been updated to version 4.0 to align with the indication extension. Lastly, the minor editorial corrections are made throughout the SmPC and package leaflet. The Applicant also requested 1 year of market protection for a new indication (Article 14(11) of Regulation (EC) 726/2004). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	21/07/2022	21/09/2022	SmPC and PL	Please refer to Scientific Discussion: EMEA/H/C/004954/II/0026

II/0029	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	01/09/2022	n/a		
PSUSA/10787 /202112	Periodic Safety Update EU Single assessment - ravulizumab	01/09/2022	n/a		PRAC Recommendation - maintenance
IB/0031	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	17/08/2022	n/a		
PSUSA/10787 /202106	Periodic Safety Update EU Single assessment - ravulizumab	27/01/2022	01/04/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10787/202106.
IB/0025/G	This was an application for a group of variations. B.II.g.3 - Deletion of an approved change management protocol related to the finished product B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	16/11/2021	n/a		
II/0016	Update of section 4.4 Special warnings and precautions for use and Section 4.8 Undesirable effects of the SmPC, with consequential updates to Section 2 and 4 of the Patient Information Leaflet regarding anaphylactic reaction, hypersensitivity,	30/09/2021	01/04/2022	SmPC and PL	SmPC new text: Administration of ravulizumab may result in infusion reactions and allergic or hypersensitivity reactions (including anaphylaxis). 'Anaphylactic reaction and hypersensitivity' have been

	and infusion-related reactions. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				added to the Table of Adverse reactions as uncommon adverse reactions. 'Infusion related reaction' has been added to the Table of Adverse reactions as common adverse reaction.
II/0010	Extension of indication for Ultomiris to include treatment of paroxysmal nocturnal haemoglobinuria (PNH) in paediatric patients with a body weight of 10 kg or above; 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 in accordance. In addition, Annex II is updated to reflect the agreed educational material (addition of a "Parent guide"). Version 2.1 of the RMP has also been submitted, in order to include the new indication. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/07/2021	01/09/2021	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Ultomiris-H-C-004954-II-0010'
IB/0023/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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	18/08/2021	n/a		
IAIN/0022/G	This was an application for a group of variations.	13/07/2021	01/09/2021	SmPC, Annex	

	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing B.II.f.1.a.3 - Stability of FP - Reduction of the shelf life of the finished product - After dilution or reconstitution			II and PL	
PSUSA/10787 /202012	Periodic Safety Update EU Single assessment - ravulizumab	08/07/2021	n/a		PRAC Recommendation - maintenance
IB/0021/G	This was an application for a group of variations. B.I.e.3 - Deletion of an approved change management protocol related to the AS B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	28/06/2021	n/a		
II/0015/G	This was an application for a group of variations. B.II.g.2 - Introduction of a post approval change management protocol related to the finished product B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	24/06/2021	n/a		
IB/0020	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/06/2021	n/a		

IB/0019	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	21/05/2021	n/a		
IAIN/0017/G	This was an application for a group of variations. B.II.g.5.a - Implementation of changes foreseen in an approved change management protocol - Requires no further supporting data B.II.g.3 - Deletion of an approved change management protocol related to the finished product	29/04/2021	n/a		
IB/0014/G	This was an application for a group of variations. B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.I.b.1.b - Change in the specification parameters	22/04/2021	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
IB/0011/G	This was an application for a group of variations. B.II.g.3 - Deletion of an approved change management protocol related to the finished product B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	27/01/2021	n/a		
IB/0012	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	18/01/2021	n/a		
PSUSA/10787 /202006	Periodic Safety Update EU Single assessment - ravulizumab	14/01/2021	n/a		PRAC Recommendation - maintenance
X/0004/G	This was an application for a group of variations. Extension application to add a new strength (1100 mg in 11 ml vial, concentration 100 mg/ml) for Ultomiris concentrate for solution for infusion, grouped with a Type II application (B.II.z) for a new	17/09/2020	18/11/2020	SmPC, Annex II, Labelling and PL	

	presentation (300 mg in 3 ml vial, concentration 100 mg/ml) including changes in the active substance concentration, excipients composition and concentrations, and minor differences in the last two steps of the manufacturing process. Annex I_2.(c) Change or addition of a new strength/potency B.II.z - Quality change - Finished product - Other variation				
IB/0009/G	This was an application for a group of variations. B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data) B.II.g.3 - Deletion of an approved change management protocol related to the finished product	23/09/2020	01/09/2021	SmPC	
PSUSA/10787 /201912	Periodic Safety Update EU Single assessment - ravulizumab	09/07/2020	n/a		PRAC Recommendation - maintenance
II/0002	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	30/04/2020	25/06/2020	SmPC, Annex II and PL	
IB/0007	B.II.g.5.b - Implementation of changes foreseen in an approved change management protocol - Requires further supporting data	22/06/2020	n/a		
II/0005	B.II.g.2 - Introduction of a post approval change	28/05/2020	n/a		

	management protocol related to the finished product				
II/0003/G	This was an application for a group of variations. 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.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place 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	16/01/2020	25/06/2020	SmPC	
IAIN/0001	A.1 - Administrative change - Change in the name and/or address of the MAH	26/07/2019	25/06/2020	SmPC, Labelling and PL	