Respreeza

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
N/0058	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/12/2021		PL	
IA/0056	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	22/11/2021	n/a		

[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).

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IG/1429	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	20/08/2021	n/a		
II/0053/G	This was an application for a group of variations. B.II.e.1.b.2 (Type II) - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products - Introduction of an alternative stopper (bromobutyl rubber) for the sterile water for injections (SWFI) 20 mL, 76 mL and 95 mL vials. B.II.e.7.a (Art. 5 unforeseen - Type IA) Container closure system - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier – To delete the registered suppliers for the primary packaging materials for WFI from the dossier. B.II.b.3.z (Art. 5 unforeseen - Type IA) Change in the manufacturing process of the finished product or intermediate product – Other variation - Deletion of one manufacturing process of the drug product manufacturing process - To delete the no longer used production procedure P-110 and filling and packaging procedure F-110 from the manufacturing	22/07/2021		SmPC	

	process for WFI. The MAH took the opportunity to correct a technical publishing error occurred in the dossier section 2.3.A.1., with eCTD Sequence 0093. The product related 2.3.A.1 was mistakenly replaced with the 2.3.A.1 concerning the solvent water for injections manufactured at CSL Behring LLC. With the current submission this error is corrected by replacing the 2.3.A.1 introduced with the eCTD Sequence 0093 with the 2.3.A.1 from the eCTD sequence 0081. Thereby reintroducing the missing product related 2.3.A.1. The content has not changed. The MAH also took the opportunity to introduce some editorial changes to section 3.2.A.1. Regarding the Product Information the specific material type of the rubber stopper stated in section 6.5. of the SmPC is changed from chlorobutyl/bromobutyl to "butyl". B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier				

IG/1356	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	16/02/2021	n/a		
IB/0047	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	22/12/2020	n/a		
IB/0049	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	04/12/2020	n/a		
IB/0048	B.I.b.z - Change in control of the AS - Other variation	30/11/2020	n/a		
IB/0045	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/10/2020	22/03/2021	SmPC and PL	
IB/0046	B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products	09/10/2020	n/a		
IA/0044	B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the	08/09/2020	n/a		

	finished product - Tightening of specification limits				
IB/0042	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	23/07/2020	n/a		
II/0041	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	16/07/2020	n/a		
IG/1269	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	15/07/2020	n/a		
II/0040	B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability	18/06/2020	n/a		
IB/0039	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	29/04/2020	n/a		
R/0036	Renewal of the marketing authorisation.	27/02/2020	23/04/2020	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Respreeza in the approved indication remains favourable and therefore recommended the renewal of the marketing

					authorisation with unlimited validity. The product information is updated in accordance with the latest QRD template version 10.1.
IB/0038	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	06/04/2020	22/03/2021	SmPC, Labelling and PL	
PSUSA/10410 /201908	Periodic Safety Update EU Single assessment - human alfa1-proteinase inhibitor (centrally authorised product)	12/03/2020	n/a		PRAC Recommendation - maintenance
IG/1209	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	25/02/2020	n/a		
IB/0034	B.I.z - Quality change - Active substance - Other variation	27/11/2019	n/a		
IA/0033/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.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	03/10/2019	n/a		

N/0032	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/08/2019	23/04/2020	PL	
II/0029/G	This was an application for a group of variations. 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.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	06/06/2019	n/a		
IB/0031	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	03/05/2019	n/a		
IG/1074	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	01/04/2019	n/a		
PSUSA/10410 /201808	Periodic Safety Update EU Single assessment - human alfa1-proteinase inhibitor (centrally authorised product)	14/03/2019	n/a		PRAC Recommendation - maintenance

N/0028	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/11/2018	31/01/2019	Labelling and PL	
IB/0026	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)	06/11/2018	n/a		
II/0024	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	04/10/2018	n/a		
IB/0025/G	This was an application for a group of variations. B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale	01/10/2018	31/01/2019	SmPC	
II/0023/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products	26/07/2018	31/01/2019	SmPC, Labelling and PL	

	B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products B.II.e.5.c - Change in pack size of the finished product - Change in the fill weight/fill volume of sterile multidose (or single-dose, partial use) parenteral medicinal products, including biological/immunological medicinal products B.II.e.5.c - Change in pack size of the finished product - Change in the fill weight/fill volume of sterile multidose (or single-dose, partial use) parenteral medicinal products, including biological/immunological medicinal products B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation				
II/0020	B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products	15/03/2018	31/01/2019	SmPC and PL	
PSUSA/10410 /201708	Periodic Safety Update EU Single assessment - human alfa1-proteinase inhibitor (centrally authorised product)	08/03/2018	n/a		PRAC Recommendation - maintenance

IB/0021	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	22/02/2018	31/01/2019	SmPC, Labelling and PL	
IG/0885	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	29/01/2018	n/a		
PSUSA/10410 /201702	Periodic Safety Update EU Single assessment - human alfa1-proteinase inhibitor (centrally authorised product)	28/09/2017	n/a		PRAC Recommendation - maintenance
IB/0017	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	24/04/2017	n/a		
IG/0788	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	12/04/2017	n/a		
II/0013	C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	06/04/2017	n/a		

IA/0015	B.II.d.2.f - Change in test procedure for the finished product - To reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number	22/03/2017	n/a		
IA/0014/G	This was an application for a group of variations. B.I.a.z - Change in manufacture of the AS - Other variation 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	09/03/2017	n/a		
PSUSA/10410 /201608	Periodic Safety Update EU Single assessment - human alfa1-proteinase inhibitor (centrally authorised product)	09/03/2017	n/a		PRAC Recommendation - maintenance
IG/0757	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP	26/01/2017	n/a		
IB/0011	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	21/12/2016	n/a		

N/0009	Update of the package leaflet with revised contact details of the local representatives for Greece and Cyprus. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/10/2016	22/05/2017	PL	
IAIN/0008	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	22/09/2016	22/05/2017	SmPC, Labelling and PL	
PSUSA/10410 /201602	Periodic Safety Update EU Single assessment - human alfa1-proteinase inhibitor (centrally authorised product)	02/09/2016	n/a		PRAC Recommendation - maintenance
II/0004/G	This was an application for a group of variations. 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.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph	30/06/2016	n/a		

	of the Ph. Eur. or national pharmacopoeia of a Member State				
II/0002	Update of sections 4.8 with change of frequency from uncommon to common for dyspnoea and nausea and 5.1 of the SmPC in order to add information from final study report for study CE1226_3001. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to align the section 4.4 of the SmPC with the RMP on hypersensitivity and anaphylactic reactions due to traces of IgA. Furthermore, the PI has been aligned to SmPC guideline. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/06/2016	22/05/2017	SmPC and PL	The safety and efficacy of Respreeza was evaluated in a randomized, double-blind, placebo-controlled, multi-center study (RAPID) followed by a 2-year open-label extension study (RAPID extension study). One-hundred forty subjects (76 Respreeza-treated subjects and 64 subjects treated with placebo in the RAPID Study) continued into the RAPID extension study and were treated with a weekly 60 mg / kg bw intravenous dose of Respreeza for up to 24 months. The RAPID extension study demonstrated that the reduced rate in lung density decline was maintained for subjects continuously treated with Respreeza for 4 years.
IB/0007	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	14/06/2016	n/a		
IG/0676/G	This was an application for a group of variations. B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or	27/04/2016	n/a		

	amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IA/0003/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the	01/04/2016	n/a		

	dossier) - Replacement or addition of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
IB/0001/G	This was an application for a group of variations. 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.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	21/12/2015	n/a		