HyQvia

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/0101	B.II.f.1.c - Stability of FP - Change in storage conditions for biological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol	03/04/2025		SmPC, Labelling and PL	The SmPC section 6.4 has been updated as follows: Store in a refrigerator (2 °C – 8 °C). The product may be stored at temperatures above +8°C and below +25°C for up to 3 months. Do not refrigerate after storing at room temperature. Discard after 3 months or after the expiry date is reached whichever occurs

[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).

					sooner. The date of removal from the refrigerator should be recorded on the outer carton. The Labelling and PL have been updated accordingly.
II/0102	Update of sections 4.8 and 5.1 of the SmPC to reflect results from the final report from study 161505; this is a Phase 3b, open-label, non-controlled, multicenter study to assess the long-term tolerability and safety of immune globulin infusion 10% (human) with recombinant human hyaluronidase (HyQvia) for the treatment of chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). The package leaflet is updated accordingly. In addition, the marketing authorisation holder has taken the opportunity to update the list of local representatives in the PL and implement minor editorial changes in sections 4.1, 4.2, 4.4, 5.2 and 6.4 of the SmPC and PL. The RMP version 16.0 has also been approved. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	27/02/2025		SmPC and PL	Study 161505 was a multi-center, open-label extension study to investigate the long-term safety (primary objective) and efficacy (secondary objective) of HyQvia in maintenance treatment of CIDP in subjects who had received prior HyQvia therapy (or placebo) in Study 161403. Overall, the final safety and efficacy results of the long-term extension study support efficacious CIDP maintenance treatment with HyQvia. The product information has been updated to reflect the final safety and efficacy results of the CIDP extension study 161505 in sections 4.8 and 5.1 of the SmPC. For more information, please refer to the Summary of Product Characteristics.
WS/2622	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	13/02/2025	n/a		

WS/2669	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	13/06/2024	n/a		
WS/2657	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	23/05/2024	n/a		
II/0096	Update of sections 4.8 and 5.1 of the SmPC in order to update long-term safety information based on final results from studies 161406 "Non-Interventional Post-Marketing Safety Study on the Long-Term Safety of HYQVIA (Global)" listed as a category 3 study in the RMP and 161302 "Non-Interventional Post-Authorization Safety Study on the Long-Term Safety of HyQvia in Subjects Treated with HyQvia". Both studies were non-interventional, prospective, uncontrolled, multicenter, open-label, post-authorization studies. The RMP version 15.0 has also been approved. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.3, to update the list of local representatives in the Package Leaflet and to introduce minor editorial changes to the PI.	16/05/2024		SmPC, Annex II and PL	Study 161406 was a non-interventional, prospective, uncontrolled, multicenter, open-label, post-marketing surveillance study. The primary objective of the study was to collect and assess additional safety data, in particular the occurrence of long-term changes in incidence and severity of related adverse events in subjects treated with HyQvia. In line with the previous EU PASS 161302, the study confirms the known safety profile for HyQvia in the adult population and in the elderly population. This information has been added in sections 4.8 and 5.1 of the SmPC. For more information, please refer to the Summary of Product Characteristics.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IAIN/0100	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	14/05/2024	n/a		
IA/0099/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	19/04/2024	n/a		
WS/2584	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	29/02/2024	n/a		
WS/2605	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	22/02/2024	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0087	Extension of indication to include treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) as maintenance therapy after stabilization with IVIg in adults, children and adolescents for HyQvia, based on final results from studies 161403 and TAK-771-1001; and interim results from study 161505. 161403 and 161505 are interventional Phase III efficacy and safety studies, while TAK-771-1001 is an interventional Phase I safety study. As a consequence, sections 4.1, 4.2, 4.4, 4.7, 4.8, 5.1,5.2 and 6.6 of the SmPC are updated. The Package Leaflet and Labelling are updated in accordance. Version 14.3 of the RMP has also been accepted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is brought in line with the latest QRD template. The variation leads to amendments to the Summary of Product Characteristics, Labelling and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	14/12/2023	25/01/2024	SmPC, Labelling and PL	Please refer to Scientific Discussion 'HyQvia-H-C-2491-II-0087'
WS/2582	This was an application for a variation following a worksharing procedure according to Article 20 of	18/01/2024	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
IB/0093/G	This was an application for a group of variations. 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 of the Ph. Eur. or national pharmacopoeia of a Member State B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	13/11/2023	n/a		
WS/2490	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.z - Quality change - Active substance - Other variation	13/07/2023	n/a		
IAIN/0091	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	12/05/2023	n/a		
IB/0089/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or	30/03/2023	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
WS/2359	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	02/03/2023	n/a		
IA/0088/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test A.7 - Administrative change - Deletion of manufacturing sites	13/02/2023	n/a		

IB/0086/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.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process 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	04/01/2023	n/a		
WS/2328	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	08/12/2022	n/a		
II/0078	Update of section 4.8 and 5.1 of the SmPC in order to update safety data in paediatric population based on final results from study 161504 – Post-Authorization Safety, Tolerability and Immunogenicity Evaluation of HyQvia in Pediatric Subjects With Primary Immunodeficiency Diseases, listed as a category 3 study in the RMP. This is a paediatric interventional Phase 4 study performed to	27/10/2022	19/10/2023	SmPC, Annex II and PL	

	acquire additional data on safety, tolerability and immunogenicity of HyQvia in paediatric (age two to <18 years) patients with Primary Immunodeficiency Diseases (PIDD). In addition, the MAH is taking this opportunity to update Annex II-D of the PI following procedure EMEA/H/C/002491/II/0070/G, and to remove the statement that this medicinal product is subject to additional monitoring from the SmPC and Package leaflet following the fulfilment of the PASS 161302. The RMP version 13.1 has also been adopted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0084	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	05/10/2022	n/a		
IA/0083	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	23/08/2022	n/a		
IAIN/0081	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	13/07/2022	n/a		

N/0079	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/06/2022	19/10/2023	PL	
WS/2240	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	19/05/2022	n/a		
SW/0080	Post Authorisation Safety Study results - EMEA/H/C/PSR/S/0037 – Variation	24/02/2022	29/04/2022	Annex II	The final study report submitted by the MAH complies with their obligation to perform a PASS to evaluate the long-term safety and use of HyQvia in patients receiving treatment with HyQvia as imposed at the time of the initial marketing authorisation.
IA/0076/G	This was an application for a group of variations. 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.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.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	24/01/2022	n/a		

	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.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.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) 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)				
WS/2060	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	21/10/2021	n/a		

	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product				
WS/2099	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	14/10/2021	n/a		
II/0070/G	This was an application for a group of variations. 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 C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	02/09/2021	04/02/2022	SmPC and PL	In view of the very limited data from the result of a non-interventional, prospective, uncontrolled, two-arm, open-label, multicentre post-authorisation pregnancy registry of women treated with HyQvia, section 4.6 of the SmPC has been updated to state that from a total of nine women enrolled in this study, and of the eight pregnancies with known outcomes, there were eight live births with normal APGAR scores. There were no specified labor or delivery complications. Four mothers were tested for anti rHuPH20 binding or neutralizing antibodies and no antibodies were detected. Subsection Breast-feeding of section 4.6 has been updated to add that one infant in the study was breastfed and that all adverse events were reported as not related to previous or current HyQvia treatment. Section B point 2 of the Package Leaflet is updated accordingly and several editorial changes that do not change the content of the previously approved SmPC are introduced in sections 3, 4.2, 4.4 and 4.7. For more information, please refer to the Summary of

					Product Characteristics.
N/0074	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/08/2021	04/02/2022	PL	
IAIN/0075	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	08/07/2021	n/a		
WS/1964	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	08/07/2021	n/a		
II/0068/G	This was an application for a group of variations. B.II.c.1.d - Change in the specification parameters and/or limits of an excipient - Change outside the approved specifications limits range B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new	08/07/2021	n/a		

	specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.II.c.2.b - Change in test procedure for an excipient - Deletion of a test procedure if an alternative test procedure is already authorised B.II.c.2.a - Change in test procedure for an excipient - Minor changes to an approved test procedure B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of				

	specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.I.d.1.b.3 - Stability of AS - Change in the storage conditions - Change in storage conditions of the AS 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 B.I.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile) 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) 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.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method 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 B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.2.c - Change in test procedure for an excipient - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent B.II.c.1.e - Change in the specification parameters and/or limits of an excipient - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product				

	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.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.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.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.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.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				
WS/2047	This was an application for a variation following a worksharing procedure according to Article 20 of	20/05/2021	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
WS/1984	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	11/02/2021	n/a		
IB/0067	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	02/02/2021	04/02/2022	Annex II	
PSUSA/1633/202005	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	14/01/2021	n/a		PRAC Recommendation - maintenance
IA/0065/G	This was an application for a group of variations. B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an	08/12/2020	n/a		

	alternative method is already authorised B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised				
WS/1924	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	26/11/2020	n/a		
WS/1882	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	17/09/2020	n/a		
II/0056	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/07/2020	03/09/2020	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion 'HyQvia-H-C-002491-II-0056'
IAIN/0062	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier	20/08/2020	n/a		

	of a medicinal product. (PMF 2nd step procedure) - Inclusion of an updated/amended PMF when changes do not affect the properties of the FP				
IB/0061	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 control/testing takes place	11/08/2020	n/a		
IAIN/0059/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer 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	20/05/2020	n/a		
N/0057	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/04/2020	03/09/2020	PL	
II/0055	B.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	17/04/2020	n/a		

II/0054	B.II.e.4.b - Change in shape or dimensions of the container or closure (immediate packaging) - The change in shape or dimensions concerns a fundamental part, which may have a significant impact on the delivery, use, safety or stability of the FP	12/03/2020	n/a		
WS/1524	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.e.2 - Introduction of a post approval change management protocol related to the AS	20/02/2020	n/a		
IA/0052/G	This was an application for a group of variations. A.6 - Administrative change - Change in ATC Code/ATC Vet Code A.7 - Administrative change - Deletion of manufacturing sites	09/01/2020	03/09/2020	SmPC, Annex II and PL	
II/0051	B.II.c.1.d - Change in the specification parameters and/or limits of an excipient - Change outside the approved specifications limits range	19/09/2019	n/a		
IAIN/0050/G	This was an application for a group of variations. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer B.V.a.1.d - PMF - Inclusion of a new, updated or	20/06/2019	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				
WS/1519/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product	14/06/2019	n/a		
WS/1500/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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.V.a.1.b - PMF - Inclusion of a new, updated or	16/05/2019	n/a		

	amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) - First-time inclusion of a new PMF NOT affecting the properties of the FP 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				
IB/0049	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	15/05/2019	n/a		
WS/1494	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	07/03/2019	n/a		
IB/0043	B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	22/10/2018	n/a		
WS/1407	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	13/09/2018	n/a		

II/0040/G	This was an application for a group of variations. Update of section 4.8 of the SmPC to include aseptic meningitis as adverse reaction. The PL is updated accordingly. Update of section 4.2 of the SmPC to include the option of hand-push administration of the rHuPH20 component (in addition to administration with a pump). This change is a correction in order to harmonise with the PL. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/07/2018	19/07/2019	SmPC and PL	The IG 10% component should be infused using a pump. The rHuPH20 may be hand-pushed or infused by a pump. A 24 gauge needle may be required to allow patients to infuse at flow rates of 300 mL/hr/infusion site. However, needles with smaller diameters may be used if slower flow rates are acceptable.
IAIN/0041	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	23/04/2018	n/a		
WS/1309	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products	08/02/2018	n/a		

PSUSA/1633/201705	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	11/01/2018	n/a		PRAC Recommendation - maintenance
R/0037	Renewal of the marketing authorisation.	09/11/2017	08/01/2018		
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/06/2017	08/01/2018	PL	
IAIN/0035	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	28/04/2017	n/a		
WS/1085	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.III.1.a.2 - Submission of a new/updated or deletion of Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	21/04/2017	n/a		
II/0033/G	This was an application for a group of variations. 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.II.c.2.c - Change in test procedure for an excipient	23/03/2017	n/a		

	- Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent				
II/0032	Update of section 4.2 and 4.8 of the SmPC in order to add information on infusion site leakage. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI in line with the latest QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	23/03/2017	08/01/2018	SmPC, Labelling and PL	Infusion site leakage can occur during or after subcutaneous administration of immunoglobulin, including HyQvia. Consider using longer needles and/or more than one infusion site. Any change of needle size would have to be supervised by the treating physician.
PSUSA/1633/ 201605	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	12/01/2017	n/a		PRAC Recommendation - maintenance
WS/1003	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	15/12/2016	n/a		
WS/0966	This was an application for a variation following a worksharing procedure according to Article 20 of	15/09/2016	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
IAIN/0029	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	11/07/2016	n/a		
WS/0882/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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 B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	09/06/2016	n/a		
II/0021	Extension of indication to include paediatric population for all authorised indications: as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	28/04/2016	01/06/2016	SmPC and PL	Please refer to the Scientific Discussion HyQvia-H-C-2491-II-021.

IAIN/0027/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.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	28/04/2016	26/05/2016	Annex II	
II/0022	Update of section 4.4 "Special warnings and precautions for use" of the HyQvia SmPC to add information that aseptic meningitis syndrome (AMS) occurs independently of high or low dosage and that it also occurs more frequently in women than men based on PV data collected on AMS and to provide new information on possible false positive reading of assays used for diagnosis of fungal infections depending on detection of beta-D-glucans. In addition, the Marketing authorisation holder (MAH) took the opportunity to implement the new Guideline on core SmPC for human normal immunoglobulin for subcutaneous and intramuscular administration (EMA/CHMP/BPWP/143744/2011 rev. 1), which came into force on 1 September 2015, as well as the current QRD template version 9.1 with the present submission.	25/02/2016	26/05/2016	SmPC, Labelling and PL	

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IB/0024	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)	02/02/2016	26/05/2016	SmPC	
IA/0026	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	27/01/2016	n/a		
WS/0825	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product	14/01/2016	n/a		
PSUSA/1633/ 201505	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	14/01/2016	n/a		PRAC Recommendation - maintenance
WS/0790	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.g - Change in the manufacturer of AS or of a	19/11/2015	26/05/2016	Annex II	

	starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier				
IB/0020	B.II.c.2.d - Change in test procedure for an excipient - Other changes to a test procedure (including replacement or addition)	20/10/2015	n/a		
IB/0018	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	30/09/2015	n/a		
WS/0720	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	16/07/2015	n/a		
II/0013	Update of sections 4.2, 4.4, 4.6 and 5.3 of the SmPC in order to update the safety information regarding pregnancy, fertility and lactation following new additional preclinical data. The Package Leaflet is updated accordingly. Furthermore, the Annex II has been revised to remove educational material based on the availability	25/06/2015	26/05/2016	SmPC, Annex II and PL	The safety of HyQvia for use in human pregnancy has not been established in controlled clinical trials and therefore should only be given with caution to pregnant women and breast-feeding mothers. SCIg products have been shown to cross the placenta, increasingly during the third trimester. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the

	of additional new data. In addition, the Marketing authorisation holder took the opportunity to update the list of local representatives in the Package Leaflet and to make minor editorial changes to the SmPC and PL (including additional minor modifications to the handling instructions and pictograms in the PL). The updated RMP version 7.0 has been submitted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				foetus and the neonate are to be expected. Development and reproductive toxicology studies have been conducted with recombinant human hyaluronidase in mice and rabbits. No adverse effects on pregnancy and foetal development were associated with anti-rHuPH20 antibodies and extensive nonclinical safety data package does not support prior theoretical concerns that anti-rHuPH20 antibodies could potentially affect fertility or pregnancy. In these studies, maternal antibodies to recombinant human hyaluronidase were transferred to offspring in utero. The effects of antibodies to the recombinant human hyaluronidase component of HyQvia on the human embryo or on human foetal development are currently unknown. If a woman becomes pregnant, the treating physician should encourage her to participate in the pregnancy registry. Immunoglobulins are excreted into the milk and may contribute to protecting the neonate from pathogens which have a mucosal portal of entry. There are currently no clinical safety data for HyQvia on fertility available. In conclusion, the available data indicates that administration of the rHuPH20 component of HyQvia to pregnant women or individuals of child-bearing potential does not impose an additional safety risk.
IAIN/0016	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	03/06/2015	26/05/2016	Annex II and PL	

IAIN/0015/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH 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 C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location 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	26/05/2015	26/05/2016	SmPC, Annex II, Labelling and PL	
IB/0012/G	This was an application for a group of variations. B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation A.7 - Administrative change - Deletion of manufacturing sites	26/03/2015	n/a		
WS/0683	This was an application for a variation following a worksharing procedure according to Article 20 of	26/03/2015	n/a		

	Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
N/0011	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/03/2015	26/05/2016	PL	
WS/0670	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	26/02/2015	n/a		
PSUSA/1633/ 201405	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	09/01/2015	n/a		PRAC Recommendation - maintenance
WS/0585/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Change in test procedure for AS B.I.b.2.e - Change in test procedure for AS or 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.b - Change in test procedure for AS or	23/10/2014	n/a		

	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/0006/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or 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.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	08/08/2014	n/a		
PSUV/0004	Periodic Safety Update	13/06/2014	n/a		PRAC Recommendation - maintenance
IAIN/0005/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.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	30/04/2014	n/a		
IAIN/0003	C.I.12 - Inclusion or deletion of black symbol and explanatory statements for medicinal products in the	18/12/2013	16/12/2014	SmPC, Labelling and	

	list of medicinal products that are subject to additional monitoring			PL	
II/0002/G	This was an application for a group of variations. Change in the manufacturing process of the active substance in Rieti (Italy). In addition, the current building complex at the Rieti site is extended as well as new equipment added. B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	18/12/2013	n/a		
IAIN/0001	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	14/06/2013	n/a		