Kiovig

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
IB/0117	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/06/2022		SmPC and 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.	19/05/2022	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).

	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)					
IA/0115/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.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.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	18/01/2022	n/a		

IAIN/0114	A.1 - Administrative change - Change in the name and/or address of the MAH	07/01/2022	n/a		
T/0113	Transfer of Marketing Authorisation	19/11/2021	03/12/2021		
WS/2060	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	21/10/2021	n/a		
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		
IAIN/0112	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.	08/07/2021	n/a		

	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 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	20/05/2021	n/a		
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		
PSUSA/1633/ 202005	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	14/01/2021	n/a		PRAC Recommendation - maintenance
IA/0106/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	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 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				
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		

IAIN/0103	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	20/08/2020	n/a		
IAIN/0101	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		
IB/0099	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/05/2020	09/06/2020	SmPC, Annex II, Labelling and PL	
II/0098	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		
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/0097	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	31/01/2020	n/a		
T/0095	Transfer of Marketing Authorisation	02/10/2019	21/10/2019	SmPC, Labelling and PL	
II/0091	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	05/09/2019	n/a		
IA/0094	A.7 - Administrative change - Deletion of manufacturing sites	30/08/2019	21/10/2019	Annex II and PL	
N/0093	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/07/2019	21/10/2019	PL	
IAIN/0092/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	20/06/2019	n/a		

	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 amended PMF in the marketing authorisation dossier of a medicinal product. (PMF 2nd step procedure) -	16/05/2019	n/a		

	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				
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/0088	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/02/2019	05/03/2019	SmPC and PL	
IAIN/0085	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/10/2018	05/03/2019	SmPC	
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		
IAIN/0082	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier	23/04/2018	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				
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
N/0079	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/06/2017	05/03/2019	PL	
IAIN/0077	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		
N/0078	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/04/2017	05/03/2019	Labelling and PL	
WS/1085	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	21/04/2017	n/a		

	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				
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 Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	15/09/2016	n/a		
IAIN/0073	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	27/07/2016	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		
IAIN/0071/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	02/06/2016	Annex II and PL	
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	14/01/2016	n/a		

	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				
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 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	19/11/2015	02/06/2016	Annex II	
II/0065/G	This was an application for a group of variations. Update of section 4.4 of the SmPC in order to include a new warning on possible false positive testing of assays used for diagnosis of fungal infections depending on detection of beta-D-glucans and to amend the existing warning on aseptic meningitis syndrome. Minor changes are made to the existing warnings on thromboembolic events and acute renal failure. The RMP is updated in relation to the new warning and to include the changes requested during the assessment of variation EMEA/H/C/0000628/II/0056.	24/09/2015	02/06/2016	SmPC, Annex II and PL	Based on new safety data the manufacturer proposes an update of the Product Information. The changes reflect the possibility of false positive readings in detection of ß-d-glucans for diagnosis of fungal infections, the higher incidence of aseptic meningitis syndrome (AMS) in female patients and its lack of dependency on dosage of administered immunoglobulin. They also make treating physicians more aware of thromboembolism and renal failure in patients requiring intravenous immunoglobulins. Due to new safety information with KIOVIG the list of adverse events has been updated.

	Update of section 4.8 of the SmPC in order to revise the frequency and MedRA SOC categorisation of adverse drug reactions based on information from several clinical studies in which KIOVIG was used as investigational medicinal product. Safety information from clinical trials is deleted from section 4.8 of the SmPC for simplification. The Package Leaflet is updated accordingly. The MAH took also the opportunity to implement QRD version 9.1 and to update the details of the local representative for Slovakia. 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				
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		

IAIN/0066	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	02/06/2015	02/06/2016	Annex II and PL	
IAIN/0064/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 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	29/05/2015	02/06/2016	Annex II and PL	
WS/0683	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	26/03/2015	n/a		

	the AS - Other variation				
N/0062	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/03/2015	02/06/2016	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 starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting	23/10/2014	n/a		

	material/reagent/intermediate, if an alternative test procedure is already authorised				
II/0056	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	26/06/2014	n/a		
IAIN/0057	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	24/04/2014	n/a		
PSUSA/1633/ 201305	Periodic Safety Update EU Single assessment - human normal immunoglobulin (IgG)	09/01/2014	n/a		PRAC Recommendation - maintenance
II/0050/G	This was an application for a group of variations. Update of section 4.8 of the SmPC and consequential update to section 4 of the PL to reflect the change of frequency of ADRs already included in the SmPC following an update of the clinical trial safety data pool. Stroke and myocardial infarction have also been included as new ADRs based on post-marketing spontaneous reporting; PL has been updated accordingly. Editorial changes have been made to section 4.2 of the SmPC.and paediatric statements have been included to sections 4.4, 4.5, 4.8, 4.9 and 5.1 of the SmPC as per previous commitments during variation IB/46. The PI is updated following the new QRD v.9. Finally the MAH proposed to	24/10/2013	03/06/2014	SmPC and PL	The MAH performed a pooled data analysis from 4 clinical trials (2 trials in PID patients and one trial in patients with ITP, part of the original MAA, and the one trial in subjects with MMN, assessed in a previous variation) and post-marketing spontaneous reports (including 2 reports of myocardial infarction and 2 of stroke) for a re-calculation of frequencies and frequency categories for a certain number of ADRs and to add Stroke and Myocardial Infarction in the Product Information (PI). As a result of the data analysis, frequencies and frequency categories have been changed for a few of the already reported ADRs in the PI, which was updated accordingly. Addition of stroke and myocardial infarction has been due to two reports of stroke and two reports of MI from post-marketing sources and the MAH has now incorporated them in the ADR list within frequency

	update the contact details of the Croatian, Portuguese and Romanian local representative. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				category "unknown". Relatedness and un-relatedness of ADRs to Kiovig treatment has been considered in the conservative approach described by the SmPC guideline. Furthermore, updates of the PI as for the results from previous procedures and the update to the current version of the QRD template have been introduced by the applicant.
IAIN/0054	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	27/06/2013	03/06/2014	Annex II	
II/0051/G	This was an application for a group of variations. This is an application for a group of variations related to the active substance manufacturing process. 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	27/06/2013	n/a		
IAIN/0053	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	31/05/2013	n/a		

II/0049	Replacement of a test for the drug product for both: release testing/batch analysis as well as for future stability study testing. B.II.d.2.c - Change in test procedure for the finished product - Replacement of a biological/ immunological/immunochemical test method or a method using a biological reagent	25/04/2013	n/a		
IAIN/0052	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	12/04/2013	n/a		
II/0048	Submission of the relevant validation data to demonstrate that the manufacturing process includes steps in accordance with the revision of the Ph. Eur. Monograph (01/2012: 0918). B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	21/02/2013	n/a		
IB/0046	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	03/08/2012	31/10/2012	SmPC, Labelling and PL	
IAIN/0047	B.V.a.1.d - PMF - Inclusion of a new, updated or amended PMF in the marketing authorisation dossier	07/06/2012	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				
WS/0232	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Submission of updated Certificate of Suitability B.III.1.a.2 - Submission of a new or updated Ph. Eur. Certificate of Suitability to the relevant Ph. Eur. Monograph - Updated certificate from an already approved manufacturer	24/05/2012	n/a		
IAIN/0045	C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database	10/05/2012	n/a		
IB/0044	B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	25/04/2012	n/a		
IA/0042	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	08/11/2011	n/a		
II/0040	Update of section 4.4 of the SmPC to add a statement regarding hyperproteinemia and hyponatremia. Furthermore, changes are proposed	23/06/2011	27/07/2011	SmPC and PL	Hyperproteinemia and increased serum viscosity may occur in patients receiving IGIV therapy. In addition, hyponatremia may occur in association with IVIG products.

	to align the SmPC with the revised Core SmPC for IVIg products. Minor editorial changes in section 4.2, 4.4 and 4.5 and PIL have been introduced. The list of local representatives is being updated in section 6 of the PIL. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				It is clinically critical to distinguish true hyponatremia from a pseudohyponatremia that is associated with concomitant decreased calculated serum osmolality or elevated osmolar gap, because treatment aimed at decreasing serum free water in patients with pseudohyponatremia may lead to volume depletion, a further increase in serum viscosity and a possible predisposition to thromboembolic events.
II/0037	Extension of indication to add the treatment of multifocal motor neuropathy (MMN) to the list of approved indications in 4.1. Consequential changes are made to section 4.2. The PIL is updated accordingly. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/06/2011	27/07/2011	SmPC, Annex II and PL	Please refer to the Scientific Discussion "Kiovig/H/C/000628/II/37" for further information.
II/0038	Change in the manufacturing process of the active substance 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	21/07/2011	21/07/2011		
IA/0041/G	This was an application for a group of variations.	01/06/2011	n/a		

	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				
IB/0039	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)	12/05/2011	n/a		
R/0036	Renewal of the marketing authorisation.	23/09/2010	06/12/2010	SmPC, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit-risk balance, the CHMP is of the opinion that the quality, safety and efficacy of KIOVIG continues to be adequately and sufficiently demonstrated and therefore considered that the benefit-risk profile of KIOVIG continues to be favourable. The CHMP recommends the renewal of the Marketing Authorisation with unlimited validity.
II/0034	Change of the manufacturing process of the active substance. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	22/07/2010	05/08/2010		

II/0033/G	This was an application for a group of variations. Changes to the finished product specifications. B.II.b.2.b.3 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing for a biol/immunol product and one of the test methods is a biol/immunol/immunochemical method B.II.d.2.z - Change in test procedure for the finished product - Other variation	22/07/2010	05/08/2010		
II/0028	Update of SmPC section 4.6 with clinical safety information obtained since original licensure of the product in January 2006. The list of local representatives in the PIL has been updated. Update of Summary of Product Characteristics and Package Leaflet	20/05/2010	01/07/2010	SmPC and PL	The MAH updated section 4.6 to include information on IGIV crossing the placenta during the third trimester. The proposed changes were supported by references to the published literature. The SPC changes provide an update of the safety information but do not affect the overall positive benefit-risk balance of this product.
II/0027	Update of SmPC section 4.8 and PIL section 4 with clinical safety information obtained since original licensure of the product. Furthermore, section 4 "Possible side effects" of the Package Leaflet has been adapted to the QRD template. Update of Summary of Product Characteristics and Package Leaflet	20/05/2010	01/07/2010	SmPC and PL	The MAH has proposed changes to section 4.8 of the SPC based on the evaluation of case reports received by the MAH in the post-marketing phase of Kiovig. The changes to the SPC and PIL provide an update of the safety information for Kiovig but do not affect the overall positive benefit-risk balance of this product.
II/0026	Update of the clinical safety information obtained since the original licensure of the product in January	20/05/2010	01/07/2010	SmPC and PL	The SPC of Kiovig was updated to include more details to the warning statements in section 4.4, particularly with

	2006. SPC sections 4.2, 4.3, 4.4 and 4.9 are updated. Update of Summary of Product Characteristics and Package Leaflet				regard to transfusion related acute lung injury (TRALI), hemolysis and aseptic meningitis (ASM). Patients with cardiac impairment have been added as being at particular risk of adverse events in case of overdose (4.9). In addition, some minor changes have been introduced in sections 4.2 and 4.3. In support of the changes of the Kiovig SPC, which is based on the core SPC for human normal immunoglobulin for intravenous administration (IVIg) (CPMP/BPWG/859/95), the company has provided the updated CCSI as well as published literature.
IA/0035	To include the PMF Annual Update 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	20/05/2010	n/a		
II/0030	To introduce a new vial size of 30g/300ml for Kiovig. New presentation(s)	18/02/2010	05/05/2010	SmPC, Labelling and PL	
II/0031	Change in the manufacturing process of the intermediate. Change(s) to the manufacturing process for the active substance	18/02/2010	11/03/2010		
IB/0029	IB_36_a_Change in shape or dimensions of the container/closure - sterile ph. forms/biologicals	26/01/2010	n/a		

II/0025	To extend the room termperature storage of the final product from 9 to 12 months within the licensed shelf life of 24 months. This change affects the product information annexes I, IIIA and IIIB. At this occassion the MAH takes the oportunity to update the local representatives in the annex IIIB. Change(s) to shelf-life or storage conditions	17/12/2009	25/01/2010	SmPC, Labelling and PL	
2PMF/0032	Inclusion of the updated or amended Plasma Master File (Baxter EMEA/H/PMF/000003/04) in the marketing authorisation dossier	08/01/2010	n/a		
IB/0024	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	14/08/2009	n/a		
IB/0023	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	14/08/2009	n/a		
IB/0022	IB_31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits	14/08/2009	n/a		
II/0021	Use of a new method as the primary method for the determination of S/D reagents concentration in the finished product as well as in the in-process controls in the manufacturing process of the drug substance. The currently approved methods shall still be used as backup methods. Quality changes	19/03/2009	23/03/2009		

II/0017	Change(s) to the manufacturing process for the active substance	24/07/2008	28/07/2008		
II/0011	Quality changes	20/09/2007	28/07/2008		
MF/0020	2PMF (2nd step of PMF certification procedure)	26/06/2008	n/a		
II/0019	Change to the manufacturing process. Change(s) to the manufacturing process for the active substance	30/05/2008	05/06/2008		
II/0018	Introduction of a new test for determination of protein in the final product. The current approved one will be used as an alternative. Change(s) to the test method(s) and/or specifications for the finished product	24/04/2008	28/04/2008		
IB/0016	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	29/11/2007	n/a		
II/0014	Quality changes	15/11/2007	22/11/2007		
IB/0015	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	26/10/2007	n/a		
II/0013	Update of Summary of Product Characteristics, Annex II, Labelling and Package Leaflet Update of the Product Information in compliance with	19/07/2007	21/08/2007	SmPC, Annex II, Labelling and PL	The SPC, labelling and PL were updated in compliance with the QRD template version 7.2. In addition, an editorial error was corrected in Annex II and the list of local representatives in the PL was updated. The MAH committed

	the current QRD template version 7.2, editorial correction in the Annex II and update of the local representatives section in the Package Leaflet. Update of Summary of Product Characteristics, Labelling and Package Leaflet				to further review the section "Possible side effects" of the PL at the next available opportunity.
MF/0012	2PMF (2nd step of PMF certification procedure)	06/06/2007	n/a		
IB/0010	IB_37_a_Change in the specification of the finished product - tightening of specification limits	06/03/2007	n/a		
IB/0009	IB_31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits	27/02/2007	n/a		
II/0008	Change(s) to the manufacturing process for the active substance	24/01/2007	29/01/2007		
II/0006	Change(s) to the manufacturing process for the active substance	16/11/2006	21/11/2006		
IB/0007	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	15/11/2006	n/a		
N/0005	To update Annex III according to the newest QRD template for vial lable and outer carton and to add the EU Marketing Authosisation numbers. In Annex III B the phone number of the local representative for Germany and the adress of the Finnish local representative were updated.	15/08/2006	n/a	SmPC, Labelling and PL	

	Furthermore, minor lingustic and QRD changes were introduced in the Danish, German, Portuguese and Swedish Annexes Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
II/0003	Change to the test procedure and/or specification of a raw material	27/07/2006	03/08/2006		
MF/0004	2PMF (2nd step of PMF certification procedure)	19/06/2006	n/a		
IB/0001	IB_38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient	02/05/2006	n/a		
IA/0002	IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance	02/05/2006	n/a		