Nplate

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
IG/1743	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)	28/06/2024		Annex II	
II/0091	Submission of an updated RMP version 22 in order to	07/03/2024	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).

	include the latest safety information collected until 31 July 2023 (data lock point). The main change consists of removing the neutralizing antibodies that cross-react with endogeneous thrombopoietin (eTPO). 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				
II/0090	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	08/02/2024	n/a		
II/0089	B.II.b.5.e - Change to in-process tests or limits applied during the manufacture of the finished product - Widening of the approved IPC limits, which may have a significant effect on overall quality of the finished product	09/11/2023	n/a		
PSUSA/2660/ 202207	Periodic Safety Update EU Single assessment - romiplostim	16/03/2023	n/a		PRAC Recommendation - maintenance
IA/0088	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	06/02/2023	n/a		

IAIN/0087/G	This was an application for a group of variations. 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 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	19/12/2022	n/a		
N/0085	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/10/2022		Labelling	
II/0083	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	01/09/2022	n/a		
IB/0084/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.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation 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	28/03/2022	n/a		

II/0081/G	This was an application for a group of variations. 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.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product or a new bioequivalence study	13/01/2022	n/a		
N/0082	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/11/2021		PL	
IB/0080	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	06/09/2021	n/a		
II/0077	Extension of indication to add the use of romiplostim in adult patients who have had ITP for ≤ 12 months and who have had an insufficient response to corticosteroids or immunoglobulins. Sections 4.1, 4.4., 4.8, 5.1 and 5.2 of the SmPC have been updated. In addition, the MAH has taken the opportunity to implement minor editorial changes in sections 4.2, 4.4, 4.8 and 5.1 of the SmPC. The Package Leaflet is updated in accordance. Version 20.1 of the RMP has also been submitted. Furthermore, the PI is brought in line with the latest QRD template (version 10.1). The variation requested amendments to the	10/12/2020	22/01/2021	SmPC and PL	Please refer to Scientific Discussion "Nplate-H-C-000942/II/0077".

	Summary of Product Characteristics 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				
II/0078	Update of sections 4.8 and 5.1 of the SmPC to reflect the main results from study 20101221 following the assessment performed under Article 46 of Regulation 1901/2006. Study 20101221 is an open-label trial to evaluate safety in children from 1 year of age to less than 18 years of age with primary ITP regardless of splenectomy status, including a protocol supplement to implement bone marrow evaluations. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH	26/11/2020	22/01/2021	SmPC	Update of sections 4.8 and 5.1 of the SmPC to reflect the main results from study 20101221 which is an open-label trial to evaluate safety in children from 1 year of age to less than 18 years of age with primary ITP. This procedure follows the assessment performed under Article 46 of Regulation 1901/2006. For more information, please refer to the Summary of Product Characteristics.
PSUSA/2660/ 201907	Periodic Safety Update EU Single assessment - romiplostim	26/03/2020	20/05/2020	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2660/201907.
IB/0076	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	21/02/2020	n/a		
II/0074	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	16/01/2020	n/a		

	Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
IB/0073	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	17/06/2019	n/a		
N/0072	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/05/2019	20/05/2020	PL	
IB/0071	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	04/01/2019	n/a		
IA/0070	B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter	06/09/2018	n/a		
IG/0946	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	04/06/2018	31/01/2019	PL	
IB/0067	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	08/03/2018	n/a		

II/0060/G	This was an application for a group of variations. Extension of Indication to include paediatric population for Nplate: to register Nplate for the use in the paediatric chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients: 1 year of age and older. As a consequence sections 2, 4.2, 4.4, 4.8, 4.9, 5.1, 5.2, 6.3, 6.5, 6.6 and 8 of the SmPC have been updated accordingly. The Package Leaflet and Labelling are updated in accordance. Furthermore, the PI is brought in line with the latest QRD template version 10. 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 C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	09/11/2017	30/01/2018	SmPC, Labelling and PL	For further information please refer to the published Assessment Report: Nplate H-C-942-II-60-AR.
II/0066	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	25/01/2018	31/01/2019	SmPC and PL	The SmPC section 6.4 has been updated as follows: This medicine may be removed from the refrigerator for a period of 30 days at room temperature (up to 25°C) when stored in the original carton.

					The PL has been updated accordingly.
IG/0853	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	10/11/2017	31/01/2019	Annex II and PL	
IA/0064/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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 B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test	28/07/2017	n/a		
IB/0063	B.IV.z - Quality change - Change in Medical Devices - Other variation	18/05/2017	n/a		
II/0062/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 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	27/04/2017	02/06/2017	Annex II and PL	

	biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes				
PSUSA/2660/ 201607	Periodic Safety Update EU Single assessment - romiplostim	09/02/2017	n/a		PRAC Recommendation - maintenance
IA/0061/G	This was an application for a group of variations. B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	25/01/2017	n/a		
IA/0059/G	This was an application for a group of variations. B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	25/11/2016	n/a		
II/0057	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	15/09/2016	n/a		

IA/0056/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	09/06/2016	02/06/2017	Annex II	
II/0055/G	This was an application for a group of variations. B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished	02/06/2016	n/a		

	product - Addition of a new test(s) and limits B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.f.1.e - Stability of FP - Change to an approved stability protocol				
PSUSA/2660/ 201507	Periodic Safety Update EU Single assessment - romiplostim	25/02/2016	21/04/2016	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2660/201507.
II/0053	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	11/02/2016	n/a		
IB/0054	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	27/01/2016	21/04/2016	Annex II	
II/0051	Extension of Indication to include second line treatment of non-splenectomised patients; as a consequence, sections 4.1, 4.2, 4.4, 4.8 and 5.1 of the SmPC have been updated and the Package Leaflet has been updated accordingly. In addition, the MAH took the opportunity to update the contact details of the local representatives in the Package Leaflet. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or	17/12/2015	22/01/2016	SmPC and PL	For further information please refer to the published Assessment Report: Nplate H-C-942-II-51-AR.

	modification of an approved one				
II/0049	Update of section 4.6 of the SmPC in order to increase clarity with reference to the presentation of results from the relevant animal studies undertaken. Further, the MAH provided the final CSR of Study 20080009; a long-term open-label prospective study to assess changes in bone marrow morphology, thereby addressing the post-authorisation measure 'MEA 005.3'. A revised RMP version 16 was provided as part of the application. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/06/2015	11/11/2015	SmPC	Studies in animals have shown that romiplostim crossed the placenta and increased foetal platelet counts. Post implantation loss and a slight increase in peri-natal pup mortality also occurred in animal studies.
WS/0660	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. 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	26/03/2015	n/a		
PSUSA/2660/ 201407	Periodic Safety Update EU Single assessment - romiplostim	12/02/2015	n/a		PRAC Recommendation - maintenance
IB/0050/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished	07/01/2015	n/a		

	product - Other changes to a test procedure (including replacement or addition) 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 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 B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation				
II/0045	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	20/11/2014	11/11/2015	Annex II	
II/0042	Introduction of a post-approval change management protocol related to the Active Substance. B.I.e.2 - Introduction of a post approval change management protocol related to the AS	23/10/2014	n/a		Introduction of a post-approval change management protocol related to the Active Substance
II/0044	To add a batch control and stability testing site for finished product B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP -	25/09/2014	n/a		To add a batch control and stability testing site for finished product

	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				
IB/0046/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 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	21/08/2014	n/a		
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/05/2014	11/11/2015	PL	
IB/0041	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	17/03/2014	n/a		
PSUV/0040	Periodic Safety Update	06/03/2014	n/a		PRAC Recommendation - maintenance
R/0037	Renewal of the marketing authorisation.	24/10/2013	20/12/2013	SmPC and PL	Based on the CHMP review of data on quality, safety and efficacy, including all variations introduced since the marketing authorisation was granted, the CHMP considers by consensus that the risk-benefit balance of Nplate in the treatment of chronic immune (idiopathic) thrombocytopenic purpura (ITP) in adult splenectomised patients who are refractory to other treatments remains favourable and

					therefore recommends the renewal of the marketing authorisation for unlimited validity. In addition, based on the review of cumulative safety data from completed and ongoing controlled trials with romiplostim the CHMP considers that the following adverse drug reactions should be included in the section 4.8 of the SmPC: upper respiratory tract infection with frequency "Very common"; gastroenteritis with frequency "Common"; palpitations with frequency "Common"; erythromelalgia with the frequency "Uncommon" . The package leaflet has been updated accordingly.
IB/0039	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	31/10/2013	n/a		
IAIN/0038	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	18/09/2013	n/a		
II/0036	Changes to the drug product specifications. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	27/06/2013	n/a		
II/0029	Update of sections 4.4 and 4.8 of the SmPC in order to update the safety information related to progression of existing Myelodysplastic Syndromes (MDS) based on the final report from study 20060198 following the assessment of FUM 029. In	27/06/2013	20/12/2013	SmPC, Annex II and PL	In this variation sections 4.4 and 4.8 of the SmPC have been updated in order to reflect the latest safety information related to progression of existing Myelodysplastic Syndromes (MDS) based on the final report from study 20060198. In this study treatment with

	addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the MAH proposed this opportunity to bring the PI in line with the latest QRD template version 9.0. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				romiplostim was prematurely stopped due to a numerical excess of disease progression to AML and an increase in circulating blasts greater than 10% in patients receiving romiplostim compared to placebo. Overall survival was similar to placebo.
IB/0035/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new tests and limits B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished	23/04/2013	n/a		

	product - Other variation				
IAIN/0034	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/03/2013	n/a		
IB/0033/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	04/03/2013	n/a		
IAIN/0032/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	14/02/2013	20/12/2013	Annex II and PL	
IA/0031	A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	14/12/2012	n/a		
IG/0247	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/12/2012	n/a		

II/0022	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	15/11/2012	20/12/2013	SmPC, Annex II, Labelling and PL	
IB/0028/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	07/11/2012	20/12/2013	SmPC	
II/0023	Update of section 4.8 of the SmPC in order to add Hypersensitivity reactions and Angioedema as Adverse Drug Reactions, to address the request of CHMP following the assessment of PSUR 5. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make minor editorial changes to section 4.8 of the SmPC. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the	20/09/2012	23/10/2012	SmPC and PL	Upon request from CHMP following cases of hypersensitivity and angioedema reported in the last PSUR, a review of the romiplostim clinical studies, Amgen safety database and bibliographic databases was conducted and these two adverse drug reactions were added in the Product Information with the frequency "very common" and "common", respectively.

	MAH				
IB/0026/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.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	16/08/2012	n/a		
IA/0027	B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place	08/08/2012	n/a		
IB/0025	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	26/06/2012	n/a		
IAIN/0024/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	16/05/2012	n/a		

IB/0021/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	30/03/2012	23/10/2012	SmPC	
II/0020/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to a biological/immunological/ immunochemical test method or a method using a biological reagent for a biological AS B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	15/03/2012	n/a		
II/0017	Changes in sections 4.4 and 4.8 of the SmPC to update recommendations for patients with myelodysplastic syndrome (MDS) on the risk of	21/07/2011	24/08/2011	SmPC, Annex II and PL	In this variation the MAH has updated sections 4.4 and 4.8 of the SmPC with available data from a randomised clinical study of patients with thrombocytopenia associated with

	progression to acute myelogenous leukaemia (AML), further to the assessment of data submitted as procedure OTH28. The package leaflet has been updated accordingly. In addition Annex II has been updated to include a revised RMP version number. The MAH took the opportunity to update the product information according to the latest QRD recommendations. Moreover, minor editorial amendments have been implemented and the list of local representatives has been updated in the package leaflet. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH				myelodysplastic syndrome (MDS) in which an increased risk of progression to acute myelogenous leukaemia (AML) was observed in patients treated with romiplostim compared to placebo. In addition, the key messages in the SmPC and package leaflet have been reinforced to highlight that a positive benefit/risk for romiplostim has only been established for the treatment of thrombocytopenia associated to chronic ITP and that romiplostim must not be used for the treatment of thrombocytopenia due to MDS or any other cause of thrombocytopenia other than ITP outside clinical trials.
IA/0019	C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV	12/08/2011	n/a		
IA/0018/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	28/06/2011	n/a		

IB/0016	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	19/05/2011	n/a		
IA/0015	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	02/03/2011	n/a		
II/0010/G	This was an application for a group of variations. Update of the SmPC further to a class labeling review on thrombopoietin stimulating agents. The changes include update of section 4.2 of the SmPC to amend the platelet count cut-off levels for dose adjustment and treatment interruption; update of section 4.8 of the SmPC to include all adverse reactions and update of sections 4.2 and 4.4 of the SmPC on the risk of thromboembolic events in patients with moderate to severe hepatic impairment. As a consequence, Annex II and Annex 127a have been revised to include additional key elements in the educational materials and to reflect the latest version of the RMP agreed. In addition, section 4.4 of the SmPC has been updated following the assessment of the procedure OTH 024 to detail that the diagnosis of ITP in adults and elderly patients should have been confirmed by the exclusion of other clinical entities presenting with thrombocytopenia and that consideration should be given to performing a bone marrow aspirate and biopsy over the course of the disease and	21/10/2010	26/11/2010	SmPC, Annex II and PL	In this group of variations, the MAH has updated the SmPC further to a class labeling review on thrombopoietin stimulating agents. The changes include update of section 4.2 of the SmPC to amend the platelet count cut-off levels for dose adjustment and treatment interruption; update of section 4.8 of the SmPC to include all adverse reactions and update of sections 4.2 and 4.4 of the SmPC on the risk of thromboembolic events in patients with moderate to severe hepatic impairment. As a consequence, Annex II and Annex 127a have been revised to include key elements in the educational materials regarding the risk of thromboembolic events and to reflect the latest version of the RMP agreed. In addition, section 4.4 of the SmPC has been updated following the assessment of the procedure OTH 024 to detail that the diagnosis of ITP in adults and elderly patients should have been confirmed by the exclusion of other clinical entities presenting with thrombocytopenia and that consideration should be given to performing a bone marrow aspirate and biopsy over the course of the disease and treatment. Moreover, section 4.8 of the SmPC has been updated to

	treatment.. Moreover, section 4.8 of the SmPC has been updated to include the assessment of neutralising antibodies during Nplate treatment and erythromelalgia as an adverse reaction; these changes were requested following the assessment of the 2nd PSUR. Furthermore, the SmPC has been updated to the latest QRD template and minor editing improvements have been implemented. The Package Leaflet has been updated according to all the changes proposed and on local representatives. C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH				include the assessment of neutralising antibodies during Nplate treatment and erythromelalgia as an adverse reaction; these changes were requested following the assessment of the 2nd PSUR.
IA/0014/G	This was an application for a group of variations.	09/11/2010	n/a	Annex II	

	C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system				
IB/0013	C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH	18/10/2010	n/a	SmPC	To amend section 4.4 of the SmPC to reflect updated information regarding the use in patients with myelodysplastic syndromes (MDS) further to the assessment of FU2 024.2.
IA/0012/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	27/08/2010	n/a	Annex II	
IB/0011	To increase the storage period of the active substance	10/06/2010	n/a		

	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				
X/0004	To introduce four additional presentations, which include all the components (i.e. solvent and reconstitution kit) necessary for the reconstitution and administration of the finished product. Annex I_2.(d) Change or addition of a new pharmaceutical form	22/10/2009	11/01/2010	SmPC, Labelling and PL	Romiplostim drug product is supplied as a sterile, preservative free lyophilized white powder ready for reconstitution. To be administered, it requires reconstitution with preservative-free sterile water for injection (sWFI). When reconstituted with the appropriate volume of solvent, romiplostim is at a concentration of 0.5 mg/mL. The change introduced by this extension application affects only the quality part of the dossier. Its scope is to introduce four additional presentations to the existing lyophilized powder presentations, which include all the components (i.e. solvent and reconstitution kit) necessary for the reconstitution and administration of the medicinal product. The purpose of the additional presentations is to enhance healthcare professionals (HCP) convenience by providing the standard components necessary to reconstitute the drug product, so there is no need to source the components separately. The manufacture of the drug product itself has not changed and only additional information has been provided on the solvent (sWFI) used to reconstitute the lyophilized powder. A complete set of information have been submitted for the solvent and injection devices included in the kit. All the new components of the reconstitution kit are CE marked and shown to be functionally and chemically compatible with

					romiplostim drug product. The manufacturing process of the solvent has been described in sufficient detail and it is considered adequately controlled. Test methods and specifications have been provided and consistency demonstrated. Stability data from samples stored at the recommended temperature of storage and under different stress conditions show that the solvent is stable. The proposed new presentations (1-pack) contain the following components: - One vial of romiplostim drug product (250 or 500 micrograms deliverable product) - One prefilled syringe containing 0.72 or 1.2 mL of solvent (sWFI) for the 250 or 500 micrograms presentations
II/0009	To introduce some changes to the manufacturing process of the active substance and to update some administrative information in the pharmaceutical documentation. Update of or change(s) to the pharmaceutical documentation	17/12/2009	08/01/2010		
II/0003	To introduce some changes to the test methods for the drug substance and the drug product. Change(s) to the test method(s) and/or specifications for the active substance	29/05/2009	08/06/2009		
IB/0002	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	06/03/2009	06/03/2009	SmPC, Labelling and	

				PL	
IB/0001	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	06/03/2009	06/03/2009	SmPC, Labelling and PL	