NeoRecormon

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion / Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
N/0104	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/07/2019		Labelling	
IG/1070	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	04/03/2019	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).

IG/1049/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method 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	17/01/2019	n/a		
IG/0997/G	This was an application for a group of variations. B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	22/11/2018	n/a		
WS/1481	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	22/11/2018	n/a		

	the AS - Minor change in the manufacturing process of the AS				
N/0099	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2018		PL	
T/0098	Transfer of Marketing Authorisation	20/02/2018	15/03/2018	SmPC, Labelling and PL	
IAIN/0097	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	24/11/2017	15/03/2018	SmPC, Annex II, Labelling and PL	
IB/0095	B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information	06/11/2017	15/03/2018	SmPC, Labelling and PL	
PSUSA/1239/ 201702	Periodic Safety Update EU Single assessment - epoetin beta	28/09/2017	n/a		PRAC Recommendation - maintenance
IB/0093/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.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch	01/03/2017	n/a		

	control/testing takes place				
IG/0736	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	19/10/2016	n/a		
N/0091	Update of Annex IIIA to add the 2D barcode unique identifier according to QRD template vs 10. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/08/2016	15/03/2018	Labelling	
II/0090/G	This was an application for a group of variations. 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.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold	01/04/2016	n/a		
IB/0089	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	16/10/2015	n/a		

IB/0087	C.I.3.a - 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 - Implementation of wording agreed by the competent authority	24/07/2015	15/07/2016	SmPC and PL	
II/0083	Update of sections 4.2 and 4.4 of the SmPC, upon request by PRAC following the assessment of PSU 047, MEA 052 and MEA 052.1, with further information regarding the potential risk of retinopathy of prematurity (RoP) with early epoetin use in prematurity. The Package Leaflet was proposed to be updated accordingly. Further, the annexes have been aligned with the latest QRD template (version 9). 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	23/07/2015	15/07/2016	SmPC, Annex II, Labelling and PL	In preterm infants a potential risk of erythropoietin to cause retinopathy cannot be excluded, therefore caution should be exercised and the decision to treat a preterm infant should be balanced against the potential benefit and risk of this treatment and available alternative options. Prevention of anaemia of prematurity: The solution is administered subcutaneously at a dose of 3 x 250 IU/kg b.w. per week. Premature infants who have already been transfused by the start of treatment with NeoRecormon are not likely to benefit as much as untransfused infants. The treatment should last for 6 weeks.
IG/0573	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	01/07/2015	n/a		
IG/0497	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	18/11/2014	n/a		

PSUV/0084	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
IB/0085/G	This was an application for a group of variations. 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.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.c.2.a - Change in the specification parameters and/or limits of the immediate packaging of the AS - Tightening of specification limits	12/06/2014	n/a		
IA/0082/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	13/12/2013	n/a		
N/0081	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/10/2013	15/07/2016	PL	
IG/0228	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/11/2012	n/a		

IB/0079/G	This was an application for a group of variations. 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 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)	15/11/2012	n/a		
II/0075/G	This was an application for a group of variations. to introduce changes to the test procedures and specifications for the active substance. 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.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.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)	15/11/2012	n/a		

	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.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.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.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.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0076	To register an existing manufacturer for the production of 2 dosage strengths of the finished product. 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, batch control, and secondary packaging, for biological/immunological medicinal products.	18/10/2012	18/10/2012		

WS/0299	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. minor changes to the manufacturing process of the active substance. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/09/2012	n/a		
N/0073	Update in the phone number of the local representative for France and Latvia in the package leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/04/2012	15/07/2016	PL	
IG/0161	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	14/03/2012	n/a		
IA/0072/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database	25/10/2011	n/a		

IA/0071	B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing	08/09/2011	n/a	Annex II and PL	
IG/0092/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in 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	08/08/2011	n/a		
IB/0070/G	This was an application for a group of variations. 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.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	28/07/2011	n/a		
IB/0069	Due to very low use of patients the MAH decided to proactively deregister presentations and strengths (100,000 IU vials, 1000 IU pre-filled syringes, 10K, 20K, 60K Recopen cartridges). C.I.7.b - Deletion of - a strength	30/05/2011	n/a	SmPC, Labelling and PL	
IB/0067/G	This was an application for a group of variations. C.I.3.a - Implementation of change(s) requested following the assessment of an USR, class labelling, a	11/03/2011	n/a	SmPC, Annex II and PL	Following the saferty review of Erythropoiesis-stimulating agents (ESAs) and CHMP communication dated 21st December 2009, the MAH wishes to update the SmPC accordingly.

	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.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				In addition, the MAH wishes to update the SmPC following the TREAT study which indicates that epoietins are not beneficial in diabetic patients with chronic renal disease suffering from moderate anaemia. Furthermore, the MAH wishes to delete the DDPS version number as per October procedural announcement.
II/0066	Roche - Update of the detailed description of the pharmacovigilance system (version 4.1). Annex II has been updated accordingly. In addition, Annex II has been updated in line with the latest QRD templates. Update of DDPS (Pharmacovigilance)	18/03/2010	29/04/2010	Annex II	With this variation the MAH submitted a new version of the DDPS (core version 4.1) in accordance with the current Pharmacovigilance guideline. After assessing the documentation the CHMP concluded that the submitted DDPS contained all required elements. Consequently, Annex II has been updated with the new version number of the agreed core DDPS. In addition, Annex II has been updated in line with the latest QRD templates.
II/0065	To implement changes to the analytical methods and release specifications. Quality changes	21/01/2010	04/02/2010		
II/0064	To implement changes to the cultivation process for the drug substance and related changes. Quality changes	21/01/2010	04/02/2010		
II/0063	This variation concerns an update of the summary of product characteristics (SPC) following the completion of a class safety review by the PhVWP and the CHMP. As a result, CHMP requested to update section 4.4 of	17/12/2009	20/01/2010	SmPC	As a result of the discussion of the updated risk management plans (RMPs) and the results of the Cochrane meta-analysis it was agreed at the PhVWP/CHMP meeting in September 2009 that all MAHs for epoetins should submit a type II

	the SPC to include more information on pure red cell aplasia (PRCA) in patients with hepatitis C treated with Interferon, Ribavirin and Epoetin and section 5.1 to include additional data on the Cochrane meta-analysis and the effects of epoetins in cancer patients. Update of Summary of Product Characteristics				variation to amend the SPC. Information with respect to the results of the Cochrane meta-analysis on the effects of epoetins in cancer patients and to the occurrence of PRCA in patients with Hepatitis C treated with Interferon, Ribavirin and Epoetin should be included into the SPC. The amendments of Sections 4.4 and 5.1 of the SPC have been implemented as recommended by the PhVWP / CHMP.
II/0062	Update of Detail Description of the Pharmacovigilance System (Pharmacovigilance). Update of DDPS (Pharmacovigilance)	22/10/2009	20/11/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated has provided a revised DDPS (Version 3.6 dated 17 September 2009). Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS.
II/0061	The MAH applied to implement the new primary packaging material for NeoRecormon pre-filled syringes drug product. Quality changes	25/06/2009	06/07/2009		
II/0060	Changes to the manufacturing process of drug product. Change(s) to the manufacturing process for the finished product	23/04/2009	07/05/2009		
II/0059	Implementation of new tability test method, in replacement of current approved. Change(s) to the test method(s) and/or specifications	19/02/2009	04/03/2009		

	for the finished product				
II/0058	The MAH applied to add F. Hoffmann-La Roche LTD, Basel, Switzerland as manufacturer for NeoRecormon pre-filled syringes and to adjust some parameters in order to harmonise all strength manufactured in Basel. Quality changes	19/02/2009	04/03/2009		
II/0057	This variation concerns an update of the SPC following the completion of a class safety review by the PhVWP and the CHMP. The safety review was initiated because recent data show a consistent unexplained excess mortality in cancer patients with anaemia treated with epoetins. As a result, CHMP requested to update section 4.4 of the SPC to include an additional ESA class warning in the epoetins with cancer indication. The Package Leaflet has been updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	25/09/2008	23/10/2008	SmPC and PL	This variation concerns an update of the SPC following the completion of a class safety review by the PhVWP and the CHMP. The safety review was initiated because recent new available data from studies that showed an increased risk of tumour progression, venous thromboembolism and shorter overall survival in cancer patients who received epoetins compared to patients who did not receive them. Following this review, the CHMP concluded, at its June 2008 meeting, that the benefits of epoetins continue to outweigh their risks in the approved indications. However, in cancer patients with a reasonably long life-expectancy, the benefit of using epoetins does not outweigh the risk of tumour progression and shorter overall survival and therefore the Committee concluded that in these patients anaemia should be corrected with blood transfusions. The decision to administer epoetin-containing medicines should be based on an informed assessment of the benefits against the risks on individual basis, taking into account the type and stage of tumour, the degree of anaemia, the patient's life-expectancy, the environment in which the patient is being treated and patient preference. As a result, Section 4.4 of the SPC and section 2 of the

					Package Leaflet are being updated to reflect these conclusions by incorporating wording requested by CHMP for inclusion for all epoetins for which a cancer indication is licensed.
II/0056	Change to the manufacturing process of the active substance Change(s) to the manufacturing process for the active substance	30/05/2008	05/06/2008		
IB/0055	IB_37_b_Change in the specification of the finished product - add. of new test parameter IB_38_c_Change in test procedure of finished product - other changes	27/03/2008	n/a		
II/0054	Update of Summary of Product Characteristics and Package Leaflet	24/01/2008	26/02/2008	SmPC and PL	This variation primarily concerns an update of the SPC following the completion of a class safety review by the PhVWP and the CHMP. The safety review was initiated because recent data show a consistent unexplained excess mortality in cancer patients with anaemia treated with epoetins, and that treatment of anaemia with epoetins in patients with chronic kidney disease to achieve relatively high target haemoglobin concentrations may be associated with an increase in the risk of mortality and cardiovascular morbidity. As a result, the main changes being implemented are: i) in section 4.1, to highlight that epoetins should be used only if associated with symptoms, ii) in Section 4.2 to establish a uniform target haemoglobin range for all epoetins, iii) in Section 4.4 to mention the observed negative benefit risk

					balance in patients treated with high target haemoglobin concentrations, and iv) in section 5.1 to include the relevant results of the trials triggering the safety review. Additional section 4.8 has also been amended to update frequency of one adverse reaction. The package leaflet has been updated accordingly. Further changes to the package leaflet have been made to update the contact details of some local representatives.
II/0052	Upscaling of the manufactruring process for Neorecormon active substance Quality changes	13/12/2007	19/12/2007		
IA/0053	IA_47_a_Deletion of a pharmaceutical form IA_47_b_Deletion of a strength IA_47_c_Deletion of a pack size(s)	01/10/2007	n/a	SmPC, Labelling and PL	
R/0050	Renewal of the marketing authorisation.	26/04/2007	25/06/2007	SmPC, Annex II, Labelling and PL	
N/0051	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/04/2007	n/a	Labelling	
II/0049	Update of Summary of Product Characteristics, Labelling and Package Leaflet	16/11/2006	04/01/2007	SmPC, Labelling and PL	The MAH has applied to update sections 4.1, 4.2 and 4.8 of the SPC in order to harmonise the wording between the oncology indications.
II/0048	Change(s) to the manufacturing process for the active substance	28/06/2006	05/07/2006		

II/0047	Change(s) to the manufacturing process for the finished product	01/06/2006	07/06/2006		
II/0046	Change(s) to the manufacturing process for the finished product	23/03/2006	29/03/2006		
II/0044	Update of Summary of Product Characteristics, Labelling and Package Leaflet	13/10/2005	17/11/2005	SmPC, Labelling and PL	
II/0043	Change(s) to the test method(s) and/or specifications for the active substance	15/09/2005	29/09/2005		
II/0042	Change(s) to the manufacturing process for the active substance	15/09/2005	29/09/2005		
II/0041	Change(s) to the manufacturing process for the finished product	15/09/2005	29/09/2005		
IA/0045	IA_01_Change in the name and/or address of the marketing authorisation holder	26/09/2005	n/a	SmPC, Labelling and PL	
II/0040	Change(s) to the manufacturing process for the finished product	27/07/2005	03/08/2005		
II/0037	Update of Summary of Product Characteristics and Package Leaflet	26/05/2005	13/07/2005	SmPC and PL	
IB/0039	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	20/05/2005	n/a		

II/0038	Change(s) to the manufacturing process for the finished product	21/04/2005	27/04/2005		
II/0035	Change(s) to the test method(s) and/or specifications for the finished product	17/02/2005	25/02/2005		
IA/0036	IA_47_b_Deletion of a strength IA_47_c_Deletion of a pack size(s)	14/12/2004	n/a	SmPC, Labelling and PL	
II/0034	Quality changes	18/11/2004	22/11/2004		
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/08/2004	n/a	PL	
II/0032		22/04/2004	n/a		
X/0031	X-3-iii_Addition of new strength	25/09/2003	23/02/2004	SmPC, Annex II, Labelling and PL	
II/0030	Change(s) to the manufacturing process for the active substance	25/04/2003	30/04/2003		
II/0026	Update of Summary of Product Characteristics and Package Leaflet	18/12/2002	17/03/2003	SmPC and PL	
I/0029	16_Change in the batch size of finished product	23/01/2003	27/01/2003		
II/0023	Update of Summary of Product Characteristics and Package Leaflet	22/08/2002	03/12/2002	SmPC and PL	

I/0028	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	08/11/2002	n/a		
I/0027	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	25/10/2002	n/a		
I/0024	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	25/10/2002	n/a		
R/0022	Renewal of the marketing authorisation.	30/05/2002	22/08/2002	SmPC, Annex II, Labelling and PL	
I/0021	15_Minor changes in manufacture of the medicinal product	21/02/2002	01/03/2002		
II/0019	Change(s) to the test method(s) and/or specifications for the active substance	15/11/2001	19/11/2001		
II/0015	Update of Summary of Product Characteristics and Package Leaflet	31/05/2001	17/09/2001	SmPC and PL	
I/0018	25_Change in test procedures of the medicinal product	27/06/2001	06/07/2001		
II/0017	Change(s) to the test method(s) and/or specifications for the active substance	27/06/2001	04/07/2001		
I/0016	16_Change in the batch size of finished product	14/05/2001	01/06/2001		
II/0014	Extension of Indication	16/11/2000	20/03/2001	SmPC and PL	
X/0013	X-3-iii_Addition of new strength	23/09/1999	10/02/2000	SmPC,	

				Labelling and PL	
X/0012	X-3-iii_Addition of new strength	23/09/1999	10/02/2000	SmPC, Labelling and PL	
X/0011	X-3-iii_Addition of new strength	23/09/1999	10/02/2000	SmPC, Labelling and PL	
II/0010	Update of Summary of Product Characteristics and Package Leaflet	23/09/1999	10/02/2000	SmPC, Labelling and PL	
II/0009	Change(s) to the manufacturing process for the finished product	28/07/1999	n/a		
I/0008	01_Change following modification(s) of the manufacturing authorisation(s)	12/03/1999	01/07/1999	SmPC, Labelling and PL	
T/0007	Transfer of Marketing Authorisation	12/03/1999	07/05/1999	SmPC, Labelling and PL	
II/0005	Update of Summary of Product Characteristics and Package Leaflet	23/07/1998	11/11/1998	SmPC, Labelling and PL	
II/0004	Update of Summary of Product Characteristics	27/05/1998	11/11/1998	SmPC	
I/0003	02_Change in the name of the medicinal product (either invented name of common name)	03/07/1998	01/10/1998	SmPC, Labelling and PL	

I/0006	12_Minor change of manufacturing process of the active substance	27/05/1998	n/a		
X/0002	X-3-iv_Change or addition of a new pharmaceutical form	22/10/1997	02/04/1998	SmPC, Annex II, Labelling and PL	
I/0001	12_Minor change of manufacturing process of the active substance 14_Change in specifications of active substance 24_Change in test procedure of active substance	22/10/1997	02/04/1998		