Retacrit

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/0113	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/07/2023		PL	
IB/0114/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a	03/07/2023	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).

	manufacturing site for the FP - Other variation 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.1.z - Replacement or addition of a manufacturing site for the FP - Other variation				
N/0112	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/12/2022		PL	
IB/0111	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	08/09/2022	n/a		
IB/0110	B.I.b.z - Change in control of the AS - Other variation	24/02/2022	n/a		
IB/0107	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	20/01/2022	n/a		
N/0106	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/10/2021		PL	
II/0105	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	23/09/2021	n/a		
PSUSA/1241/ 202012	Periodic Safety Update EU Single assessment - epoetin zeta	02/09/2021	n/a		PRAC Recommendation - maintenance

IB/0103	B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	01/06/2021	n/a		
IB/0104	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	21/05/2021	n/a		
II/0100	Submission of the final study report of a joint post-authorisation safety cohort study of Retacrit/Silapo (epoetin zeta) administered subcutaneously for the treatment of renal anemia (PASCO II) listed as a category 3 study in the RMP. The primary objective of the observational study was to estimate the incidence of pure red cell aplasia (PRCA), neutralising antibodies, lack of efficacy and thromboembolic events under treatment with Retacrit/Silapo (epoetin zeta). The RMP version 16 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/05/2021	n/a		
N/0102	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/03/2021	22/10/2021	PL	
IA/0099	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the	26/11/2020	n/a		

	finished product, including quality control sites (excluding manufacturer for batch release)				
IB/0098	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/10/2020	22/10/2021	SmPC, Annex II, Labelling and PL	
IB/0097	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	18/09/2020	n/a		
IA/0096	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	27/07/2020	n/a		
II/0094	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	14/05/2020	n/a		
IA/0095/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	17/04/2020	31/07/2020	Annex II and PL	
N/0093	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/12/2019	31/07/2020	PL	

IA/0092	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)	28/11/2019	n/a		
IA/0091	B.III.2.z - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Other variation	25/11/2019	n/a		
IB/0090	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	16/08/2019	31/07/2020	SmPC, Labelling and PL	
N/0089	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/04/2019	31/07/2020	PL	
N/0088	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/10/2018	31/07/2020	PL	
IA/0087/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.7 - Administrative change - Deletion of manufacturing sites	19/10/2018	n/a		

T/0086	Transfer of Marketing Authorisation	12/09/2018	28/09/2018	SmPC, Labelling and PL	
IB/0085	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	03/08/2018	06/09/2018	SmPC, Labelling and PL	
PSUSA/1241/ 201712	Periodic Safety Update EU Single assessment - epoetin zeta	12/07/2018	n/a		PRAC Recommendation - maintenance
IB/0083	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	17/04/2018	n/a		
IB/0082	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)	10/01/2018	n/a		
N/0081	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	06/11/2017	06/09/2018	PL	
IAIN/0080	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	26/09/2017	06/09/2018	SmPC and PL	
IA/0079	A.7 - Administrative change - Deletion of manufacturing sites	18/08/2017	n/a		

IAIN/0078	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	20/07/2017	18/09/2017	Annex II and PL	
II/0077	Submission of the final report from the registry based healthcare database study linked to PASCO (PMS-830-07-0043)) listed as a category 3 study in the RMP. This is an observational study on the incidence of thromboembolic events in patients with renal anaemia treated with erythropoietin-zeta as compared with erythropoietin-alpha and other erythropoiesis-stimulating agents. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/07/2017	n/a		The submitted study is a registry based health care database study (HDBS-study) linked to PASCO (Post-Authorisation Safety Cohort Observation of Epoetin zeta Administered Intravenously for the Treatment of Renal Anaemia). The study aimed to compare the crude incidence rate (with 95% CIs) of thromboembolic events in patients with renal anaemia treated with epoetin zeta vs. other epoetins (including epoetin alpha). Overall, no increased thromboembolic risk for epoetin zeta compared to the other epoetins in clinical practice can be derived from the data provided. No new safety concern associated with epoetin zeta was identified. The findings did not warrant changes to the product information.
II/0075	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	23/02/2017	n/a		
N/0076	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/02/2017	18/09/2017	Labelling and PL	
IB/0074	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	11/11/2016	n/a		

IB/0073/G	This was an application for a group of variations. 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 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 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 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 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 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 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 B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g.	16/09/2016	18/09/2017	SmPC, Annex II, Labelling and PL	

	tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes 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 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 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 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 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 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 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 B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g.				

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	tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes 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				
N/0072	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/06/2016	18/09/2017	PL	
IG/0693	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	02/06/2016	n/a		
IA/0070/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.7 - Administrative change - Deletion of manufacturing sites	08/04/2016	n/a		
IB/0069	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	30/03/2016	n/a		
IG/0645	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	17/12/2015	n/a		

IB/0067	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	02/12/2015	n/a		
PSUSA/1241/ 201412	Periodic Safety Update EU Single assessment - epoetin zeta	10/09/2015	n/a		PRAC Recommendation - maintenance
IB/0065	To update the Product Information in order to fulfil the Post-Authorisation Measure LEG 36.4 (ESAs: Outcome of statistical analysis of clinical trial data in chronic kidney disease (CKD) patients on dialysis/not on dialysis). Sections 4.2, 4.4 and 5.1 of the SmPC and sections 2 and 3 of the PIL were updated accordingly. Furthermore annex II has been updated to comply with the latest version of the QRD template. In addition, minor grammatical, typographical and QRD template related updates/corrections have been updated in the annexes. C.I.3.z - 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 - Other variation	27/07/2015	12/08/2015	SmPC, Annex II and PL	
IA/0066	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/07/2015	n/a		
II/0061	B.II.b.2.b - Change to importer, batch release	25/06/2015	n/a		

	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				
IA/0063	A.1 - Administrative change - Change in the name and/or address of the MAH	12/06/2015	12/08/2015	SmPC, Labelling and PL	
IG/0555	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	22/05/2015	n/a		
II/0059	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	23/04/2015	n/a		
IAIN/0060/G	This was an application for a group of variations. 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 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 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	13/04/2015	12/08/2015	SmPC, Labelling and PL	

IB/0058/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.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 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 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 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 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 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 B.II.e.5.a.1 - Change in pack size of the finished	08/01/2015	12/08/2015	SmPC, Labelling and PL	

	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 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 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 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 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 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 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 B.II.e.5.a.1 - Change in pack size of the finished				

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II/0057	B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS	18/12/2014	n/a		
II/0053/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	25/09/2014	n/a		
IG/0477	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	03/09/2014	n/a		

	PSMF location				
IB/0055	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data is required to be submitted by the MAH	25/07/2014	19/08/2014	SmPC and PL	
IB/0054/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) A.7 - Administrative change - Deletion of manufacturing sites	27/02/2014	n/a		
IB/0051/G	This was an application for a group of variations. 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 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 control/testing takes place	16/12/2013	n/a		

	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)				
IG/0382	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	02/12/2013	n/a		
II/0047	Upscaling of the manufacturing process of the drug substance. B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS	19/09/2013	n/a		
IAIN/0050	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	30/08/2013	19/08/2014	SmPC and PL	
IG/0317	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/07/2013	n/a		
IG/0286	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	12/04/2013	n/a		
IB/0045/G	This was an application for a group of variations. B.V.c.1.c - Change management protocol - Update of the quality dossier to implement changes, requested	08/04/2013	n/a		

	by the EMA/NCA, following assessment of a change management protocol - Implementation of a change for a biological/immunological medicinal product 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				
R/0041	Renewal of the marketing authorisation.	20/09/2012	15/11/2012	SmPC, Annex II, Labelling and PL	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of Retacrit continues to be adequately and sufficiently demonstrated and considers that the benefit/risk profile of this medicinal product continues to be favourable. The CHMP recommends the renewal of the Marketing Authorisation for Retacrit, subject to the conditions and obligations as laid down in Annex II to the Opinion. The CHMP recommends that the renewal be granted with unlimited validity. The MAH is requested to submit three-yearly PSURs unless otherwise specified by the CHMP.
IB/0044	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	09/10/2012	n/a		
IAIN/0043	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	29/05/2012	n/a		
II/0040	To register a new manufacturing site for the finished product	24/05/2012	n/a		

	B.II.g.2 - Design Space - Introduction of a post approval change management protocol related to the finished product				
IAIN/0042/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.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.d - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the safety database C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities 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	27/04/2012	n/a		
IA/0039/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 of the finished product, including quality control sites (excluding manufacturer for batch release) A.7 - Administrative change - Deletion of manufacturing sites	23/01/2012	n/a		

II/0036	Addition of the indication " Retacrit can be used to reduce exposure to allogeneic blood transfusions in adult non-iron deficient patients prior to major elective orthopaedic surgery, having a high perceived risk for transfusion complications. Use should be restricted to patients with moderate anaemia (e.g. Hb 10-13 g/dl) who do not have an autologous predonation programme available and with expected moderate blood loss (900 to 1800 ml)" in section 4.1 of the Summary of Product Characteristics (SmpC). Sections 4.2, 4.3, 4.4 and 4.8 of the SmPC and sections 1, 2 and 3 of the Package Leaflet, outlining the mode of administration, contraindications, undesirable effects, special warnings and precautions for use, have been updated as a consequence. Furthermore, Annex II has been updated in order to include the new version number of the Risk Management Plan (version 8.0) and has been aligned in accordance with the latest QRD template (version 7.3.1, March 2010). Minor editorial changes have also been implemented. 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	26/07/2011	SmPC, Annex II and PL	In this application, the MAH submitted data from a phase III study (411-54-07-08-0000) comparing efficacy and safety (including immunogenicity) of subcutaneously administered test and reference product in patients with renal anaemia to support an extension of the current indication to the use of epoetin zeta as an alternative to blood transfusions in adult patients about to undergo major orthopaedic (bone) surgery where there is a potentially high risk from blood transfusion complications. The CHMP considered the extrapolation of efficacy and safety data to the new indication, licensed for the reference product, acceptable based on demonstrated similarity in physicochemical characteristics, efficacy and safety to the reference product; same mechanism of action/ receptor involved, and the absence of additional/unique safety concerns in the new indication. As a consequence, sections 4.1, 4.2, 4.3 4.4 and 4.8 of the SmPC were updated. The Package Leaflet was also updated accordingly.
IB/0037	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	26/05/2011	n/a	SmPC	

II/0031	to introduce change to the Epoetin Reference Standard Material. B.I.b.z - Change in control of the AS - Other variation	17/02/2011	28/02/2011		
IA/0035	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	02/02/2011	n/a		
IB/0034	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)	19/01/2011	n/a		
IB/0032	B.I.a.z - Change in manufacture of the AS - Other variation	19/01/2011	n/a		
IB/0033	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	17/01/2011	n/a	SmPC, Annex II and PL	
T/0030	Transfer of Marketing Authorisation	21/09/2010	11/10/2010	SmPC, Labelling and PL	Transfer of the marketing authorisation holder from Hospira Enterprises B.V. to Hospira UK Limited.
IB/0028	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	06/09/2010	n/a		

IB/0027	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	06/09/2010	n/a		
IB/0026	B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	06/09/2010	n/a		
IA/0029	A.1 - Administrative change - Change in the name and/or address of the MAH	03/09/2010	n/a	SmPC, Labelling and PL	
II/0020	Addition of a subcutaneous route of administration in the indication of "anaemia associated with CRF on haemodyalisis and patients on peritoneal dialysis" and "severe anaemia of renal origin accompanied by clinical symptoms in adult patients with renal insufficiency not yet undergoing analysis". SPC sections 4.2 and 4.4, and the Package Leaflet sections outlining the mode of administration of Epoetin zeta have been amended. Conditions or restrictions with regard to the safe and effective use of the medicinal product as detailed in Annex IIB have been lifted. Update of Summary of Product Characteristics and Package Leaflet	18/02/2010	06/04/2010	SmPC, Annex II and PL	The scope of this variation is to apply for the addition of the subcutaneous route of administration in the indication "Treatment of anaemia associated with chronic renal failure in adult and paediatric patients on haemodialysis and adult patients on peritoneal dialysis" and "Treatment of severe anaemia of renal origin accompanied by clinical symptoms in adult patients with renal insufficiency not yet undergoing dialysis". As a result of this variation, the respective SPC/PL-sections outlining the mode of administration of Epoetin zeta have been amended. Consequently the section "Conditions or restrictions with regard to the safe and effective use of the medicinal product" in Annex IIB has been removed as it currently refers to off-label SC use of Epoetin zeta.
IB/0024	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,	08/03/2010	n/a	SmPC and PL	

	or amendments to reflect a Core SPC - Changes with NO new additional data are submitted by the MAH				
II/0022	This variation concerns an update of the 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 the SPC to include more information on 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 and Package Leaflet	19/11/2009	23/12/2009	SmPC and PL	As a result of the discussion of the updated 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 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.
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/12/2009	n/a	PL	
IA/0021	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	21/10/2009	n/a	Annex II and PL	
II/0019	The MAH applied to introduce changes to the premises of the manufacturing process of the active substance. 11_Change in or addition of manufacturer(s) of active substance	24/09/2009	05/10/2009		
II/0016	Inclusion of in-use storage statement in Product Information	20/11/2008	07/01/2009	SmPC and PL	

	Change(s) to shelf-life or storage conditions				
II/0015	This variation concerns an update of the 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 the SPC to include an additional ESA class warning in the epoetins with cancer indication. In addition, the MAH has made some additional changes to Sections 4.2 and 5.1 of the current SPC The Package Leaflet has been updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	23/10/2008	21/11/2008	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. 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. In addition The MAH has made changes in section 4.2 and 5.1 of the SPC in order to clarify the posology and method of administration of the product and align the text with CHMP recommendations.
IA/0018	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	06/10/2008	n/a		
IA/0017	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	06/10/2008	n/a		
II/0006	The Marketing Authorisation Holder applied for a modification of analytical methods used in the manufacturing process of the active substance. Change(s) to the manufacturing process for the active substance	25/09/2008	03/10/2008		
IB/0012	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	04/09/2008	04/09/2008	SmPC, Labelling and	

				PL	
IB/0011	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	04/09/2008	04/09/2008	SmPC, Labelling and PL	
IB/0010	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	04/09/2008	04/09/2008	SmPC, Labelling and PL	
IB/0009	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	04/09/2008	04/09/2008	SmPC, Labelling and PL	
IB/0008	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	04/09/2008	04/09/2008	SmPC, Labelling and PL	
IB/0007	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	04/09/2008	04/09/2008	SmPC, Labelling and PL	
IA/0014	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	19/08/2008	n/a		
IA/0013	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	19/08/2008	n/a		
IB/0005	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	14/08/2008	n/a	SmPC	
II/0001	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	26/06/2008	13/08/2008	SmPC, Labelling 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

	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. The package leaflet has also been updated accordingly. The MAH also took this opportunity to perform some minor changes in section 6.4 of the SPC, in the Package Leaflet and in the outer labelling and to amend the list of local representatives in the Package Leaflet. Update of Summary of Product Characteristics, Labelling and Package Leaflet				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. The package leaflet has also been updated accordingly. The MAH also took this opportunity to perform some minor changes in section 6.4 of the SPC, in the Package Leaflet and in the outer labelling and to amend the list of local representatives in the Package Leaflet.
IB/0004	IB_37_a_Change in the specification of the finished	11/08/2008	n/a		

	product - tightening of specification limits				
IB/0003	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	11/08/2008	n/a		
IA/0002	IA_05_Change in the name and/or address of a manufacturer of the finished product	18/07/2008	n/a		