



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Binocrit

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
WS/2615	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.4 of the SmPC in order to allow for iron supplementation in accordance with patient</p>	11/07/2024	n/a		Recommendations regarding iron supplementation were updated. Specifically, selection of the best treatment options for iron supplementation should consider the patient's needs, current treatment guidelines on iron supplementation in combination with dose instructions approved and outlined in the Summary of Product

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).



	<p>needs and up-to date treatment guidelines by removing the restrictions to exclusively use the oral route of administration for iron supplementation. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI, bring it in line with the latest QRD template version 10.3, align it with the reference product and update instructions for use.</p> <p>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority</p>				<p>Characteristics of the iron medication.</p> <p>For more information, please refer to the Summary of Product Characteristics.</p>
WS/2624	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.e.z - Change in container closure system of the Finished Product - Other variation</p>	11/01/2024	n/a		
N/0107	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/11/2023		PL	
WS/2534	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.4 of the SmPC in order to allow for iron supplementation in accordance with patient needs and up-to date treatment guidelines by removing the restrictions to exclusively use the oral route of administration for iron supplementation. In</p>	09/11/2023		SmPC, Annex II, Labelling and PL	<p>Recommendations regarding iron supplementation were updated. Specifically, selection of the best treatment options for iron supplementation should consider the patient's needs, current treatment guidelines on iron supplementation in combination with dose instructions approved and outlined in the Summary of Product Characteristics of the iron medication.</p> <p>For more information, please refer to the Summary of</p>

	<p>addition, the MAH took the opportunity to introduce minor editorial changes to the PI, bring it in line with the latest QRD template version 10.3, align it with the reference product and update instructions for use.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>				Product Characteristics.
IB/0104	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)	11/09/2023	n/a		
IG/1658/G	<p>This was an application for a group of variations.</p> <p>B.II.e.1.b.3 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Deletion of an immediate packaging container without a complete deletion of a strength or pharmaceutical form</p> <p>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)</p>	01/09/2023	n/a		
IG/1650/G	<p>This was an application for a group of variations.</p> <p>A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder</p>	21/08/2023		Annex II	

	<p>or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient</p> <p>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</p> <p>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)</p> <p>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)</p> <p>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</p> <p>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</p>				
WS/2459	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or</p>	12/05/2023	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0102	B.II.e.3.b - Change in test procedure for the immediate packaging of the finished product - Other changes to a test procedure (including replacement or addition)	18/04/2023	n/a		
WS/2354/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p>	13/10/2022	n/a		
WS/2292	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product</p>	15/09/2022	n/a		
WS/2225/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.	05/05/2022	n/a		

	<p>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</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS</p> <p>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol</p>				
PSUSA/1237/202108	Periodic Safety Update EU Single assessment - epoetin alfa	07/04/2022	n/a		PRAC Recommendation - maintenance
IB/0097	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)	21/02/2022	n/a		
WS/2144	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation</p>	14/10/2021	n/a		

WS/2013	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	08/07/2021	n/a		
WS/2072	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.f.1.z - Stability of FP - Change in the shelf-life or storage conditions of the finished product - Other variation</p>	24/06/2021	n/a		
WS/1981	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Based on the review of the submitted data, this application regarding the following change: Variation requested Type Annexes affected B.II.g.2 B.II.g.2 - Introduction of a post approval change management protocol related to the finished product Type II None</p> <p>1is recommended for approval.</p>	20/05/2021	n/a		Not applicable

	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product				
WS/1998/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p>	11/03/2021	n/a		
IG/1232	A.7 - Administrative change - Deletion of manufacturing sites	17/04/2020	n/a		
IG/1181	A.7 - Administrative change - Deletion of manufacturing sites	12/12/2019	n/a		
IG/1166	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	15/11/2019	n/a		
IG/1153/G	<p>This was an application for a group of variations.</p> <p>B.I.d.1.a.1 - Stability of AS - Change in the re-test period/storage period - Reduction</p> <p>B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change</p>	31/10/2019	n/a		

	to an approved stability protocol				
WS/1688	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation</p>	19/09/2019	n/a		
WS/1675	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	12/09/2019	14/11/2019	SmPC, Labelling and PL	
PSUSA/1237/ 201808	Periodic Safety Update EU Single assessment - epoetin alfa	16/05/2019	n/a		PRAC Recommendation - maintenance
WS/1548	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal</p>	07/03/2019	n/a		

	product and is not related to a protocol				
WS/1546/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation</p>	31/01/2019	n/a		
IG/1058	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	29/01/2019	n/a		
WS/1507	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	06/12/2018	14/11/2019	SmPC, Labelling and PL	

WS/1470	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>	04/10/2018	n/a		
WS/1465/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p> <p>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</p>	04/10/2018	n/a		
WS/1463	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	20/09/2018	n/a		

WS/1419	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.z - Quality change - Finished product - Other variation</p>	13/09/2018	n/a		
WS/1406	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Extension of indication to include the treatment of symptomatic anaemia (haemoglobin concentration of ≤ 10 g/dl) in adults with low- or intermediate-1-risk primary myelodysplastic syndromes (MDS) who have low serum erythropoietin (< 200 mU/ml) for Binocrit, Epoetin alfa Hexal and Abseamed; as a consequence, sections 4.1, 4.2, 4.8, 5.1 of the SmPC are updated with safety and efficacy information. The Package Leaflet and the risk management plan (finally agreed version 17.1) are updated in accordance. In addition, the worksharing applicant (WSA) took the opportunity to align information with the reference medicinal product and with the EC guideline on Excipients, to improve the quality and readability of the translations in the product information and to update the Annex A in line with EMA guideline.</p> <p>C.I.2.b - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following assessment of the same change for the reference</p>	26/07/2018	31/08/2018	SmPC, Labelling and PL	Please refer to Scientific Discussion Abseamed-H-C-WS-1406, Binocrit-H-C-WS-1406, Epoetin alpha Hexal-H-C-WS-1406

	product - Change(s) require to be further substantiated by new additional data to be submitted by the MAH				
IG/0970/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p>	17/08/2018	n/a		
IB/0071	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)	06/07/2018	n/a		
IA/0072	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	29/06/2018	n/a		
WS/1367	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>	19/04/2018	n/a		

IG/0882	B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information	21/12/2017	n/a		
WS/1290	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	14/12/2017	n/a		
WS/1287	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	14/12/2017	n/a		
IG/0847/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.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	04/10/2017	31/08/2018	SmPC, Annex II and PL	

	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
WS/1175	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	22/06/2017	n/a		
WS/1155	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	05/05/2017	n/a		
IB/0062/G	<p>This was an application for a group of variations.</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p> <p>B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS</p>	15/03/2017	n/a		

	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
IG/0752	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)	12/12/2016	n/a		
IG/0746	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	08/12/2016	n/a		
WS/1032	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	13/10/2016	07/09/2017	SmPC, Labelling and PL	
WS/1011	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation</p>	13/10/2016	n/a		

WS/0981	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>	15/09/2016	n/a		
PSUSA/1237/201508	Periodic Safety Update EU Single assessment - epoetin alfa	14/04/2016	n/a		PRAC Recommendation - maintenance
WS/0877	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of sections 4.2 and 4.4 of the SmPC in order to add administration by subcutaneous (s.c.) route in addition to the intravenous (i.v.) route in treatment of anaemia in patients with chronic renal failure based on clinical study HX575-308 (SENSE) to address MEA 024.1. The Package Leaflet is updated accordingly. In addition, the Worksharing applicant (WSA) took the opportunity to make minor editorial changes in the SmPC and to update the list of local representatives in the Package Leaflet for Abseamed and Binocrit and to bring the PI in line with the latest QRD template version 9.1. Moreover, the updated RMP version 15 has been submitted.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>	25/02/2016	31/03/2016	SmPC, Annex II, Labelling and PL	<p>In patients with chronic renal failure where intravenous access is routinely available (haemodialysis patients) administration of Abseamed/Binocrit/ Epoetin alfa Hexal by the intravenous route is preferable.</p> <p>Where intravenous access is not readily available (patients not yet undergoing dialysis and peritoneal dialysis patients) Abseamed/Binocrit/ Epoetin alfa Hexal may be administered as a subcutaneous injection.</p> <p>During the maintenance phase, Abseamed/Binocrit/ Epoetin alfa Hexal can be administered either 3 times per week, and in the case of subcutaneous administration, once weekly or once every 2 weeks.</p> <p>The maximum dosage should not exceed 150 IU/kg, 3 times per week, 240 IU/kg (up to a maximum of 20,000 IU) once weekly, or 480 IU/kg (up to a maximum of 40,000 IU) once every 2 weeks.</p> <p>Chronic renal failure patients treated with epoetin alfa by the subcutaneous route should be monitored regularly for loss of efficacy, defined as absent or decreased response to epoetin alfa treatment in patients who previously responded to such therapy. This is characterised by a</p>

					sustained decrease in haemoglobin despite an increase in epoetin alfa dosage.
WS/0866	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p>	14/01/2016	n/a		
WS/0811/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p> <p>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</p>	17/09/2015	n/a		
WS/0783	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.a.1.f - Change in the manufacturer of AS or of a</p>	06/08/2015	n/a		

	starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
WS/0780/G	<p>This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.I.b.z - Change in control of the AS - Other variation</p> <p>B.III.1.z - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Other variation</p> <p>B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure</p> <p>B.I.z - Quality change - Active substance - Other variation</p>	06/08/2015	n/a		
WS/0764	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>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</p>	25/06/2015	31/07/2015	SmPC, Labelling and PL	

WS/0717	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>B.II.f.1.e - Stability of FP - Change to an approved stability protocol</p>	23/04/2015	n/a		
IG/0529	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	05/02/2015	n/a		
IG/0480	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	17/09/2014	n/a		
IB/0046/G	<p>This was an application for a group of variations.</p> <p>B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits</p> <p>B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)</p>	23/05/2014	n/a		
IG/0373	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	12/11/2013	n/a		

WS/0442	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Relocation of a quality control testing site for the active substance.</p> <p>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place</p>	24/10/2013	n/a		
WS/0423	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Move of a quality control testing site for the active substance.</p> <p>B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place</p>	19/09/2013	n/a		
IB/0043	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/09/2013	n/a		
IB/0041	C.I.2.a - Change in the SPC, Labelling or PL of a generic/hybrid/biosimilar products following	17/07/2013		SmPC, Annex	

	assessment of the same change for the reference product - Implementation of change(s) for which NO new additional data are submitted by the MAH			II and PL	
IG/0287/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>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</p>	11/03/2013	21/03/2014	SmPC, Labelling and PL	
IG/0281	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	11/03/2013	21/03/2014	SmPC, Labelling and PL	
IB/0038	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	20/02/2013	n/a		
WS/0307	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>to replace the quality control testing site for the active substance.</p>	18/10/2012	n/a		

	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
WS/0265	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>to add an alternative storage site in the manufacture of the drug substance.</p> <p>B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer</p>	21/06/2012	21/06/2012		
R/0033	Renewal of the marketing authorisation.	19/04/2012	18/06/2012	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 Binocrit 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 Binocrit, 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 yearly PSURs unless otherwise specified by the CHMP.

IG/0183	A.7 - Administrative change - Deletion of manufacturing sites	25/05/2012	n/a		
WS/0233	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>to introduce changes to the manufacturing process of HX575 drug substance (DS)</p> <p>B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol</p>	24/05/2012	n/a		
WS/0184	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>To change the batch size of the active substance production.</p> <p>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)</p>	15/12/2011	15/12/2011		
N/0023	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/12/2011	18/06/2012	PL	
WS/0093	This was an application for a variation following a worksharing procedure according to Article 20 of	19/05/2011	19/05/2011		

	<p>Commission Regulation (EC) No 1234/2008.</p> <p>To change shelf life specifications for the finished product</p> <p>B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range</p>				
IG/0063	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	20/04/2011	n/a		
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/03/2011	n/a	PL	Update to the Greek local representative contact details in the Package Leaflet.
WS/0084	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>This was an application for a type IB variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Deletion of the requirement for distribution of cool boxes with the marketed products from Annex II and Annex 127a of the conditions of the Marketing Authorisation. Annex II.B has also been updated to delete the version number of the detailed description of the pharmacovigilance system (DDPS).</p>	20/01/2011	14/03/2011	Annex II	The requirement of distributing cool boxes with epoetin alfa has been questioned with the main arguments that stability of the product is granted by the label for 3 days out of fridge and that no other MAH of an erythropoiesis-stimulating agent (ESA) bears a similar requirement. The current wording of the cool box requirement can also be misinterpreted as obligation to provide one cool box with each box of epoetin alfa. The requirement has been in place for Abseamed/Binocrit/Epoetin Alfa only as it was suggested by the applicants themselves at the time of marketing authorization.

	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
IG/0050	A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS	23/02/2011	n/a		
WS/0078	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>To change the active substance specifications.</p> <p>B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS</p>	20/01/2011	20/01/2011		
WS/0051	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Change in the immediate packaging of the finished product.</p> <p>B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products</p>	20/01/2011	20/01/2011		

IA/0021/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p> <p>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</p>	08/10/2010	08/10/2010	SmPC, Labelling and PL	
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WS/0013	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>This was an application for a type IB variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>Update of section 4.4 of the Summary of Product Characteristics (SmPC) and Section 2 of the Package Leaflet (PL) in order to implement the CHMP/PhVWP agreed wording for all erythropoiesis stimulating agents (ESA) regarding the need to maintain patient medication records and the information concerning any modification to the ESA prescribed. The Package Leaflet has also been aligned with the SmPC with regards to wording on pure red cell aplasia in patients with hepatitis C.</p> <p>Minor linguistic changes were introduced to the Dutch, Greek and German annexes. The list of local</p>	22/07/2010	18/08/2010	SmPC, Annex II and PL	<p>Two cases of pure red cell aplasia (PRCA) occurred during a clinical study investigating erythropoiesis stimulating agents (ESAs), where anti-epoetin antibodies were detected.</p> <p>While investigations on the cause of PRCA in these cases are still ongoing, the CHMP and Pharmacovigilance Working Party (PhVWP) considered it important that accurate medication histories are maintained for patients treated with epoetins, recording the trade name or the scientific name with the name of the manufacturer. It is recommended that the product information of all ESAs includes a request to maintain patient medication records.</p> <p>The scope of this variation is to implement the CHMP/PhVWP agreed wording for all erythropoiesis stimulating agents (class labelling) to the Summary of Product Characteristics and Package Leaflet of Abseamed/Binocrit/Epoetin Hexal, as requested by the CHMP.</p>

	<p>representatives in the Package Leaflet was also updated. Additionally, minor changes to the product information were introduced.</p> <p>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</p>				<p>SmPC Section 4.4: Special warnings and precautions for use</p> <p>."In order to improve the traceability of erythropoiesis-stimulating agents (ESAs), the trade name of the administered ESA should be clearly recorded (or stated) in the patient file."</p> <p>PL: Take special care with other products that stimulate red blood cell production:</p> <p>Binocrit/Epoetin alfa Hexal/Abseamed is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional will always record the exact product you are using.</p> <p>The Package Leaflet has also been updated with regards to wording on PRCA in patients with hepatitis receiving a combination of ESAs with interferon and ribavirin.</p> <p>Additionally, minor changes to the annexes were introduced. Furthermore minor linguistic changes were introduced to the Dutch, Greek and German annexes.</p> <p>Also the contact details of local representatives were updated.</p>
IG/0013/G	<p>This was an application for a group of variations.</p> <p>C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV</p> <p>C.I.9.e - Changes to an existing pharmacovigilance</p>	28/07/2010	n/a	Annex II	

	system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD				
IB/0020	<p>To add the already approved Lek Pharmaceutical d.d site (menges, Slovenia) as an additional manufacturing site regarding release and stability testing for the finished product.</p> <p>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</p>	28/04/2010	n/a		
II/0017	<p>Establishment of an additional filing suite in combination with the upscale of the batch size for drug product</p> <p>Quality changes</p>	18/03/2010	24/03/2010		
II/0018	<p>This variation concerns an update of the SPC following the completion of a class safety review by the PhVWP and the CHMP.</p> <p>As a result, CHMP requested to update section 4.4 of 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.</p>	17/12/2009	20/01/2010	SmPC	<p>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 variation to amend the summary of product characteristics (SPC).</p> <p>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</p>

	<p>Minor linguistic and formatting changes have also been introduced.</p> <p>Update of Summary of Product Characteristics</p>				<p>treated with Interferon, Ribavirin and Epoetin should be included into the SPC.</p> <p>The amendments of Sections 4.4 and 5.1 of the SPC have been implemented as recommended by the PhVWP / CHMP. Minor linguistic and formatting changes have also been implemented.</p>
II/0015	<p>To add an additional manufacturing site for the drug substance.</p> <p>Quality changes</p>	19/11/2009	16/12/2009	Annex II	
IA/0019	<p>To replace the manufacturer responsible for batch release</p> <p>IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing</p>	19/11/2009	n/a	Annex II and PL	
X/0010	<p>The Marketing Authorisation Holder applied to add three presentations to the existing range, comprising the new strengths 20,000, 30,000, and 40,000 IU in pre-filled syringes.</p> <p>Annex I_2.(c) Change or addition of a new strength/potency</p>	25/06/2009	01/10/2009	SmPC, Labelling and PL	
IA/0016	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	09/09/2009	n/a		
II/0014	The MAH applied for chnges in the label of the syringe for the drug product.	23/07/2009	25/08/2009	SmPC and PL	

	Update of Summary of Product Characteristics and Package Leaflet				
II/0012	The MAH applied to introduce additional process lines for the drug substance. Quality changes	23/04/2009	08/05/2009		
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/05/2009	n/a	Labelling	
II/0006	Extension of indication to increase the yield of autologous blood from patients in a predonation program. Update of sections 4.1, 4.2, 4.3, 4.4, 4.6 and 4.8 of the SPC. Labelling and Package Leaflet have been updated accordingly. Update of Summary of Product Characteristics, Labelling and Package Leaflet	23/10/2008	21/11/2008	SmPC, Labelling and PL	Epoetin alfa has been shown to stimulate erythropoiesis in anaemic patients with chronic renal failure (CRF), including those on dialysis and those who do not require regular dialysis. In addition, severe anaemia caused by non-renal disease can be corrected or alleviated following treatment with epoetin alfa, e.g. in cancer patients on chemotherapy. Response to epoetin alfa in these patients is manifested by increased haematocrit, haemoglobin, reduced transfusion requirements and increase in quality of life. In patients with moderate anaemia undergoing major elective surgery accompanied by considerable blood loss, epoetin alfa can be used to increase the yield of autologous blood in a predonation program. Epoetin alfa treatment was shown to reduce the exposure to allogeneic blood transfusion in patients undergoing major elective orthopaedic surgery. An application for a "Similar Biological Medicinal Product" via the centralised procedure under Article 10(4) of Directive 2001/83/EC as amended, also making reference to its Annex 1 was submitted to get marketing approval.

					The application was based on a comparability concept against the reference medicinal product Erypo® (Janssen-Cilag), as authorized in Germany which has been registered in Europe for more than 10 years.
IA/0011	IA_05_Change in the name and/or address of a manufacturer of the finished product	13/11/2008	n/a	Annex II and PL	
II/0009	<p>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.</p> <p>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.</p> <p>Update of Summary of Product Characteristics and Package Leaflet</p>	25/09/2008	29/10/2008	SmPC and PL	<p>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.</p> <p>As a result, Section 4.4 of the SPC and section 2 of the Package Leaflet are being updated to reflect these</p>

					conclusions by incorporating wording requested by CHMP for inclusion for all epoetins for which a cancer indication is licensed.
II/0008	The Marketing Authorisation Holder applied for revised storage conditions for sterile formulated bulk. Change(s) to the manufacturing process for the finished product	25/09/2008	03/10/2008		
IA/0007	IA_05_Change in the name and/or address of a manufacturer of the finished product	17/07/2008	n/a		
II/0001	New presentation(s)	30/05/2008	08/07/2008	SmPC, Labelling and PL	
II/0004	The Marketing Authorisation Holder applied to change the method and specification for the analysis of sialic acids per mol epoetin. Change(s) to the test method(s) and/or specifications for the active substance	26/06/2008	30/06/2008		
II/0003	Change(s) to the manufacturing process for the active substance	30/05/2008	05/06/2008		
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/05/2008	n/a	PL	
II/0002	Update of Summary of Product Characteristics, Labelling and Package Leaflet	24/01/2008	29/02/2008	SmPC, Labelling and	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

				PL	<p>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.</p> <p>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.</p> <p>In addition, minor details in the labelling and the PL have been updated.</p>
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