Neulasta

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IG/1743	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	28/06/2024		Annex II	
IB/0123	C.I.11.z - Introduction of, or change(s) to, the	17/10/2023	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).

	obligations and conditions of a marketing authorisation, including the RMP - Other variation				
II/0121	Submission of the final report from PASS study 20170701 listed as a category 3 study in the RMP. This is a cross-sectional survey study to assess the effectiveness of the Neulasta Patient Alert Card and to measure medication errors related to the use of the Neulasta On-Body Injector. The RMP version 9.0 was accepted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/07/2023	n/a		This variation concerns the final study report of the category 3 post-authorization safety study (PASS) 20170701 to evaluate the effectiveness of the patient alert card and to measure medication errors related to the use of the Neulasta On-Body Injector (OBI). Of the 62 respondents who completed all relevant sections of the study questionnaire, the median composite endpoint for awareness and behavioural intent reached the predefined cut-off level. The questionnaire design did not allow estimation of medication errors with the OBI in clinical practice. However, as concurrently to this procedure the OBI was withdrawn from the European market, no further regulatory actions were considered necessary following the results of this study.
IB/0122	B.II.e.z - Change in container closure system of the Finished Product - Other variation	27/06/2023		SmPC, Labelling and PL	
PSUSA/2326/ 202201	Periodic Safety Update EU Single assessment - pegfilgrastim	29/09/2022	n/a		PRAC Recommendation - maintenance
IB/0120	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	15/09/2022	n/a		
II/0116	Submission of the final report from study 20170701 listed as a category 3 study in the RMP (MEA-060.5). This is an observational study to assess the effectiveness of the Neulasta patient alert card and	02/12/2021	16/12/2022	PL	Package leaflet (Patient instructions for use) new text: The on-body injector can be worn in a shower. After showering, check the on-body injector to ensure it has not become dislodged.

	to measure medication errors related to the use of the On-Body Injector. Data provided justified additional activity to be included in the Patient Instruction for use in the package leaflet. The MAH took the occasion to amend local representative details for Malta, Germany and to align the PI to the recent QRD template version 10.2. The RMP version 8.0 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				For more information, please refer to the Summary of Product Characteristics.
II/0117	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	18/11/2021	n/a		
IB/0118/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation 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 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	26/10/2021	n/a		

IB/0115	B.II.z - Quality change - Finished product - Other variation	04/05/2021	n/a		
II/0114	Update of section 6.6 of the SmPC in order to add a new warning that the medicine should be allowed to reach room temperature before use, based on cumulative reviews of post-marketing reports of medication errors with the on-body injector and in response to the PAM EMEA/H/C/000420/MEA/060.3. The MAH also took the opportunity to introduce an editorial change in section 4.4 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/03/2021	13/12/2021	SmPC	Allow the pre-filled syringe for manual administration and pre-filled syringe co-packed with the on-body injector (Onpro kit) for automatic administration to come to room temperature for 30 minutes before using the syringe.
II/0113	Submission of the final report from study 20160176 listed as a category 3 study in the RMP. This is a retrospective cohort study with primary outcome the time from index date to diagnosis of MDS or AML (safety). As a result, section 4.4 and 4.8 of the SmPC is updated to add a new warning on Myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML), and to add them in the list of adverse drug reactions (ADRs) with frequency uncommon; the Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.1. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission	26/11/2020	13/12/2021	SmPC, Annex II and PL	In the post-marketing observational study setting, myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) have been associated with the use of pegfilgrastim in conjunction with chemotherapy and/or radiotherapy in breast and lung cancer patients.

	of studies to the competent authority				
IB/0112	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	27/02/2020	n/a		
IB/0111/G	This was an application for a group of variations. 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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	25/11/2019	n/a		
IA/0110/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	22/11/2019	n/a		
PSUSA/2326/ 201901	Periodic Safety Update EU Single assessment - pegfilgrastim	19/09/2019	22/11/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/2326/201901.
IA/0108	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)	04/04/2019	n/a		
IB/0107	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	29/03/2019	22/11/2019	SmPC and PL	
II/0099	Submission of an updated RMP (version 6.2) in order to add study 20160176, a retrospective cohort study of female breast cancer patients aged 66 years and over selected from the US SEER-Medicare database to estimate the risk of acute myeloid leukemia/myelodysplastic syndrome for breast cancer patients, as a new Pharmacovigilance activity (category 3). In addition, the MAH submitted the draft protocol for study 20160176. 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	14/03/2019	n/a		
IB/0105	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	04/10/2018	n/a		
IAIN/0106	C.I.z - Changes (Safety/Efficacy) of Human and	13/09/2018	31/10/2018	SmPC and PL	

	Veterinary Medicinal Products - Other variation				
IB/0103	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	02/07/2018	n/a		
IG/0946	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	04/06/2018	31/10/2018	PL	
IAIN/0101	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	17/05/2018	31/10/2018	SmPC and PL	
WS/1177/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.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	26/04/2018	n/a		

	material/intermediate				
II/0093/G	This was an application for a group of variations. Update of sections 3, 4.2, 4.4, 4.8, 5.1, 6.4, 6.5, 6.6 and 8 of the SmPC. The Labelling, Package Leaflet and the RMP (version 4.2) are updated accordingly. In addition the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet, to include some editorial changes and correct some typos throughout the product information, and to bring the product information in line with the latest QRD template version 10. B.II.e.5.c - Change in pack size of the finished product - Change in the fill weight/fill volume of sterile multidose (or single-dose, partial use) parenteral medicinal products, including biological/immunological medicinal products B.IV.1.a.3 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Spacer device for metered dose inhalers or other device which may have a significant impact on the delivery of the AS	22/02/2018	31/10/2018	SmPC, Annex II, Labelling and PL	
IG/0853	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	10/11/2017	19/02/2018	Annex II and PL	

WS/1159	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	06/07/2017	n/a		
IB/0096	B.I.b.z - Change in control of the AS - Other variation	31/05/2017	n/a		
WS/1099/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.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.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.e - Change in the specification parameters	18/05/2017	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a non-significant specification parameter B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product B.II.d.3 - Variations related to the introduction of real-time release or parametric release in the manufacture of the finished product B.II.f.1.e - Stability of FP - Change to an approved stability protocol				
IAIN/0094	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	10/03/2017	19/02/2018	Annex II and PL	

WS/1022/G	This was an application for a group of variations following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant effect on the overall quality of the AS B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.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) B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other	19/01/2017	n/a		

	changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol				
IA/0090	A.7 - Administrative change - Deletion of manufacturing sites	07/09/2016	n/a		
PSUSA/2326/ 201601	Periodic Safety Update EU Single assessment - pegfilgrastim	02/09/2016	n/a		PRAC Recommendation - maintenance
IB/0089	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	07/07/2016	n/a		
IB/0087	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	18/03/2016	n/a		
WS/0834	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	10/12/2015	n/a		

II/0085	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	16/07/2015	n/a		
II/0084	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/05/2015	26/05/2016	SmPC and PL	
WS/0660	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate	26/03/2015	n/a		
II/0082	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	26/02/2015	n/a		
II/0078	Introduction of a Post Approval Change Management Protocol for the finished product B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	25/09/2014	n/a		

IB/0081	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	22/09/2014	n/a		
IB/0080	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/08/2014	13/11/2014	SmPC and PL	
N/0079	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/05/2014	13/11/2014	PL	
II/0076	to add a site responsible for lot release testing of Neulasta finished product. B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method	22/05/2014	n/a		
II/0075	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	22/05/2014	13/11/2014	SmPC and PL	
IA/0077	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	13/05/2014	n/a		
II/0072	change in manufacturing process of filgrastim B.I.a.2.c - Changes in the manufacturing process of	23/01/2014	n/a		

	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				
IA/0074	A.7 - Administrative change - Deletion of manufacturing sites	09/12/2013	n/a		
II/0070	Update of section 4.6 of the SmPC with details of Amgen's pregnancy surveillance program (PSP) and lactation surveillance program (LSP) and section 4.9 on information on overdose. The Package Leaflet is updated accordingly. Amgen also addressed in this submission the Quality Review of Documents (QRD) groups comments on the SmPC, PL (including the instructions for use) and labelling made during the recently concluded procedure to introduce minor changes to the Automatic Needle Guard for the 6mg pre-filled syringes (procedure number EMEA/H/C/000420/IB/0067). Furthermore, the PI is being brought in line with the latest QRD template version 9.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/11/2013	13/11/2014	SmPC, Annex II, Labelling and PL	The MAH implemented a pregnancy surveillance programme (PSP) and lactation surveillance programme (LSP) to facilitate the reporting of all available information on the use of Amgen products during pregnancy and lactation. This information has been included in the SmPC and PL to help increase awareness of the programmes among healthcare professionals. The MAH also updated the PI according to the latest QRD version 9.0.
IA/0073/G	This was an application for a group of variations. B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved	18/11/2013	n/a		

	manufacturer B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
PSUV/0071	Periodic Safety Update	19/09/2013	15/11/2013	SmPC and PL	Update of section 4.4 of the SmPC to add a statement on traceability in line with other products in the class. The Package leaflet is updated accordingly. Please refer to: Neulasta-H-C-420-PSUV-0071 EPAR - Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
IAIN/0069	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	20/09/2013	n/a		
WS/0399	This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008. Update of sections 4.4 and 4.8 of the SmPC to add capillary leak syndrome as a new adverse drug reaction and include a related warning further to the assessment of a signal by the PRAC. The Package Leaflet is updated accordingly. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	25/07/2013	03/09/2013	SmPC and PL	Capillary leak syndrome has been reported in recipients of granulocyte-colony stimulating factor (filgrastim and pegfilgrastim) including patients undergoing chemotherapy and a healthy donor undergoing peripheral blood progenitor cell mobilisation. It has been reported rarely in cancer patients undergoing chemotherapy following administration of Neulasta. Capillary leak syndrome is characterised by hypotension, hypoalbuminaemia, oedema and hemoconcentration. Patients who develop symptoms of capillary leak syndrome should be closely monitored and receive standard symptomatic treatment, which may include a need for intensive care. This information is reflected in the revised product information.

IB/0067	B.IV.1.z - Change of a measuring or administration device - Other variation	02/08/2013	15/11/2013	Labelling and PL	
N/0068	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/07/2013	03/09/2013	PL	
II/0065/G	This was an application for a group of variations. to approve an alternative primary container closure system B.II.e.1.b.2 - Change in immediate packaging of the finished product - Type of container - Sterile medicinal products and biological/immunological medicinal products B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	27/06/2013	n/a		
IB/0064	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	23/04/2013	n/a		
IAIN/0063	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/03/2013	n/a		
IG/0247	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/12/2012	n/a		
IAIN/0061/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a	29/11/2012	03/09/2013	Annex II and PL	

	manufacturing site for the FP - Secondary packaging site B.II.b.2.b.1 - Change to batch release arrangements and quality control testing of the FP - Not including batch control/testing				
IB/0060	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	14/11/2012	n/a		
II/0058	Introduction of a post approval change management protocol for the finished product. B.II.g.2 - Design Space - Introduction of a post approval change management protocol related to the finished product	18/10/2012	n/a		
IB/0059	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	11/09/2012	n/a		
IB/0057/G	This was an application for a group of variations. B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished	08/08/2012	n/a		

	product - Addition of a new tests and limits B.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test				
IA/0056/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	19/07/2012	n/a		
N/0053	Update in the local representative details for Czech Republic, Denmark, Cyprus, Spain, Greece, Latvia, Netherlands, Poland and Portugal in the package leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2012	03/09/2013	PL	
IA/0054	A.7 - Administrative change - Deletion of manufacturing sites	21/05/2012	n/a		

IB/0052	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	14/03/2012	n/a		
IB/0051	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	17/01/2012	n/a		
N/0050	The MAH has updated the Package Leaflet to improve the instructions for injecting with Neulasta pre-filled syringe, with or without automatic needle guard. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2011	25/05/2012	PL	
IB/0049	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	03/11/2011	n/a		
IB/0048	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	24/10/2011	n/a	SmPC	
IB/0047	B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new tests and limits	15/09/2011	n/a		

II/0046	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	14/04/2011	27/05/2011	SmPC and PL	
WS/0043/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. Changes in the manufacturing process, test procedures and specification parameters of the active substance. Change of specifications to comply with Ph. Eur. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.III.2.a.2 - Change of specification(s) of a former non Pharmacopoeial substance to comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	16/12/2010	16/12/2010		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - 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.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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 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				
IB/0045/G	This was an application for a group of variations. 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 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	16/12/2010	n/a		
IB/0044	Removal of the 'Sureclick' prefilled pen presentation (EU/1/02/227/003) from the approved list of presentations for Neulasta. C.I.7.a - Deletion of - a pharmaceutical form	15/09/2010	n/a	SmPC, Labelling and PL	
N/0043	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/05/2010	n/a	Labelling and PL	
II/0041	Changes to the manufacturer of a starting material used in the manufacturing process for the active	21/01/2010	02/02/2010		

	substance Change(s) to the manufacturing process for the active substance				
N/0042	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/01/2010	n/a	PL	
II/0040	Upon request of the CHMP, the MAH submitted an update of the SPC sections 4.2, 4.8, 5.1 and 5.2 to add information for physicians on recommended use in paediatric patients based on a clinical study 990130 and a publication. Update of Summary of Product Characteristics	24/09/2009	23/10/2009	SmPC	The safety and efficacy data from study 990130 in paediatric patients lead to the amendment of section 4.2 and introduction of new information in sections 4.8, 5.1 and 5.2 of the SPC. Section 4.2 Paediatric patients The experience in children is limited. See sections 4.8, 5.1 and 5.2. Section 4.8 A higher frequency of serious adverse events in younger children aged 0-5 years (92%) has been observed compared to older children aged 6-11 and 12-21 years respectively (80% and 67%) and adults. The most common adverse study medicinal product reaction was bone pain (see section 5.1 and 5.2). Section 5.1 In a phase II (n = 37) multicentre, randomised, open-label study of paediatric sarcoma patients receiving 100 ?g/kg pegfilgrastim following cycle 1 of vincristine, doxorubicin and cyclophosphamide (VAdriaC/IE) chemotherapy, a longer duration of severe neutropenia (neutrophils < 0.5 x

					109) was observed in younger children aged 0-5 yrs (8.9 days) compared to older children aged 6-11 years and 12-21 years (6 days and 3.7 days, respectively) and adults. Additionally a higher incidence of febrile neutropenia was observed in younger children aged 0-5 yrs (75%) compared to older children aged 6 11 years and 12-21 years (70% and 33%, respectively) and adults (see sections 4.8 and 5.2). Section 5.2 Paediatric patients The pharmacokinetics of pegfilgrastim were studied in 37 paediatric patients with sarcoma, who received 100 ?g/kg pegfilgrastim after the completion of VAdriaC/IE chemotherapy. The youngest age group (0-5 years) had a higher mean exposure to pegfilgrastim (AUC) (± Standard Deviation) (47.9 ± 22.5 ?g·hr/ml) than older children aged 6-11 years and 12-21 years (22.0 ± 13.1 ?g·hr/ml and 29.3 ± 23.2 ?g·hr/ml, respectively) (see section 5.1). With the exception of the youngest age group (0 5 years), the mean AUC in paediatric subjects appeared similar to that for adult patients with high risk stage II-IV breast cancer and receiving 100 ?g/kg pegfilgrasti
IA/0039	IA_28_Change in any part of primary packaging material not in contact with finished product	17/04/2009	17/04/2009	SmPC, Labelling and PL	
IB/0038	IB_37_b_Change in the specification of the finished product - add. of new test parameter	14/08/2008	n/a		
II/0036	Change(s) to the manufacturing process for the finished product	30/05/2008	05/06/2008		

II/0037	The MAH has applied to amend section 4.8 of the SPC to included information about the potential for elevated Liver Function Tests (LFTs) in patients treated with pegfilgrastim. Update of Summary of Product Characteristics	19/03/2008	21/04/2008	SmPC	The MAH has applied to amend section 4.8 of the SPC to included information about the potential for elevated Liver Function Tests (LFTs) in patients treated with pegfilgrastim.
II/0035	Change(s) to the manufacturing process for the active substance	21/02/2008	26/02/2008		
II/0034	Update of Summary of Product Characteristics and Package Leaflet	13/12/2007	17/01/2008	SmPC and PL	Amendment to section 4.8 of the SPC with regard to the frequency of Sweet's syndrome. The Package Leaflet has also been amended accordingly.
II/0033	Change(s) to the manufacturing process for the active substance	15/11/2007	21/11/2007		
II/0032	Update of Summary of Product Characteristics and Package Leaflet	18/10/2007	20/11/2007	SmPC and PL	Update of section 4.8 of the Summary of Product Characteristics to include: injection-site reactions, erythema and flushing. The package leaflet is updated accordingly. This variation fulfils a commitment made by the MAH which resulted from the recent renewal procedure.
II/0031	Update of Summary of Product Characteristics to amend sections 4.2 and 5.2 with data from a study investigating the effects of renal impairment on the pharmacokinetics of pegfilgrastim. This variation fulfils a commitment made by the MAH which resulted from the recent renewal procedure. Update of Summary of Product Characteristics	18/10/2007	20/11/2007	SmPC	

R/0030	Renewal of the marketing authorisation.	24/05/2007	16/07/2007		
II/0029	Change(s) to the manufacturing process for the finished product	22/03/2007	27/03/2007		
II/0028	Change to the test procedure and/or specification of a raw material	22/03/2007	27/03/2007		
II/0027	Change(s) to the manufacturing process for the active substance	24/01/2007	29/01/2007		
II/0026	Update of Summary of Product Characteristics and Package Leaflet	16/11/2006	03/01/2007	SmPC, Annex II, Labelling and PL	Update to sections 4.4 and 4.8 of the SPC following a review of the Company Core Data Sheet and a recent assessment of the 7th PSUR. Update to sections 2 and 4 of the Package Leaflet with regards to information on allergy to latex and very rare events of cutaneous vasculitis. Update to section 6 of the Package Leaflet on how to administer the medicinal product.
II/0025	Change(s) to the manufacturing process for the active substance	27/07/2006	18/08/2006		
II/0023	Change(s) to the manufacturing process for the active substance	27/04/2006	03/05/2006		
IA/0024	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	17/01/2006	n/a		
IB/0022	IB_37_a_Change in the specification of the finished product - tightening of specification limits	10/01/2006	n/a		
II/0020	The Marketing Authorisation Holder applied to add a	15/09/2005	28/10/2005	SmPC,	

	new prefilled pen presentation to the product range. New presentation(s)			Labelling and PL	
II/0015	Sections 4.8 and 5.1 of the SPC were updated to reflect new data on the use of Neulasta in patients with de novo acute myeloid leukaemia. Update of Summary of Product Characteristics	15/09/2005	28/10/2005	SmPC	Sections 4.8 and 5.1 of the SPC were updated to reflect new data on the use of Neulasta in patients with de novo acute myeloid leukaemia.
II/0018	Change(s) to the manufacturing process for the active substance	27/07/2005	31/08/2005	Annex II	
II/0019	Update of Summary of Product Characteristics and Package Leaflet	23/06/2005	01/08/2005	SmPC and PL	Sections 4.4 and 4.8 of the SPC were amended to update the safety information in relation to pulmonary effects and to add "leucocytosis" further to the assessment of the 5th PSUR. The Patient Leaflet was amended accordingly.
IA/0021	IA_28_Change in any part of primary packaging material not in contact with finished product	29/06/2005	n/a		
II/0017	Update of Summary of Product Characteristics	16/03/2005	29/04/2005	SmPC	Sections 4.8 and 5.1 of the SPC were amended to reflect the results from a phase 3 study showing that the addition of pegfilgrastim to docetaxel in patients with breast cancer had a beneficial effect on the primary endpoint of the incidence of febrile neutropenia.
II/0016	The Marketing Authorisation Holder applied to update the manufacturing process for the active substance. Quality changes	16/03/2005	21/03/2005		

II/0014	The Marketing Authorisation Holder applied to change the active substance and product specifications. Quality changes	16/03/2005	21/03/2005		
II/0013	Update of Summary of Product Characteristics and Package Leaflet	15/12/2004	25/01/2005	SmPC and PL	
IB/0012	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	09/08/2004	n/a		
II/0007	Change(s) to the manufacturing process for the active substance	29/07/2004	02/08/2004		
IB/0010	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	01/07/2004	n/a	SmPC and PL	
II/0009	Change(s) to the manufacturing process for the finished product	23/06/2004	29/06/2004		
II/0008	Change(s) to shelf-life or storage conditions	23/06/2004	23/06/2004		
IA/0011	IA_28_Change in any part of primary packaging material not in contact with finished product IA_41_a_01_Change in pack size - change in no. of units within range of appr. pack size	18/06/2004	18/06/2004	SmPC, Labelling and PL	
II/0004	Change(s) to the manufacturing process for the active substance	22/04/2004	27/04/2004		

II/0002	Update of Summary of Product Characteristics and Package Leaflet	20/11/2003	29/01/2004	SmPC and PL	
II/0003	Change(s) to the manufacturing process for the active substance	17/12/2003	15/01/2004		
II/0001	Update of or change(s) to the pharmaceutical documentation Change(s) to the manufacturing process for the active substance	22/05/2003	02/06/2003		