Omnitrope

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
IAIN/0077/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)	19/09/2023		Annex II and PL	

[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).

	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 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 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) 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				
IA/0074	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	13/02/2023	n/a		
II/0073	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/12/2022		SmPC and PL	
II/0071	Update of section 4.8 of the SmPC in order to add 'headache' and 'hypothyroidism' to the list of adverse drug reactions (ADRs) with frequency not known	02/09/2021	14/10/2022	SmPC and PL	In line with the results of the clinical study EP00-501 (PATRO children), SmPC section 4.8 was updated as to include that two adverse drug reactions ('headache' and

	based on final results from study EP00-501 (PATRO children), which were assessed in accordance with Article 46 of Regulation (EC) No1901/2006; this is a an international, non-interventional, non-controlled, longitudinal, open and multicenter study, designed to record the safety and effectiveness data of paediatric patients treated with Omnitrope in various indications within routine clinical practice; the Package Leaflet is updated accordingly. Section 5.1 of the SmPC was updated to include the study results of study EP00-501. In addition, the MAH took the opportunity to align the summary of the safety profile and the tabulated list of ADRs, to introduce statements in the PI as per the Excipients guideline and to bring the PI in line with the latest QRD template version 10.2. The requested variation proposed amendments to the Summary of Product Characteristics and Package Leaflet. C.I.3.b - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Change(s) with new additional data submitted by the MAH				'hypothyroidism'). SmPC section 5.1 was also updated to include the effectiveness results. For more information, please refer to the Summary of Product Characteristics.
IA/0072	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	03/06/2021	n/a		
II/0070	B.I.a.1.j - Change in the manufacturer of AS or of a	15/04/2021	n/a		

	starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method				
PSUSA/2772/ 202003	Periodic Safety Update EU Single assessment - somatropin	10/12/2020	11/02/2021	SmPC and PL	In view of available data on risk(s) from clinical trial(s), the literature, spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge, the PRAC Rapporteur considers a causal relationship between somatropin and acute pancreatitis is at least a reasonable possibility. The PRAC Rapporteur concludes that Section 4.4 of the SmPC of products containing somatropin should be amended to add a warning on pancreatitis. Additionally, the PRAC Rapporteur considers a causal relationship between somatropin and gynecomastia is established and concludes that section 4.8 of the SmPC of products containing somatropin should be amended, to add the adverse reaction gynecomastia with a frequency uncommon. The Package leaflet is updated accordingly.
IB/0068	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	14/11/2020	11/02/2021	SmPC, Annex II, Labelling and PL	
IA/0069	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	05/11/2020	n/a		

IB/0066	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	28/09/2020	n/a		
IA/0067	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	18/09/2020	n/a		
IA/0064	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	29/06/2020	n/a		
IB/0063	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	02/06/2020	n/a		
II/0062/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) 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	12/03/2020	n/a		

	B.I.c.1.z - Change in immediate packaging of the AS - Other variation B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) 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				
II/0060	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	25/07/2019	n/a		
IB/0061	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	03/07/2019	n/a		
IB/0059	B.II.z - Quality change - Finished product - Other variation	26/04/2019	n/a		
IAIN/0058	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	05/04/2019	n/a		
IB/0057	B.II.b.2.a - Change to importer, batch release	03/01/2019	n/a		

	arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place				
IA/0056	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	14/09/2018	n/a		
IA/0055	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)	29/08/2018	n/a		
IA/0054/G	This was an application for a group of variations. 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	19/07/2018	n/a		
IB/0053	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	18/07/2018	n/a		
PSUSA/2772/ 201703	Periodic Safety Update EU Single assessment - somatropin	14/12/2017	27/02/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/2772/201703.
IB/0052	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	07/02/2018	n/a		
II/0047	II: B.I.b.2 d) - To replace the currently used analytical release method immuno-ligand assay (ILA) by an enzyme-linked immunosorbent assay (ELISA) used to determine the concentration of host cell proteins (HCPs) in EP2000 active substance. The corresponding specification limits for the new analytical method are being defined in parallel. Consequentially, the current external contract partner for testing E. coli HCPs by ILA (Charles River Biopharmaceutical Services GmbH) has been removed. The requested variation proposed no amendments to the Product Information. 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	19/10/2017	n/a		
IB/0051	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	27/09/2017	n/a		

IAIN/0050/G	This was an application for a group of variations. 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.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 B.II.e.3.a - Change in test procedure for the immediate packaging of the finished product - Minor changes to an approved test procedure	15/09/2017	27/02/2018	Annex II and PL	
IB/0049	B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale	27/07/2017	27/02/2018	SmPC and PL	
II/0045	II: B.II.b.3.b – To introduce a new alternative pre-filter model (Sartorius Sartopure PP3) in the pre-filtration process step immediately prior to sterile filtration of the compounded finished product solution, to update and harmonize the quality control strategy used for all strengths to include several new process-parameters and in-process controls and to harmonise the compounded solution pH adjustment step between finished product strengths In addition, the MAH is also proposing minor editorial changes to modules 3.2.S, 3.2.P and 3.2.R.	16/03/2017	n/a		

	B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product				
N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/02/2017	27/02/2018	PL	
PSUSA/2772/ 201509	Periodic Safety Update EU Single assessment - somatropin	13/05/2016	n/a		PRAC Recommendation - maintenance
IB/0044	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	11/03/2016	n/a		
II/0042	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	17/12/2015	n/a		
IA/0041/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits	03/03/2015	n/a		

IB/0040	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/02/2015	16/03/2015	SmPC and PL	
IB/0039	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)	08/01/2015	n/a		
PSUSA/2772/ 201403	Periodic Safety Update EU Single assessment - somatropin	06/11/2014	n/a		PRAC Recommendation - maintenance
IA/0038	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	15/09/2014	n/a		
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/06/2014	18/07/2014	PL	
IA/0035	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	29/04/2014	n/a		
IB/0034/G	This was an application for a group of variations. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	10/02/2014	n/a		

	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product				
IAIN/0033	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	14/11/2013	n/a		
II/0030/G	This was an application for a group of variations. Grouped variations as follows: Update of section 4.4 of the SmPC, upon CHMP request set out in the conclusions of PSU 031.1 assessment report, in order to include a new warning regarding the risk of pancreatitis. Update the SmPC and Package Leaflet in accordance with the originator's PI Genotropin (UK). The Package Leaflet was proposed to be updated accordingly. 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 product - Change(s) require to be further substantiated by new additional data to be submitted by the MAH C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC -	19/09/2013	18/07/2014	SmPC, Annex II, Labelling and PL	Since Omnitrope is a biosimilar of Genotropin the MAH proposed to align the PI to the current European PI of Genotropin. The proposed amendments comprised of rephrasing the available information and adding information available in Genotropin's PI. Furthermore, in section 4.4 and 4.8 a warning on pancreatitis was included and the ADR was listed in the ADR table respectively, according to the CHMP request set out in the AR conclusions of PSU 31.1. The CHMP considered that the proposed PI changes for Ominitrope were acceptable.

	Change(s) with new additional data submitted by the MAH				
IB/0032	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	11/09/2013	n/a		
IAIN/0031/G	This was an application for a group of variations. 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.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is	17/07/2013	18/07/2014	SmPC, Labelling and PL	

	not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking				
II/0028/G	This was an application for a group of variations. Introduction of a post approval change management protocol related to the AS. B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS	27/06/2013	n/a		
IB/0029	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	24/04/2013	n/a		
IB/0027	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	30/01/2013	n/a		

	product in accordance with an approved stability protocol				
IA/0026	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	18/12/2012	n/a		
A20/0021	Article 20 Review On 10 December 2010, the European Commission initiated a procedure under Article 20 of Regulation (EC) No 726/2004 for somatropin-containing medicinal products authorised in the centralised procedure and requested the CHMP to assess all the available data and its impact on the risk benefit balance for somatropin-containing medicinal products and to give its opinion on measures necessary to ensure the safe and effective use of these medicinal products and whether the marketing authorisations for these products should be maintained, varied, suspended or revoked. The scope of the review was to assess the long-term safety of growth hormone treatments in light of the emerging safety data from the French SAGHE study in particular with regards the potential increased risk of mortality due to diseases of the circulatory system, bone tumours and subarachnoid or intracerebral haemorrhage in children and when high doses are used.	15/12/2011	02/03/2012	SmPC, Annex II and PL	Please refer to the Assessment Report: Omnitrope-H-607-A20-21-Assessment Report-Article 20

IB/0025/G	This was an application for a group of variations. B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol B.II.a.1.z - Change or addition of imprints, bossing or other markings including replacement, or addition of inks used for product marking - Other variation 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.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	04/10/2011	n/a	SmPC, Labelling and PL	
II/0023/G	This was an application for a group of variations. Change to in-process test and specification parameters of the active substance. 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	21/07/2011	21/07/2011		

	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits				
IA/0024	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)	08/07/2011	n/a		
X/0017	Extension Application of the Marketing Authorisation. Annex I_2.(c) Change or addition of a new strength/potency	14/04/2011	16/06/2011	SmPC, Labelling and PL	This extension application concerned a higher strength liquid formulation (Omnitrope 10 mg/ml solution for injection – multi dose for subcutaneous administration). The new formulation has been modified compared to the marketed Omnitrope 5 mg/ml powder for solution for injection and the Genotropin 5 mg/ml formulations. The MAH has applied for all clinical indications for the new formulation, which have previously been approved for the Omnitrope 5.0 mg/ml formulation. In view of the demonstrated physicochemical comparability and the comparable pharmacokinetic profiles, no clinically relevant differences are to be expected between the various formulations tested. In line with the previous extension procedure for the 6.7 mg/ml formulation the balance of the benefits and risks of treatment with the newly proposed 10 mg/ml formulation is therefore the same as for the already registered 5 mg/ml powder formulation.
IA/0022	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a	18/04/2011	n/a		

	DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH				
R/0018	Renewal of the marketing authorisation.	16/12/2010	28/02/2011	SmPC, Annex II and PL	
IA/0020	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	30/11/2010	n/a		
IA/0019/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance 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 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	25/11/2010	n/a	Annex II	
II/0016	Changes of category and limit of the in-process control plasmid retention Quality changes	20/05/2010	01/06/2010		

II/0015	Extension of shelf-life for the active substance Change(s) to shelf-life or storage conditions	19/11/2009	25/11/2009		
II/0014	Change in the manufacturing process of the finished product. Change(s) to the manufacturing process for the finished product	24/09/2009	30/09/2009		
II/0012	Changes to the specifications for the active substance Change(s) to the test method(s) and/or specifications for the active substance	29/05/2009	05/06/2009		
IB/0013	IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	12/05/2009	n/a		
II/0011	Changes to the manufacturing procedure of the active substance and alternative manufacturing site for active substance. Change(s) to the manufacturing process for the active substance	23/04/2009	28/04/2009		
II/0009	Update of Summary of Product Characteristics an Package Leaflet to harmonise all authorised presentations and to bring the product information in line with the reference product.	21/02/2008	18/03/2008	SmPC, Labelling and PL	The product information has been updated in line with the reference product with the following information: -deletion of a contraindication in patients with Prader Willy Syndrome (PWS)

	Update of Summary of Product Characteristics, Labelling and Package Leaflet				-description without gender differences of the risk factors potentially causing death in patients with PWS and one or more of the following: severe obesity, history of severe breathing problems, especially during sleep, or infection of the lungs or airways. In addition, other minor amendments have been introduced to harmonise all presentations throughout the product information.
II/0008	Change(s) to the manufacturing process for the active substance	13/12/2007	19/12/2007		
II/0007	Change(s) to the test method(s) and/or specifications for the finished product	15/11/2007	21/11/2007		
X/0002	The Marketing Authorisation Holder applied to extend the range of presentations to include a higher strength liquid formulation (solution for injection) in glass cartridges for use with the Omnitrope 10 Pen. Annex I_2.(c) Change or addition of a new strength/potency	19/07/2007	19/09/2007	SmPC, Labelling and PL	The new 6.7mg/ml formulation has been modified compared to the existing liquid 3.3mg/ml presentation and now contains phenol as a preservative. The main advantage with the new presentation is the elimination of the reconstitution step and use of the pen device and the higher strength facilitates administration of the product.
II/0006	Change(s) to the test method(s) and/or specifications for the active substance	19/07/2007	10/08/2007		
II/0003	The Marketing Authorisation Holder applied for the addition of statements in the Summary of Product Characteristics and Package Leaflet on the presence of benzyl alcohol for the 5 mg/ml strengths and statements on sodium for the 1.3 and 5 mg/ml	22/03/2007	15/05/2007	SmPC, Labelling and PL	A statement to avoid the use of the product in newborns and premature babies, due to the presence of benzyl alcohol was introduced to the SPC and PL for the 5 mg/ml strengths. In addition, a statement on the very low concentration of sodium in the medicinal product was

	strengths. The Package Leaflet was amended with a list of local representatives. In addition, corrections regarding the storage information, corrections to the list of local representatives (Estonia, Slovenia, Italy and Finland) and minor editorial changes were included in the Summary of Product Characteristics, Labelling and Package Leaflet for the 3.3 mg/ml strengths. Update of Summary of Product Characteristics, Labelling and Package Leaflet				added for the 1.3 and 5 mg/ml strengths. This harmonises text with earlier presentations.
X/0001	The Marketing Authorisation Holder applied to extend the range of 1.3 mg/ml and 5.0 mg/ml (powder for solution for injection) presentations to include a liquid formulation (solution for injection) in glass cartridges for use with the Omnitrope 5 Pen. Annex I_2.(c) Change or addition of a new strength/potency	22/02/2007	20/04/2007	SmPC, Labelling and PL	The new formulation has been modified compared to the existing presentations, above, however, like the 5.0mg/ml presentation, contains benzyl alcohol as a preservative. The main advantage with the new presentation is the elimination of the reconstitution step and use of the pen device, facilitating administration of the product.
II/0004	Change(s) to the manufacturing process for the active substance	22/03/2007	10/04/2007		
IB/0005	IA_37_a_Change in the specification of the finished product - tightening of specification limits IB_38_c_Change in test procedure of finished product - other changes	07/02/2007	n/a		