Arixtra

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
N/0091	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/03/2024		PL	
T/0090	Transfer of Marketing Authorisation	18/01/2024	16/02/2024	SmPC, Labelling and	

[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).

				PL	
IA/0089	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	30/10/2023	n/a		
II/0087	To update section 4.8 of the SmPC to update the ADR table following the assessment of PSUSA (EMEA/H/C/PSUSA/00001467/202112). The Package Leaflet is updated accordingly. C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	28/09/2023	16/02/2024	SmPC and PL	
IAIN/0088/G	This was an application for a group of variations. 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.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	13/07/2023	16/02/2024	Annex II and PL	
N/0086	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/10/2022	16/02/2024	PL	

PSUSA/1467/202112	Periodic Safety Update EU Single assessment - fondaparinux	07/07/2022	n/a		PRAC Recommendation - maintenance
N/0084	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/11/2021	16/02/2024	PL	
N/0083	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/09/2021	16/02/2024	PL	
T/0082	Transfer of Marketing Authorisation	19/02/2021	17/03/2021	SmPC, Labelling and PL	
N/0081	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/12/2020	17/03/2021	PL	
IA/0080	A.7 - Administrative change - Deletion of manufacturing sites	15/05/2020	n/a		
IB/0079/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation 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.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size B.I.b.1.c - Change in the specification parameters	19/09/2019	n/a		

	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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.a.3.b - Change in batch size (including batch size ranges) of AS or intermediate - Downscaling down to 10-fold B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
PSUSA/1467/ 201812	Periodic Safety Update EU Single assessment - fondaparinux	14/06/2019	n/a		PRAC Recommendation - maintenance
IB/0078	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	05/04/2019	n/a		
IA/0076/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.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	22/11/2018	n/a		

	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.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.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				
N/0075	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/11/2018	17/03/2021	PL	
PSUSA/1467/201712	Periodic Safety Update EU Single assessment - fondaparinux	28/06/2018	23/08/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/1467/201712.
IA/0074/G	This was an application for a group of variations. B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits 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)	13/07/2018	n/a		

	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 B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier				
N/0072	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/03/2018	23/08/2018	Labelling	
PSUSA/1467/ 201612	Periodic Safety Update EU Single assessment - fondaparinux	06/07/2017	n/a		PRAC Recommendation - maintenance
PSUSA/1467/ 201512	Periodic Safety Update EU Single assessment - fondaparinux	21/07/2016	15/09/2016	SmPC	Please refer to Arixtra PSUSA-00001467-201512 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
IB/0069/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size	25/02/2016	n/a		
IAIN/0068	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	09/12/2015	n/a		

II/0067	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	19/11/2015	n/a		
PSUSA/1467/ 201412	Periodic Safety Update EU Single assessment - fondaparinux	11/06/2015	n/a		PRAC Recommendation - maintenance
IA/0065	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	06/10/2014	n/a		
IAIN/0064/G	This was an application for a group of variations. 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.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	06/10/2014	30/09/2015	Annex II and PL	
PSUV/0062	Periodic Safety Update	11/09/2014	n/a		PRAC Recommendation - maintenance
T/0063	Transfer of Marketing Authorisation	25/07/2014	26/08/2014	SmPC, Labelling and PL	Transfer of the Marketing Authorisation from Glaxo Group Ltd to Aspen Pharma Trading Limited.
II/0061	Submission of a revised RMP version 1.9, which has been aligned with the new RMP format and which	26/06/2014	n/a		N/A

	includes an amendment of the current timeline for completion of the Superficial Vein Thrombosis post-marketing observational study from December 2013 to December 2014. The requested variation proposed no amendments to the PI. C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
N/0060	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/06/2014	26/08/2014	Labelling and PL	
N/0059	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/11/2013	26/08/2014	PL	
II/0056	Update of section 4.8 of the SmPC in order to add angioedema and anaphylactoid/anaphylactic reaction as new adverse reaction for all strengths. The Package Leaflet was proposed to be updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template version 9. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/04/2013	29/11/2013	SmPC, Annex II and PL	During the time period covered by the last fondaparinux PSUR, two reports were identified that described possible anaphylactic reactions. Following this the MAH committed to conduct a comprehensive review of anaphylaxis to further investigate a causal association between anaphylaxis and the use of fondaparinux. Following the review conducted by the MAH and assessed by the CHMP section 4.8 of the SmPC was updated in order to add angioedema and anaphylactoid/anaphylactic reaction as new adverse reaction for all strengths.

IG/0279	A.1 - Administrative change - Change in the name and/or address of the MAH	18/04/2013	29/11/2013	SmPC, Labelling and PL	
IG/0275	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/03/2013	n/a		
IB/0055/G	This was an application for a group of variations. B.II.b.1.f - Replacement or addition of a manufacturing site for part or all of the manufacturing process of the FP - Site where any manufacturing operation(s) take place, except batch release, batch control, and secondary packaging, for sterile medicinal products (including those that are aseptically manufactured) excluding biological/ immunological medicinal products A.7 - Administrative change - Deletion of manufacturing sites B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation 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 B.II.b.3.a - Change in the manufacturing process of	19/12/2012	n/a		

	the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions				
IB/0054	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	14/12/2012	29/11/2013	SmPC, Annex II, Labelling and PL	To update section 4.8 - Undesirable effects of the EU SmPC for the higher doses (5mg, 7,5mg, and 10 mg solution for injection) only with the following adverse reactions; abdominal pain (rare), hepatic enzymes increased (uncommon) and pruritus (rare). The following adverse reactions; gastritis, constipation, diarrhoea, and bilirubinaemia (reported in post marketing experience) will also be added as a statement under the table in section 4.8 for the higher dose (5mg, 7,5mg, and 10 mg) SmPCs. The possible side effects section of the Package leaflet has been updated in line with the updates to section 4.8 of the SmPCs.
IB/0052	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	13/04/2012	n/a		
IG/0150/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.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	05/04/2012	n/a		

IB/0051	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	15/12/2011	04/07/2012	SmPC, Labelling and PL	
II/0049	Update the Summary of Product Characteristics under section 4.4 Special Warnings and Precautions for Use, with the addition of a Latex Warning. Consequently, the Package Leaflet has also been updated. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	22/09/2011	20/10/2011	SmPC and PL	Fondaparinux sodium is supplied as a sterile, preservative-free injectable solution for subcutaneous and intravenous use, in a single dose pre-filled syringe. The needle guard of the syringe contains natural rubber (i.e. latex). Therefore a warning on the potential allergic reactions that might be caused by the latex has been added to the SmPC and PL.
II/0048	Update of section 5.1 of the SmPC of the 2.5mg strength with data and information from a post-approval safety study conducted as a commitment following approval of the Acute Coronary Syndrom (ACS) indications. Consequently, section 4.4 of the SmPC of the 2.5mg strength is updated to reflect information on the risk of guiding cathete thrombus. Additionally, the SmPC and PL reflect some typo corrections and terminology improvements. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	14/04/2011	18/05/2011	SmPC and PL	This Type II variation is to update the Summary of Product Characteristics (SmPC sections 4.2, 4.4 and 5.1) of the 2.5mg strength to include data from the study FUTURA and a warning on the risk of guiding cathete thrombus. FUTURA is a post-approval safety study to evaluate the safety of two dose regimens of unfractionated heparin (UFH) as adjunctive to fondaparinux during percutaneous coronary intervention (PCI) in non-ST segment elevation myocardial infarction (NSTEMI) patients being treated initially with fondaparinux. The study was conducted as a commitment following approval of the Acute Coronary Syndrome (ACS) indication. The study results showed a trend for lower incidences of minor bleedings and large haematomas at the injection sites for the low dose group. However, an opposite trend was observed for ischemic complications at day 30. The study had an appropriate design and seems to have

					been well performed. It has provided results that are of clinical interest and a short description of the main results in the SmPC is judged to be justified.
II/0047	Update of sections 4.2, 5.1 and 5.2 of the SmPC with data from a phase II pilot dose-finding and pharmacokinetic study of fondaparinux in paediatric patients with Deep Vein Thrombosis (DVT). This update affects only the SmPCs relevant to the DVT indication (i.e. strengths 5, 7.5 and 10 mg). C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	20/01/2011	28/02/2011	SmPC	ART113100 was a phase II pilot dose-finding and pharmacokinetic study of fondaparinux in patients with Deep Vein Thrombosis (DVT), aged 1-18 years and with a body weight greater than 8.3 kg. Data from this study were used to create a PK model for the paediatric population to compare concentrations achieved in paediatric patients receiving 0.1mg/kg/day to concentrations known to be efficacious in adults. The PK modelling used data from study ART113100 and study BDR3780, a bioequivalence study in adult healthy subjects. The BDR3780 clinical study report was part of the original Marketing Authorisation Application for Arixtra. The limited data provided in paediatrics collectively suggest that the exposure in children with dosing 0.1 mg/kg is somewhat lower than that observed in adults and that there is a trend for increased exposure with increased age within the paediatric population. From the results of this small uncontrolled study no firm conclusions can be drawn on an optimal concentration range to target in children in the treatment of thrombosis in the deep venous system. However, the CHMP was of the opinion that it could be of value for the prescribers to know what concentrations could be expected with a dose that, when adjusted to body-weight, is similar to what is recommended for adults. Therefore the CHMP agreed on the update of the SmPC to include data on this study. As the data concerns children with deep venous thrombosis, this information is only included in the SmPCs relevant for

					this indication, i.e. the 5, 7.5 and 10 mg strengths.
IG/0034/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details of the QPPV C.I.9.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.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system 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 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	06/01/2011	n/a	Annex II	

II/0045	Please refer to the Scientific discussion: Arixtra-H-403-II-45. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/07/2010	31/08/2010	SmPC, Labelling and PL	
II/0044	Addition of an alternative active substance manufacturer. Quality changes	20/05/2010	01/06/2010		
IB/0046	To wash the wet Step 3 process intermediate DEFGH3 with aqueous acetonitrile in addition to or as an alternative to washing by water alone. B.I.a.2.e - Changes in the manufacturing process of the AS - Minor change to the restricted part of an ASMF	22/03/2010	n/a		
II/0043	Update of the Detailed Description of the Pharmacovigilance System (DDPS) including change of the Qualified Person for Pharmacovigilance (QPPV). Consequently, Annex II has been updated with the new version number. Update of DDPS (Pharmacovigilance)	17/12/2009	20/01/2010	Annex II	The DDPS has been updated (version 7.2) to reflect the change of the QPPV as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS. The CHMP considers that the Pharmacovigilance System as described by the MAH fulfils the requirements.
II/0042	Changes to the specifications (appearance) and test methods of some starting materials, intermediates and reagents used in the synthesis of the active	24/09/2009	05/10/2009		

	substance. Quality changes				
II/0041	Update of Detail Description of the Pharmacovigilance System (Pharmacovigilance) Changes to QPPV Update of DDPS (Pharmacovigilance)	19/02/2009	25/03/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated (Version 6.2 November 2008) to reflect the change of the Qualified Person for Pharmacovigilance (QPPV) as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS.
II/0038	The MAH applied for changes in the specification, test procedures and shelf-life of the finished product . Quality changes Update of Package Leaflet	19/02/2009	25/03/2009	SmPC and PL	
II/0039	he MAH applied for the addition of an alternative site of manufacture, packaging and quality control testing of the 2.5 mg/0.5 mL strength with consequential changes in the manufacturing and packaging process. Quality changes	19/02/2009	04/03/2009		
II/0037	The MAH applied for changes in the secondary packaging of the finished product. Update of or change(s) to the pharmaceutical documentation	20/11/2008	22/12/2008	SmPC and PL	

IA/0040	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	16/12/2008	n/a		
II/0036	New presentation(s)	24/07/2008	22/08/2008	SmPC, Labelling and PL	
II/0035	Update of Summary of Product Characteristics and Package Leaflet	21/02/2008	19/03/2008	SmPC and PL	Further to the results of a PK study in patients with moderate hepatic impairment, the SPC has been updated to inform physicians that no dose adjustment is necessary (section 4.2) and to include the main study findings (5.2). In addition, the warning statement (section 4.4) on Heparin Induced Thrombocytopenia (HIT) type II has been amended to reflect that rare spontaneous reports of HIT in patients treated with fondaparinux have been received, although no causal association between treatment with fondaparinux and the occurrence of HIT has been established. Finally, the statement on the prolongation of the aPTT during treatment with fondaparinux therapy (section 5.1) has been updated to inform that rare spontaneous reports of aPTT prolongation have been received.
N/0034	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/10/2007	n/a	PL	
II/0033	Update of or change(s) to the pharmaceutical documentation	20/09/2007	09/10/2007	SmPC	
II/0032	Update of Summary of Product Characteristics and Package Leaflet	19/07/2007	03/09/2007	SmPC and PL	Amendment of the posology (Section 4.2) for the prevention of venous thromboembolism (VTE) in patients

					with moderate renal impairment. Related changes are also proposed to Section 4.4 of the SPC and Sections 2 and 3 of the Package Leaflet. In addition, the MAH applied for minor changes to Section 4.2, 5.1 and 9 of the SPC and to Section 6 of the Package Leaflet. The Package Leaflet has been updated accordingly.
X/0025	New intravenous use of the 2.5 mg strength to be administered as the first dose of fondaparinux in patients with STEMI eligible for treatment with fondaparinux (subsequent doses are administered by subcutaneous injection). Annex I_2.(e) Change or addition of a new route of administration	21/06/2007	29/08/2007	SmPC, Labelling and PL	Please refer to the Scientific discussion: Arixtra-H-403-X-25 and II-24.
II/0024	Extension of Indication of the 2.5 mg strength to include a new indication in the treatment of Acute Coronary Syndromes as follows: Treatment of unstable angina or non-ST segment elevation myocardial infarction (UA/NSTEMI) in patients for whom urgent (<120mins) invasive management (PCI) is not indicated (see sections 4.4 and 5.1). Treatment of ST segment elevation myocardial infarction (STEMI) in patients who are managed with thrombolytics or who initially are to receive no other form of reperfusion therapy The new indication is based on the results of the OASIS-5 (UA/NSTEMI) and OASIS-6 (STEMI) trials.	21/06/2007	29/08/2007	SmPC, Annex II, Labelling and PL	Please refer to the Scientific discussion: Arixtra-H-403-II-24.

	Extension of Indication				
IA/0031	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	25/04/2007	n/a		
R/0027	Renewal of the marketing authorisation.	22/02/2007	20/04/2007	SmPC, Annex II, Labelling and PL	
IB/0030	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	07/12/2006	n/a	SmPC	
IA/0028	IA_13_a_Change in test proc. for active substance - minor change	25/09/2006	n/a		
IA/0026	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	31/08/2006	n/a		
IA/0023	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	24/07/2006	n/a		
IB/0022	IB_41_a_02_Change in pack size - change in no. of units outside range of appr. pack size	07/02/2006	07/02/2006	SmPC, Labelling and PL	
II/0012	Extension of Indication. The MAH applied for the addition of a new indication, namely "Prevention of Venous Thromboembolic Events (VTE) in patients undergoing abdominal surgery who are judged to be at high risk of thromboembolic complications, such as patients undergoing abdominal cancer surgery	26/05/2005	07/07/2005	SmPC and PL	Please refer to the Scientific discussion: Arixtra-H-403-II-12

	(see section 5.1)" Extension of Indication				
IA/0020	IA_09_Deletion of manufacturing site	13/05/2005	n/a		
II/0010	Extension of Indication. The MAH applied for the addition of a new indication regarding `Prevention of VTE in medical patients who are at risk for thromboembolic complications due to restricted mobility during acute illness' Extension of Indication	15/12/2004	25/01/2005	SmPC and PL	Please refer to the Scientific discussion: Arixtra-H-403-II-10.
IB/0019	IB_38_c_Change in test procedure of finished product - other changes	17/01/2005	n/a		
IB/0018	IB_37_a_Change in the specification of the finished product - tightening of specification limits	17/01/2005	n/a		
IB/0017	IB_10_Minor change in the manufacturing process of the active substance IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	17/01/2005	n/a		
T/0014	Transfer of Marketing Authorisation	03/12/2004	12/01/2005	SmPC, Annex II, Labelling and PL	Transfer of MAH from Sanofi-Synthélabo Recherche to GlaxoSmithKline.
IA/0015	IA_05_Change in the name and/or address of a manufacturer of the finished product	01/12/2004	n/a	SmPC, Annex II and PL	

X/0007	Extension of Indication X-3-iii_Addition of new strength	29/07/2004	12/11/2004	SmPC, Labelling and PL	
N/0013	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/09/2004	25/01/2005	PL	
IB/0011	IB_38_c_Change in test procedure of finished product - other changes	21/07/2004	n/a		
IB/0009	IB_37_a_Change in the specification of the finished product - tightening of specification limits	13/01/2004	n/a		
IB/0008	IB_10_Minor change in the manufacturing process of the active substance IB_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening	13/01/2004	n/a		
II/0004	Update of Summary of Product Characteristics and Package Leaflet	24/07/2003	07/11/2003	SmPC and PL	
X/0005	X-3-iii_Addition of new strength	24/07/2003	24/10/2003	SmPC, Annex II, Labelling and PL	
I/0006	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	07/08/2003	22/09/2003		
II/0001	Update of Summary of Product Characteristics	18/12/2002	20/03/2003	SmPC	
I/0002	20_Extension of shelf-life as foreseen at time of authorisation	01/12/2002	15/01/2003	SmPC	

I/0003	20a_Extension of shelf-life or retest period of the active substance	02/12/2002	11/12/2002		