Ferriprox

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
PSUSA/940/201808	Periodic Safety Update EU Single assessment - deferiprone	14/03/2019	n/a		PRAC Recommendation - maintenance
II/0126/G	This was an application for a group of variations. Update of sections 4.2, 4.4 and 5.2 of the SmPC in order to update safety information on the use of Ferriprox in patients with renal or hepatic impairment, based on the final results of two clinical studies	31/01/2019	11/03/2019	SmPC 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).

	LA39-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Renal Function and Healthy Volunteers) and LA40-0412 (An Open-Label Study to Compare the Pharmacokinetic Profiles of a Single Dose of Ferriprox in Subjects with Impaired Hepatic Function and Healthy Volunteers). The studies are listed as category 3 study in the RMP. The Package leaflet and labelling are updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to make some minor edits in the PI. The RMP version 13.1 has also been submitted to include consequential changes regarding these two clinical studies, to introduce minor changes requested to be addressed at the next regulatory procedure and to update the RMP format in line with the GVP Module V Rev 2 template. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
IA/0129	B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method	25/10/2018	n/a		
IA/0127/G	This was an application for a group of variations.	10/10/2018	n/a		

	B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.c - Change in the specification parameters and/or limits of an excipient - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IAIN/0125/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.III.2.a.1 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - AS	27/07/2018	n/a		
IA/0124	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)	28/06/2018	n/a		
IA/0123	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	27/04/2018	n/a		

PSUSA/940/201708	Periodic Safety Update EU Single assessment - deferiprone	12/04/2018	n/a		PRAC Recommendation - maintenance
IB/0120	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	12/12/2017	n/a		
IA/0122	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	08/12/2017	n/a		
IA/0119	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	30/11/2017	n/a		
IB/0118/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 B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation	13/11/2017	n/a		
IA/0117	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	20/07/2017	n/a		
IB/0116/G	This was an application for a group of variations.	04/07/2017	12/04/2018	SmPC, Annex II, Labelling	

	A.1 - Administrative change - Change in the name and/or address of the MAH B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)			and PL	
PSUSA/940/201608	Periodic Safety Update EU Single assessment - deferiprone	23/03/2017	24/05/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/940/201608.
IA/0115	B.II.e.5.b - Change in pack size of the finished product - Deletion of a pack size(s)	18/05/2017	12/04/2018	SmPC, Labelling and PL	
IB/0112	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	31/01/2017	n/a		
IAIN/0114	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	17/01/2017	n/a		
IA/0113	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	12/01/2017	n/a		
IA/0110	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	01/09/2016	n/a		

IB/0109	B.II.e.1.a.2 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Semi-solid and non-sterile liquid pharmaceutical forms	01/09/2016	n/a		
IA/0108	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	24/06/2016	n/a		
II/0103	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	28/04/2016	26/05/2016	SmPC, Annex II and PL	
PSUSA/940/201508	Periodic Safety Update EU Single assessment - deferiprone	17/03/2016	n/a		PRAC Recommendation - maintenance
IA/0107	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	22/12/2015	n/a		
IA/0105	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)	22/10/2015	n/a		
II/0089/G	This was an application for a group of variations. Update of section 5.1 of the SmPC with the results of Study LA37-1111; a double-blind randomized, crossover, thorough QT/QTc trial to evaluate the potential of deferiprone to prolong the QT interval in	22/10/2015	26/05/2016	SmPC, Annex II and PL	Study LA37-1111 was conducted to evaluate the effect of single therapeutic (33 mg/kg) and supratherapeutic (50 mg/kg) oral doses of deferiprone on the cardiac QT interval duration in healthy subjects. The maximum difference between the LS means of the therapeutic dose and placebo was 3.01 msec (95% one-sided UCL: 5.01 msec), and

	healthy subjects. Further, the MAH took the opportunity to update the SmPC, Annex II and Package Leaflet in line with the QRD template version 9, and to update the contact details of the Croatian local representative in the Package Leaflet. The updated RMP version 8.1 was agreed as part of this procedure. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				between the LS means of the supratherapeutic dose and placebo was 5.23 msec (95% one-sided UCL: 7.19 msec). Ferriprox was concluded to produce no significant prolongation of the QT interval.
IA/0104	A.7 - Administrative change - Deletion of manufacturing sites	24/09/2015	n/a		
IA/0102	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)	04/09/2015	n/a		
IA/0101/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.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	12/08/2015	n/a		

IAIN/0100	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	22/07/2015	n/a		
IB/0099	B.II.e.1.a.2 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Semi-solid and non-sterile liquid pharmaceutical forms	23/04/2015	n/a		
IA/0098	B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	23/04/2015	n/a		
IA/0097	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	26/03/2015	n/a		
PSUSA/940/201408	Periodic Safety Update EU Single assessment - deferiprone	12/03/2015	n/a		PRAC Recommendation - maintenance
IAIN/0096/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the QPPV and/or QPPV contact details and/or back-up procedure C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to	05/02/2015	n/a		

	the DDPS that does not impact on the operation of the PhV system				
IA/0095	B.III.2.b - Change to comply with Ph. Eur. or with a national pharmacopoeia of a Member State - Change to comply with an update of the relevant monograph of the Ph. Eur. or national pharmacopoeia of a Member State	19/12/2014	n/a		
IA/0094	A.7 - Administrative change - Deletion of manufacturing sites	04/12/2014	n/a		
IA/0092	B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method	01/12/2014	n/a		
IAIN/0091/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(s) in the safety database and/or major contractual arrangements for the fulfilment of PhV obligations, and/or change of the site undergoing PhV activities C.I.9.c - 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 PhV system	08/08/2014	n/a		
IA/0090	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	30/07/2014	n/a		

IA/0088	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	25/04/2014	n/a		
PSUV/0087	Periodic Safety Update	10/04/2014	n/a		PRAC Recommendation - maintenance
II/0084	Update of section 4.8 of the SmPC in order to add hypersensitivity reactions, rash and urticaria as ADRs in the course of Ferriprox treatment in conclusion to the assessment of the 22nd PSUR. The Package Leaflet is updated accordingly. In addition, the MAH took the opportunity to make a minor editorial change to section 5.2 of the SmPC and to update the list of local representatives in the Package Leaflet. Furthermore, the PI is being brought in line with version 8.3 (January 2013) of the QRD template. 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 - Change(s) with new additional data submitted by the MAH	25/04/2013	23/04/2014	SmPC, Annex II, Labelling and PL	As a follow-up to the assessment of the 22nd yearly PSUR, covering the period from 1 September 2010 to 31 August 2011, hypersensitivity reactions, rash and urticaria were included in the list of ADRs observed in the course of Ferriprox treatment following relevant cases from spontaneous reporting which were accompanied with positive dechallenge and rechallenge suggesting a causal relationship between these events and Ferriprox.
IAIN/0086	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/04/2013	n/a		
IAIN/0085	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging	20/03/2013	n/a		

	site				
IAIN/0083	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	05/12/2012	n/a		
IA/0082/G	This was an application for a group of variations. B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method 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.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	25/10/2012	n/a		
IA/0080/G	This was an application for a group of variations. 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.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	12/09/2012	n/a		

IB/0079	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	01/08/2012	25/10/2012	SmPC	
IA/0078/G	This was an application for a group of variations. B.II.e.1.a.1 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Solid pharmaceutical forms 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	24/05/2012	n/a		
N/0076	Update of name and contact information of local representatives for Bulgaria, Hungary, Poland, Romania, Slovenia and Slovakia for the package leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/03/2012	25/10/2012	PL	
IB/0077	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	21/03/2012	25/10/2012	SmPC	
IA/0075/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	02/12/2011	n/a		

	B.II.b.4.b - Change in the batch size (including batch size ranges) of the finished product - Downscaling down to 10-fold				
IA/0074	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 currently approved batch size	30/08/2011	n/a		
N/0070	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/08/2011	n/a	Annex II and PL	
IB/0073/G	This was an application for a group of variations. 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 B.I.c.2.d - Change in the specification parameters and/or limits of the immediate packaging of the AS - Addition or replacement of a specification parameter as a result of a safety or quality issue	22/08/2011	n/a		
IA/0072	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	18/07/2011	n/a		
IA/0071	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	27/06/2011	n/a		

IB/0069/G	This was an application for a group of variations. B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	18/04/2011	n/a		
IA/0067	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	06/01/2011	n/a		
IA/0065/G	This was an application for a group of variations. B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits B.II.c.1.b - Change in the specification parameters and/or limits of an excipient - Addition of a new specification parameter to the specification with its corresponding test method B.II.c.1.a - Change in the specification parameters and/or limits of an excipient - Tightening of specification limits	03/12/2010	n/a		
IA/0066	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the	29/11/2010	n/a		

	dossier) - Replacement or addition of a supplier				
N/0064	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/09/2010	n/a	PL	
II/0063	Update of sections 4.6 and 5.3 of the Summary of Product Characteristics (SmPC) with new information from non-clinical studies. Minor editorial amendments were also introduced in the SmPC, Labelling and Package Leaflet (PL). C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	24/06/2010	06/08/2010	SmPC, Labelling and PL	No effects of deferiprone on fertility and early embryonic development were noted in animals. A delay in time to confirmed mating was noted in female rats, which was attributed to a prolongation of the oestrous cycle.
X/0058	Annex I_2.(c) Change or addition of a new strength/potency	20/05/2010	28/07/2010	SmPC, Labelling and PL	
II/0062	C.I.4 - Variations related to significant modifications of the Summary of Product Characteristics due in particular to new quality, pre-clinical, clinical or pharmacovigilance data Update of section 5.1 of the Summary of Product Characteristics (SmPC) with new information from two clinical studies investigating the potential cardioprotective effect of deferiprone-mediated iron chelation. Changes to improve readability and clarity were introduced in sections 4.2, 4.4 and 4.8 of the SmPC and in the Labelling. Annex II has been updated to reflect the switch to the annual PSUR cycle. Editorial changes were made to the SmPC. The Product	20/05/2010	05/07/2010	SmPC, Annex II, Labelling and PL	Following review of a newly submitted prospective clinical study with the objective to examine the effect of deferiprone on protecting myocardial tissue from iron deposition (study LA 16-0102) and a previously reviewed retrospective study with similar objectives (LA 12-9907), section 5.1 of the SmPC was revised significantly. The studies described in 5.1 show that Ferriprox is effective in removing transfusional iron overload and in protecting myocardial tissue from iron deposition and consequent loss of cardiac function. Moreover, the warning and posology recommendation on agranulocytosis was moved from section 4.4 to section 4.2 of the SmPC and the wording on the posology recommendation was expanded. The structure of section 4.8 of the SmPC was

	Information has been updated in accordance with the latest QRD template (version 7.3.1, March 2010). C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				revised based on the recommendation of the SmPC Guideline (Revision 2, September 2009).
II/0061/G	This was an application for a group of variations. To introduce changes in the in-process testing and minor changes in the manufacturing process of the finished product. B.II.b.3.a - Change in the manufacturing process of the finished product - Minor change in the manufacturing process of an immediate release solid oral dosage form or oral solutions 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.e - Change to in-process tests or limits applied during the manufacture of the finished product - Widening of the approved IPC limits, which may have a significant effect on overall quality of the finished product	22/04/2010	04/05/2010		
IB/0060	B.II.e.1.a.2 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Semi-solid and non-sterile liquid pharmaceutical forms	26/02/2010	n/a		

IA/0068	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products	05/01/2010	n/a		
IA/0059	IA_28_Change in any part of primary packaging material not in contact with finished product	26/11/2009	n/a		
R/0054	Renewal of the marketing authorisation.	25/06/2009	21/09/2009	SmPC, Annex II, Labelling and PL	Based on quality, efficacy and safety documentation submitted, the CHMP is of the opinion that the renewal can be granted with unlimited validity and agree to renew the Marketing Authorisation of Ferriprox. The MAH will continue to submit 6 monthly PSURs, unless otherwise specified by the CHMP. The Product information has been updated to implement QRD changes as part of this renewal.
N/0057	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	25/06/2009	n/a	PL	
II/0053	To add an alternative child-resistant (CR) cap for Ferriprox 100 mg/ml oral solution and consequently a new supplier for the alternative closure. Quality changes	19/03/2009	25/03/2009		
IA/0056	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	17/03/2009	n/a		
IA/0055	IA_23_b_Change in source of excip./reagent to veg./synthetic material - other cases	11/03/2009	n/a		

N/0051	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/02/2009	n/a	PL	
IA/0050	IA_08_b_02_Change in BR/QC testing - repl./add. manuf. responsible for BR - incl. BC/testing	22/10/2008	n/a	Annex II and PL	
IA/0049	IA_29_b_Change in qual./quant. composition of immediate packaging - all other pharm. forms	27/08/2008	n/a		
IB/0047	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	08/07/2008	n/a		
IB/0046	IB_14_a_Change in manuf. of active substance without Ph. Eur. certificate - change in manuf. site	04/07/2008	n/a		
IA/0048	IA_13_a_Change in test proc. for active substance - minor change	04/07/2008	n/a		
IB/0045	IB_31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits	30/04/2008	n/a		
II/0043	The MAH applied for an update of Section 4.8 of the SPC to add headache and fatigue following the assessment of the 15th PSUR. Furthermore, the incidences of agranulocytosis and neutropenia have been amended and the entire Section 4.8 has been amended in line with the SPC guideline and QRD templates. Section 4 of the package leaflet has been amended accordingly. In addition, the MAH applied to relocate the patient/carer reminder card from Annex IIIA	19/03/2008	23/04/2008	SmPC, Labelling and PL	Following the review of the 15th Periodic Safety Update Report , the CHMP requested that the product information should be amended to include headache (common) and fatigue (common) to Section 4.8 of the SPC. The PL has been amended accordingly. Furthermore, the incidence of agranulocytosis and neutropenia has been corrected in Section 4.8 of the SPC. In addition the patient/carer reminder card has been relocated from Annex IIIA (Labelling) to Annex IIIB (PL). Cross-reference statements have been included to the PL.

	(labelling) to Annex IIIB (PL). Cross-reference statements have been included to the beginning and to Section 2 of the PL. Finally, the MAH took the opportunity to update the information in Braille in the Labelling and the list of local representatives for Belgium and Luxembourg in the Package Leaflet. Update of Summary of Product Characteristics, Labelling and Package Leaflet				Finally, the information in Braille in the labelling and the list of local representatives for Belgium and Luxembourg in the Package Leaflet have been updated.
IB/0044	IB_33_Minor change in the manufacture of the finished product	27/11/2007	n/a		
X/0036	Ferriprox, 100 mg/ml, oral solution has been authorised. Annex I_2.(d) Change or addition of a new pharmaceutical form	20/09/2007	19/11/2007	SmPC, Labelling and PL	Ferriprox, 100 mg/ml, oral solution has been authorised.
T/0042	Transfer of Marketing Authorisation	08/06/2007	29/06/2007	SmPC, Labelling and PL	Transfer from Apotex Europe Ltd. to Apotex Europe B.V.
IA/0041	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	07/02/2007	n/a		
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	02/02/2007	n/a	PL	
II/0039	Update of sections 4.2, 4.4, 4.8 and 4.9 following the assessment of the 13th PSUR, and further updates to	14/12/2006	26/01/2007	SmPC, Annex II, Labelling	Update of the information pertaining to chronic overdose and the risk of neurological disorders and strengthening the

	sections 4.4 and 4.5. Update of Summary of Product Characteristics, Labelling and Package Leaflet			and PL	wording on neutropenia and agranulocytosis and the monitoring of patient's neutrophil counts. In addition, the latest QRD template (V 7.2) is being implemented.
IA/0038	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	09/08/2006	n/a		
N/0037	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/03/2006	n/a	PL	
IA/0035	IA_38_a_Change in test procedure of finished product - minor change to approved test procedure	10/03/2006	n/a		
II/0034	Update of Summary of Product Characteristics (4.9) and Package Leaflet (3). Update of Summary of Product Characteristics and Package Leaflet	14/12/2005	30/01/2006	SmPC and PL	Inclusion of case of chronic overdose reported with deferiprone.
IA/0033	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	27/07/2005	n/a		
II/0032	Quality changes	16/03/2005	23/03/2005		
IB/0031	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	23/12/2004	n/a	SmPC	
IB/0030	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	03/12/2004	n/a		

IA/0029	IA_13_a_Change in test proc. for active substance - minor change	08/11/2004	n/a		
IA/0028	IA_05_Change in the name and/or address of a manufacturer of the finished product	20/10/2004	n/a		
IA/0027	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	20/10/2004	n/a		
R/0026	Renewal of the marketing authorisation.	23/06/2004	02/09/2004		
II/0023	changes to the specification of the active substance and finished product Change(s) to the test method(s) and/or specifications for the active substance	03/06/2004	09/06/2004		
II/0017	Extension of Indication Update of Summary of Product Characteristics and Package Leaflet	24/03/2004	07/05/2004	SmPC and PL	
IA/0025	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	30/03/2004	n/a		
IA/0024	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	30/03/2004	n/a		
IA/0021	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec. IA_37_a_Change in the specification of the finished product - tightening of specification limits	10/03/2004	n/a		

IB/0018	IB_30_b_Change in supplier of packaging components - replacement/addition	03/02/2004	n/a		
IA/0020	IA_22_a_Submission of TSE Ph. Eur. certificate for exc. - Approved/new manufacturer	28/01/2004	n/a		
IA/0019	IA_29_b_Change in qual./quant. composition of immediate packaging - all other pharm. forms	28/01/2004	n/a		
II/0016	Update of Summary of Product Characteristics and Package Leaflet	26/06/2003	03/10/2003	SmPC and PL	
I/0014	31_Change in container shape	16/04/2003	28/04/2003		
I/0013	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	16/04/2003	28/04/2003		
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/04/2003	12/05/2003	PL	
I/0012	03_Change in the name and/or address of the marketing authorisation holder	04/03/2003	10/04/2003	SmPC, Labelling and PL	
I/0011	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	25/03/2003	31/03/2003		
I/0010	13_Batch size of active substance	21/06/2002	28/06/2002		
S/0009	Annual re-assessment.	13/12/2001	12/04/2002	Annex II	
S/0005	Annual re-assessment.	16/11/2000	05/02/2002		

II/0008	Update of or change(s) to the pharmaceutical documentation Change(s) to the test method(s) and/or specifications for the active substance	25/04/2001	02/05/2001		
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/01/2001	06/03/2001	Labelling and PL	
I/0004	20a_Extension of shelf-life or retest period of the active substance	16/11/2000	n/a		
I/0003	11_Change in or addition of manufacturer(s) of active substance	15/11/2000	n/a		
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/10/2000	01/12/2000	PL	
I/0001	03_Change in the name and/or address of the marketing authorisation holder	09/12/1999	22/02/2000	SmPC, Labelling and PL	