Fareston

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/0050/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	13/11/2018		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).

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IA/0049	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	08/10/2018	n/a		
IA/0048/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.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)	07/09/2018	n/a		
PSUSA/2999/ 201709	Periodic Safety Update EU Single assessment - toremifene	31/05/2018	26/07/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2999/201709.
IB/0046	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/06/2017	12/06/2018	SmPC, Annex II, Labelling and PL	
IA/0045	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	06/06/2017	n/a		

IAIN/0044/G	This was an application for a group of variations. 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 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	18/08/2016	23/12/2016	Annex II and PL	
IAIN/0043	B.II.f.1.a.1 - Stability of FP - Reduction of the shelf life of the finished product - As packaged for sale	14/01/2016	23/12/2016	SmPC	
PSUSA/2999/ 201409	Periodic Safety Update EU Single assessment - toremifene	25/06/2015	20/08/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2999/201409.
IAIN/0042/G	This was an application for a group of variations. B.II.b.1.b - Replacement or addition of a manufacturing site for the FP - Primary packaging site B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	26/05/2015	n/a		
IAIN/0041	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	20/05/2015	n/a		

PSUSA/2999/201309	Periodic Safety Update EU Single assessment - toremifene	26/06/2014	26/08/2014		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2999/201309.
IB/0038	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	21/02/2014	26/08/2014	SmPC, Annex II, Labelling and PL	Update of the Package Leaflet based on the results of a User Testing report. The MAH also took the opportunity to update the PI in line with the latest version of the QRD template (9.0).
IA/0037	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)	17/02/2011	n/a		
N/0036	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/01/2011	n/a	PL	
IB/0035	IB_33_Minor change in the manufacture of the finished product	27/01/2010	n/a		
IB/0034	IB_33_Minor change in the manufacture of the finished product	27/01/2010	n/a		
IA/0033	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	02/12/2009	n/a		
II/0032	Update of Summary of Product Characteristics, Labelling and Package Leaflet	22/01/2009	02/03/2009	SmPC, Labelling and PL	This type II variation concerns the addition of new contraindications in section 4.3 of the SPC and new information in sections 4.4, 4.8, 4.9 and 5.3 of the SPC in relation to a dose-related risk of QTc prolongation following exposure to Fareston. Further, section 4.5 of the SPC has been amended to highlight that Fareston should not be used

					concurrently with other substances that prolong the QT interval. The Package Leaflet has been updated accordingly. The MAH also took the opportunity to update the annexes in line with the latest QRD template. Both in preclinical investigations and in humans, changes in cardiac electrophysiology have been observed following exposure to Fareston (toremifene), in the form of QT prolongation. For reasons of drug safety, toremifene is therefore contraindicated in patients with: - Congenital or documented acquired QT prolongation - Electrolyte disturbances, particularly in uncorrected hypokalaemia - Clinically relevant bradycardia - Clinically relevant heart failure with reduced left-ventricular ejection fraction - Previous history of symptomatic arrhythmias Toremifene should also not be used concurrently with other drugs that prolong the QT interval. An additive effect on QT interval prolongation between Fareston and the following drugs other medicinal products that may prolong the QTc interval cannot be excluded. This might lead to an increased risk of ventricular arrhythmias, including torsade de pointes. Therefore co-administration of Fareston with any of the following medicinal products is contraindicated: - antiarrhythmics class IA (e.g. quinidine, hydroquinidine, disopyramide) or - antiarrhythmics class III (e.g. amiodarone, sotalol, dofetilide, ibutilide), - neuroleptics (e.g. phenothiazines, pimozide, sertindole,

					haloperidol, sultopride), - certain antimicrobials agents (moxifloxacin, erythromycin IV, pentamidine, antimalarials particularly halofantrine), - certain antihistaminics (terfenadine, astemizol
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/05/2008	n/a	PL	
IA/0030	IA_05_Change in the name and/or address of a manufacturer of the finished product	30/04/2008	n/a	Annex II and PL	
IA/0029	IA_09_Deletion of manufacturing site	31/03/2008	n/a		
IA/0028	IA_23_b_Change in source of excip./reagent to veg./synthetic material - other cases	06/11/2007	n/a		
IB/0027	IB_26_b_Change in the specification of immediate packaging - addition of new test parameter	15/12/2006	n/a		
IB/0026	IB_30_b_Change in supplier of packaging components - replacement/addition	15/12/2006	n/a		
T/0023	Transfer of Marketing Authorisation	02/06/2006	11/07/2006	SmPC, Labelling and PL	The MAH applied for a transfer of the Marketing Authorisation of Fareston from Orion Corporation (old) to Orion Corporation (new).
R/0022	Renewal of the marketing authorisation.	17/11/2005	02/02/2006	SmPC, Annex II, Labelling and PL	
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/03/2005	n/a	PL	

N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/07/2004	n/a	Annex II, Labelling and PL	
IA/0020	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec. IA_13_a_Change in test proc. for active substance - minor change	29/06/2004	n/a		
IA/0018	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	21/06/2004	n/a		
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	20/11/2003	22/12/2003	PL	
I/0016	12_Minor change of manufacturing process of the active substance	19/05/2003	28/05/2003		
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/06/2002	18/07/2002	PL	
I/0014	24_Change in test procedure of active substance	11/07/2001	n/a		
I/0013	24_Change in test procedure of active substance 25_Change in test procedures of the medicinal product	11/07/2001	n/a		
II/0012	Update of or change(s) to the pharmaceutical documentation	29/03/2001	06/04/2001		
II/0010	Update of Summary of Product Characteristics	16/11/2000	20/03/2001	SmPC	
R/0011	Renewal of the marketing authorisation.	25/01/2001	n/a	SmPC, Annex	

				II, Labelling and PL	
I/0009	19_Change in specification of excipients in the medicinal product (excluding adjuvants for vaccines)	14/02/2000	17/05/2000		
N/0008	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/11/1999	20/01/2000	PL	
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/07/1999	07/09/1999	PL	
I/0004	15_Minor changes in manufacture of the medicinal product 01_Change following modification(s) of the manufacturing authorisation(s)	19/04/1999	25/05/1999		
I/0006	14_Change in specifications of active substance	18/05/1999	n/a		
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	19/04/1999	18/06/1999	PL	
II/0003	Update of Summary of Product Characteristics	19/10/1997	11/03/1998	SmPC	
T/0001	Transfer of Marketing Authorisation	14/06/1996	02/10/1996	SmPC, Labelling and PL	
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/08/1996	14/08/1996	PL	