Mozobil

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/0047	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/11/2021		PL	
IA/0046	A.7 - Administrative change - Deletion of manufacturing sites	17/06/2021		Annex II and PL	
N/0045	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/10/2020		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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PSUSA/2451/ 201912	Periodic Safety Update EU Single assessment - plerixafor	04/09/2020	n/a		PRAC Recommendation - maintenance
IA/0044	A.7 - Administrative change - Deletion of manufacturing sites	20/05/2020	n/a		
IA/0042	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	18/02/2020	n/a		
N/0041	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	18/02/2020		PL	
II/0040/G	This was an application for a group of variations. B.I.a.1.c - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions 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.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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	12/12/2019	n/a		

	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 B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue B.I.b.1.h - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition or replacement (excl. Biol. or immunol. substance) of a specification parameter as a result of a safety or quality issue B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting				

	material/intermediate B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate				
IA/0039	A.7 - Administrative change - Deletion of manufacturing sites	14/08/2019	n/a		
II/0034	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	28/03/2019	13/05/2019	SmPC and PL	
IA/0038/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.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	23/01/2019	n/a		
IG/1003	A.1 - Administrative change - Change in the name and/or address of the MAH	20/12/2018	13/05/2019	SmPC, Labelling and PL	
IAIN/0036/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a	11/10/2018	13/05/2019	Annex II and PL	

	manufacturing site for the FP - Secondary packaging site 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/0035	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	21/12/2017	n/a		
II/0032	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/09/2017	19/10/2017	SmPC and PL	Based on the results of study MSC12830 (MOZ11809), the recommended dose of plerixafor by subcutaneous injection (SC) is now according to a weight-based dosing, as follows: • 20 mg fixed dose or 0.24 mg/kg of body weight for patients weighing ≤83 kg (see section 5.2). • 0.24 mg/kg of body weight for patients weighing >83 kg. The results of the study are now detailed in section 5.3. RMP version 9.0 is accepted.
PSUSA/2451/ 201612	Periodic Safety Update EU Single assessment - plerixafor	20/07/2017	18/09/2017	SmPC	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/2451/201612.
II/0030/G	This was an application for a group of variations. Update of section 4.4 of the SmPC in order to reflect the final report from study ARD12858 (MOZ23510) "A pilot, exploratory, randomised, phase 2 safety study evaluating tumour cell (plasma cell)	22/06/2017	18/09/2017	SmPC and PL	Update of section 4.4 of the SmPC in order to reflect the final report from study ARD12858 (MOZ23510) "A pilot, exploratory, randomised, phase 2 safety study evaluating tumour cell (plasma cell) mobilisation and apheresis product contamination in plerixafor plus non-pegylated G-CSF mobilised patients and in non pegylated G-CSF alone

	mobilisation and apheresis product contamination in plerixafor plus non-pegylated G-CSF mobilised patients and in non pegylated G-CSF alone mobilised patients" listed as a category 3 study in the RMP. Submission of the final report from study OBS13611 (MOZ18009), a multicenter, noninterventional registry designed to evaluate the long-term outcomes for patients who received plerixafor for stem cell mobilisation and completed hematopoietic stem cell transplantation (HSCT) compared with patients who received other mobilisation methods and completed HSCT, listed as a category 3 study in the RMP. Submission of the final report from study OBS13612 (MOZ19310), monitoring the plerixafor off-label transplant use, in patients and donors in EBMT centers performing autologous transplants and/or allogeneic transplants, listed as a category 3 study in the RMP. In addition, the MAH took this opportunity to update the local representatives in the Package Leaflet. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission				mobilised patients" listed as a category 3 study in the RMP. Submission of the final report from study OBS13611 (MOZ18009), a multicenter, noninterventional registry designed to evaluate the long-term outcomes for patients who received plerixafor for stem cell mobilisation and completed hematopoietic stem cell transplantation (HSCT) compared with patients who received other mobilisation methods and completed HSCT, listed as a category 3 study in the RMP. Submission of the final report from study OBS13612 (MOZ19310), monitoring the plerixafor off-label transplant use, in patients and donors in EBMT centers performing autologous transplants and/or allogeneic transplants, listed as a category 3 study in the RMP. In addition, the MAH took this opportunity to update the local representatives in the Package Leaflet

	of studies to the competent authority				
IAIN/0033	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	12/06/2017	n/a		
II/0026/G	This was an application for a group of variations. B.II.b.1.d - Replacement or addition of a manufacturing site for the FP - Site which requires an initial or product specific inspection 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	14/01/2016	n/a		
II/0027/G	This was an application for a group of variations. B.II.e.1.a.3 - Change in immediate packaging of the finished product - Qualitative and quantitative composition - Sterile medicinal products and biological/immunological medicinal products B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products B.II.e.4.c - Change in shape or dimensions of the container or closure (immediate packaging) - Sterile medicinal products B.II.e.6.b - Change in any part of the (primary)	17/12/2015	n/a		

	packaging material not in contact with the finished product formulation - Change that does not affect the product information B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier				
IB/0028	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	01/10/2015	n/a		
IA/0029	B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	24/09/2015	n/a		
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/07/2015	02/03/2016	PL	
IA/0024	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	21/05/2015	n/a		
IB/0023	To update section 4.2 of the SmPC as requested by the PRAC/CHMP within LEG024 procedure in order to fulfil a post-authorisation measure resulting from the assessment of PSUR 07 (PSUV/0021). In addition, minor formatting amendments to SmPC and PL have been performed.	24/03/2015	02/03/2016	SmPC and PL	

	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation				
PSUV/0021	Periodic Safety Update	24/07/2014	22/09/2014	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUV/0021.
II/0020	Submission of the final non-clinical study report to address FUM003.4/MEA003.4. The objective of the study was to investigate whether there is a difference in tumour engraftment and progression when injecting rodents with tumour cells which do not express CXCR4 compared with tumour cells expressing CXCR4. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	25/04/2014	n/a		The MAH submitted a study which aim was to investigate whether there was a difference in tumour engraftment and progression when injecting SCID mice with tumour cells which do not express CXCR4 compared with tumour cells expressing CXCR4. Results of this study indicate that expression of CXCR4 on tumour cells may enhance tumour engraftment and thus increase the risk of disease relapse. However, a conclusion on whether the risk of relapse due to contaminating tumour cells is greater following G-CSF + plerixafor when compared to G-CSF mobilisation alone cannot be drawn based on this experiment.
IG/0418	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	11/04/2014	n/a		
R/0019	Renewal of the marketing authorisation.	20/02/2014	11/04/2014	SmPC, Annex II, Labelling and PL	Based on the review of the available information the CHMP is of the opinion that the quality, the safety and the efficacy of Mozobil continues to be adequately and sufficiently demonstrated and considers that the benefit/risk profile of this medicinal product continues to be favourable. The CHMP recommends the renewal of the Marketing Authorisation for Mozobil, subject to the conditions and obligations as laid down in Annex II to the Opinion. The

					CHMP recommends that the renewal be granted with unlimited validity.
IB/0018/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.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol	15/10/2013	n/a		
IA/0017/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.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.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	13/09/2013	n/a		
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/08/2013	11/02/2014	PL	

IG/0283	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/03/2013	n/a		
II/0014	Update of sections 4.4 and 4.8 of the SmPC in order to reflect information regarding post-marketing reports of anaphylactic reactions. The Package Leaflet is updated accordingly. In addition, the MAH deleted a sentence regarding laboratory monitoring which is considered redundant. Furthermore, the MAH proposed this opportunity to bring the PI in line with the latest QRD template version 8.3 and introduce a few minor editorial changes. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/02/2013	11/02/2014	SmPC, Annex II, Labelling and PL	Following a review of the company safety database, 3 spontaneous reports of anaphylactic reaction have been received during the Mozobil post-marketing period of 15 December 2008 through 30 April 2012. Based on the assessment of the cases, a causal relationship with Mozobil could not be excluded. Therefore, section 4.8 of the SmPC have been updated to add anaphylactic reactions, including anaphylactic shock, as new adverse reactions with the frequency 'uncommon' and to include a related warning in section 4.4. The Package leaflet has been updated accordingly.
IB/0013	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	17/12/2012	n/a		
N/0012	Update of the local representatives contact details in the Package Leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/07/2012	11/02/2014	PL	
N/0010	Update in the local representative for Spain in the package leaflet.	25/04/2012	11/02/2014	PL	

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IA/0011/G	This was an application for a group of variations. B.I.c.1.a - Change in immediate packaging of the AS - Qualitative and/or quantitative composition B.I.c.3.b - Change in test procedure for the immediate packaging of the AS - Other changes to a test procedure (including replacement or addition) B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	20/04/2012	n/a		
IG/0122	To update the Detailed Description of the Pharmacovigilance System (DDPS) to version 9, to include a change in the major contractual arrangements. 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	25/11/2011	n/a		
IG/0116	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	28/10/2011	22/12/2011	Annex II	

IA/0007	A.7 - Administrative change - Deletion of manufacturing sites	20/10/2011	n/a		
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/06/2011	n/a	PL	
IA/0005	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	29/03/2011	n/a		
IB/0004	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	14/09/2010	n/a		
IA/0003/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	09/09/2010	n/a		

II/0001	This type II variation concerns an update of section 5.3 of the SmPC to include additional nonclinical safety pharmacology data regarding the effects of plerixafor on receptors other than CXCR4. These data are provided as part of the FUM 002 as agreed by the CHMP at the time of initial marketing auhtorisation. Sections 4.5 and 5.2 of the SmPC are also updated to include in vitro pharmacokinetics data regarding the evaluation of plerixafor for P-glycoprotein substrate or inhibition potential. Furthermore, the MAH submitted an updated RMP to reflect the new available data. Consequently the version number of the RMP (version 2) was updated in Annex II. The MAH also took the opportunity to update the Product Information in line with the latest QRD template. Update of Summary of Product Characteristics	21/01/2010	15/03/2010	SmPC and Annex II	The MAH submitted the results of the general receptor radioligand binding study, the results of a patch clamp study investigating the effect of plerixafor on Ca-channels expressed in mammalian cells and an evaluation of the P-Glycoprotein substrate and inhibition potential of plerixafor using MDCKII-MDR1 cells. The receptor screening shows that plerixafor has moderate or strong binding affinity for a number of different receptors predominantly located on pre-synaptic nerve endings in the CNS and/or the PNS (N-type calcium channel, potassium channel SKCA, histamine H3, acetylcholine muscarinic M1 and M2, adrenergic alpha-1B and alpha-2C, neuropeptide Y/Y1 and glutamate NMDA polyamine receptors). An interaction of plerixafor with one or more of these receptors could be responsible for plerixafor-induced acute toxicity signs observed in animal studies. This information has been added to section 5.3 of the SmPC. The study submitted evaluating P-gp substrate and inhibition potential of plerixafor in well characterized in vitro cell systems shows that plerixafor is not a substrate for the P-gp transporter and does not inhibit this transporter. Based on the results of this study, sections 4.5 and 5.2 of the SmPC were updated. The results of these studies were also taken into account in an updated RMP. Annex II of the product information was also updated to reflect the new version number of the RMP (version 2). Furthermore, the Product Information was updated in line with the latest QRD template.
IA/0002	IA_38_a_Change in test procedure of finished	12/01/2010	n/a		

	product - minor change to approved test procedure				