EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Tractocile

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion/ Notification [1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IAIN/0077	A.1 - Administrative change - Change in the name and/or address of the MAH	30/03/2022		SmPC, Labelling and PL	
N/0076	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/02/2022		Labelling 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/0075	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)	21/12/2021	n/a		
PSUSA/264/202101	Periodic Safety Update EU Single assessment - atosiban	30/09/2021	n/a		PRAC Recommendation - maintenance
IB/0073/G	This was an application for a group of variations. 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.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	08/12/2020	n/a		
IB/0072/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.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	12/12/2018	n/a		

	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.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				
N/0071	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/11/2018		Labelling and PL	
PSUSA/264/201801	Periodic Safety Update EU Single assessment - atosiban	04/10/2018	n/a		PRAC Recommendation - maintenance
IA/0070	B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	28/06/2018	n/a		
IA/0068/G	This was an application for a group of variations. 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 B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant	02/05/2018	n/a		

	specification parameter (e.g. deletion of an obsolete parameter)				
IA/0067	A.7 - Administrative change - Deletion of manufacturing sites	24/04/2017	n/a		
IAIN/0066	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	15/09/2016	n/a		
N/0065	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	23/06/2016	19/12/2016	Labelling	
IA/0064/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	13/01/2016	19/12/2016	Annex II and PL	
PSUSA/264/201501	Periodic Safety Update EU Single assessment - atosiban	08/10/2015	n/a		PRAC Recommendation - maintenance
IB/0062/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 A.4 - Administrative change - Change in the name	28/11/2013	n/a		

	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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
N/0061	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	05/11/2013	09/01/2014	PL	
IAIN/0060	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	19/06/2013	n/a		
II/0059	Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and to update the safety information following the review of respiratory events and lung oedema as requested in the assessment of the latest PSUR. The Package Leaflet was proposed to be updated accordingly.	17/01/2013	09/01/2014	SmPC, Annex II, Labelling and PL	Following assessment of cumulative data on atosiban and comprehensive analysis of all respiratory disorders in which lung edema could be considered as underlying patho-physiological substrate, it was concluded by the CHMP that the concomitant administration of other medicinal products with tocolytic activity and multiple pregnancies are risk

	In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the MAH used this opportunity to bring the PI in line with the latest QRD template version 8.2. 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				factors of pulmonary oedema. Therefore, atosiban should be used with caution in case of multiple pregnancy and/or concomitant administration of other medicinal products with tocolytic activity.
N/0058	Update the contact details for the local representatives for Cyprus in the package leaflet. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	30/08/2012	09/01/2014	PL	
IA/0057	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	01/08/2012	n/a		
IB/0056/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits	24/05/2012	n/a		

	applied during the manufacture of the AS - Other variation B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.c.2.c - Change in the specification parameters and/or limits of the immediate packaging of the AS - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
N/0055	The MAH has amended the list of local representatives in the package leaflet. Also a typographical error in the Dutch translation of the package leaflet was corrected. Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	07/05/2012	09/01/2014	PL	
IA/0054/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 A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used	17/01/2012	n/a		

	in the manufacture of the AS A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test 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 B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised 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.c.2.c - Change in the specification parameters and/or limits of the immediate packaging of the AS - Deletion of a non-significant specification parameter				

	(e.g. deletion of an obsolete parameter) A.7 - Administrative change - Deletion of manufacturing sites				
IB/0053	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)	19/07/2011	n/a	SmPC, Labelling and PL	To extend the shelf life of the finished product from 2 to 4 years. In addition, the Marketing Authorisation Holder is taking the opportunity of introducing changes to Annex I and IIIA as requested during the renewal procedure, of correcting typo mistakes in the Danish, German, Finnish, Hungarian, Icelandic, Italian and Norwegian language versions, and to update the list of local representatives.
IA/0052	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	15/03/2011	n/a	Annex II	
R/0051	Renewal of the marketing authorisation.	22/10/2009	23/12/2009	SmPC, Annex II, Labelling and PL	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the CHMP is of the opinion that the quality, safety and efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considered that that the benefit risk profile of Tractocile continues to be favorable. The CHMP recommends the renewal of the Marketing Authorisation for Tractocile with unlimited validity.
II/0049	Quality changes	24/09/2009	30/09/2009		
IA/0050	IA_05_Change in the name and/or address of a manufacturer of the finished product	19/05/2009	n/a	Annex II and PL	

IA/0048	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	26/11/2008	n/a		
IA/0047	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	26/11/2008	n/a		
IA/0046	IA_09_Deletion of manufacturing site	26/11/2008	n/a		
T/0045	Transfer of Marketing Authorisation	13/10/2008	04/11/2008	SmPC, Labelling and PL	
IB/0044	IB_38_c_Change in test procedure of finished product - other changes	26/03/2008	n/a		
IB/0043	IB_38_c_Change in test procedure of finished product - other changes	26/03/2008	n/a		
IB/0041	IB_33_Minor change in the manufacture of the finished product	29/02/2008	n/a		
IA/0042	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	26/02/2008	n/a		
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/11/2007	n/a	PL	
II/0035	Addition of a manufacturing site for the finished product. Quality changes	18/10/2007	24/10/2007		

N/0034	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/07/2007	n/a	PL	
IB/0036	IB_36_a_Change in shape or dimensions of the container/closure - sterile ph. forms/biologicals	06/06/2007	n/a		
IA/0038	IA_05_Change in the name and/or address of a manufacturer of the finished product	22/05/2007	n/a		
IA/0037	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	22/05/2007	n/a		
N/0033	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/03/2007	n/a	PL	
II/0023	Change(s) to the manufacturing process for the active substance Change(s) to the manufacturing process for the active substance	22/02/2007	27/02/2007		
IA/0032	IA_27_a_Change to test proc. of immediate packaging - minor change to approved test procedure	17/10/2006	n/a		
IA/0031	IA_28_Change in any part of primary packaging material not in contact with finished product	17/10/2006	n/a		
IA/0030	IA_20_a_Change in test procedure for an excipient - minor change to approved test procedure	17/10/2006	n/a		

IA/0029	IA_25_b_02_Change to comply with Ph. - compliance with EU Ph. update - excipient	17/10/2006	n/a		
II/0022	Change(s) to the manufacturing process for the finished product	27/07/2006	18/08/2006		
IA/0020	IA_08_b_01_Change in BR/QC testing - repl./add. manuf. responsible for BR - not incl. BC/testing	15/12/2005	n/a	Annex II and PL	
IA/0019	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	15/12/2005	n/a		
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	17/10/2005	n/a	PL	
IA/0018	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	10/10/2005	n/a		
IA/0016	IA_07_a_Replacement/add. of manufacturing site: Secondary packaging site	01/10/2005	n/a		
R/0013	Renewal of the marketing authorisation.	18/11/2004	31/01/2005	SmPC, Annex II, Labelling and PL	
IA/0015	IA_08_a_Change in BR/QC testing - repl./add. of batch control/testing site	16/12/2004	n/a		
IA/0014	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	06/10/2004	n/a		

IB/0012	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	07/09/2004	n/a		
IB/0010	IB_17_a_Change in re-test period of the active substance	06/09/2004	n/a		
IB/0009	IB_13_b_Change in test proc. for active substance - other changes (replacement/addition)	06/09/2004	n/a		
IA/0011	IA_25_b_01_Change to comply with Ph. - compliance with EU Ph. update - active substance	27/07/2004	n/a		
II/0007	Update of the Summary of Product Characteristics to amend the statement about embryotoxicity and to reflect that no studies on the pre-implantation embryonic phase, but only studies from the time of implantation up to parturition were conducted. In addition the Package Leaflet has been updated to include the local representatives of the new Member States. Update of Summary of Product Characteristics and Package Leaflet	26/02/2004	17/06/2004	SmPC, Labelling and PL	The statement about embryotoxicity in section 4.6 of the SPC have been updated in order to reflect the available evidence. It has also been reflected in sections 4.6 and 5.3 of the SPC that that no studies on the pre-implantation embryonic phase, but only studies from the time of implantation up to parturition were conducted. The Package Leaflet has been updated to include the local representatives of the new Member States.
II/0006	Update of the Summary of Product Characteristics to include information from the results of study PTL096 in order to discourage off-label use of atosiban in women before the 24th week of gestational age. Update of Summary of Product Characteristics	21/11/2002	04/03/2003	SmPC	Further to the evaluation of a detailed analysis of all cases of infant deaths in study PTL-096 included in the 3th PSUR, the CHMP requested that the data of study PTL-096 were added in section 5.1 of the SPC in order to discourage any off-label use of atosiban in women before 24 competed weeks of gestational age.

II/0005	Update of the Summary of Product Characteristics to include new information from drug-drug interaction studies. In addition information on the Pharmacotherapeutic group and ATC code have been included in the Summary of Product Characteristics. Update of Summary of Product Characteristics	27/06/2002	10/09/2002	SmPC	The results of an in vitro study and two in vivo studies evaluating the role of the cytochrome P450 metabolism for atosiban and its potential for interaction with co-administered drugs commonly used in pregnant women including imminent preterm labour patients were submitted. Based on the results of the in vitro study it was concluded that it is highly unlikely that atosiban is involved in the cytochrome P450 mediated drug-drug interactions. The results of the in vivo studies showed no interaction between Tractocile and betamethason and no relevant interaction was observed between Tractocile and labetalol. No interaction studies were performed with antibiotics, ergot alkaloids, and anti-hypertensive agents other than labetalol. Sections 4.5 and 5.2 of the SPC have been updated to reflect this information. Also section 5.1 of the SPC have been updated to include the ATC code.
N/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/06/2001	19/07/2001	PL	
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/01/2001	11/03/2001	PL	
I/0002	15a_Change in IPCs applied during the manufacture of the product	09/08/2000	n/a		
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	31/03/2000	17/05/2000	PL	