



Emadine

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
IA/0060	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	28/06/2024	n/a		
IA/0059	B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	24/04/2024	n/a		

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).



	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
PSUSA/1207/202305	Periodic Safety Update EU Single assessment - emedastine	11/01/2024	n/a		PRAC Recommendation - maintenance
IB/0057	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	31/07/2023	n/a		
IB/0055/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	12/05/2023	n/a		
IAIN/0054/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release A.1 - Administrative change - Change in the name and/or address of the MAH	12/12/2022	24/03/2023	SmPC, Annex II, Labelling and PL	
IAIN/0053/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release B.II.b.2.c.2 - Change to importer, batch release arrangements and quality control testing of the FP -	04/04/2022	24/03/2023	Annex II and PL	

	Including batch control/testing 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				
T/0052	Transfer of Marketing Authorisation	25/06/2021	02/08/2021	SmPC, Labelling and PL	
PSUSA/1207/ 202005	Periodic Safety Update EU Single assessment - emedastine	14/01/2021	n/a		PRAC Recommendation - maintenance
IAIN/0051	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	04/12/2020	n/a		
IB/0049/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.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits 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	23/08/2019	n/a		

	data				
IA/0048/G	<p>This was an application for a group of variations.</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier</p> <p>B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier</p> <p>B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier</p>	23/05/2019	n/a		

IA/0047	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/08/2018	26/08/2019	SmPC, Annex II, Labelling and PL	
T/0046	Transfer of Marketing Authorisation	20/03/2018	23/04/2018	SmPC, Labelling and PL	
PSUSA/1207/201705	Periodic Safety Update EU Single assessment - emedastine	11/01/2018	n/a		PRAC Recommendation - maintenance
T/0044	Transfer of Marketing Authorisation	06/04/2017	16/05/2017	SmPC, Labelling and PL	
IB/0043/G	<p>This was an application for a group of variations.</p> <p>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</p> <p>A.7 - Administrative change - Deletion of manufacturing sites</p> <p>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</p> <p>B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits</p>	30/01/2017	n/a		

	<p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.d.1.a.1 - Stability of AS - Change in the re-test period/storage period - Reduction</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p> <p>B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation</p>				
IA/0042/G	This was an application for a group of variations.	13/05/2016	n/a		

	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.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)				
IA/0041	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	29/03/2016	n/a		
IAIN/0040	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	06/01/2016	04/01/2017	Annex II and PL	
PSUSA/1207/201405	Periodic Safety Update EU Single assessment - emedastine	09/01/2015	n/a		PRAC Recommendation - maintenance
IG/0452	C.1.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	28/07/2014	n/a		
II/0037	Update of sections 2, 4.2, 4.3, 4.6, 4.7, 4.8 and 4.9 of the SmPC following a review of the available	20/03/2014	16/03/2015	SmPC, Annex II, Labelling	The MAH submitted a variation in order to update the sections 2, 4.2, 4.3, 4.6, 4.7, 4.8 and 4.9 of the SmPC

	<p>clinical data and post-marketing experience with the product. The corresponding sections of the Labelling and Package Leaflet have been updated. The product information has also been updated in accordance with the recommendations of the SmPC Guideline and the latest QRD template version 9. Local representatives were updated for the following countries: Denmark, Norway, Slovakia, Iceland, Finland and Sweden.</p> <p>C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data</p>			and PL	<p>following the MAH's review of the available data supporting the safety profile for Emadine eye drops, solution. The review has taken into consideration data from clinical studies and post-marketing experience with the product. As a result of the review the MAH has revised the overall safety profile for Emadine eye drops in section 4.8 of the SmPC the frequency category of five adverse events (headache, eye irritation, dry eye, corneal staining and blurred vision) has been reassigned from Common to Uncommon for consistency with the requirements in the EU SmPC guideline. According to this document ADRs with crude incidence rate between 0.1 to 1% ($\geq 1/1000$ to $< 1/100$) should be assigned to the uncommon frequency category; section 4.6 of the SmPC the following sentence was added 'Studies in animals have shown no evidence of impaired fertility (see Section 5.3). No human fertility data are available.' and for the section 5.3 of the SmPC for which the following sentence was reworded to 'There was no evidence of impaired fertility or decreased reproductive capacity in rats administered orally dosages of Emedastine difumarate up to 30 mg/kg/day.'</p>
IB/0033	B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	24/07/2013	n/a		
IG/0324	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/07/2013	n/a		
N/0035	Update of the local representatives contact details in the Package Leaflet, including addition of a local representative for Croatia.	18/07/2013	05/03/2014	PL	Update of the local representatives contact details in the Package Leaflet, including addition of a local representative for Croatia.

	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)				
IB/0032	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	21/06/2013	n/a		
IG/0274	A.1 - Administrative change - Change in the name and/or address of the MAH	19/03/2013	05/03/2014	SmPC, Labelling and PL	
WS/0075	<p>This was an application for a variation following a worksharing procedure according to Article 20 of Commission Regulation (EC) No 1234/2008.</p> <p>To replace the current resin which is used for the closures for the drop-trainer packaging system, with two new resins.</p> <p>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</p>	20/01/2011	20/01/2011		
N/0027	<p>Update of the local representatives contact details for Czech Republic, Finland, Iceland, and Slovakia. The MAH also took the opportunity to make minor linguistic amendments in annexes III A and B, and updated the Agency's website address to reflect its new name.</p> <p>Minor change in labelling or package leaflet not</p>	30/11/2010	n/a	Labelling and PL	

	connected with the SPC (Art. 61.3 Notification)				
II/0025	to add a new sterility test method to the release and shelf-life specifications for the Emadine single dose container presentations Quality changes	22/07/2010	19/08/2010		
IB/0026	To change the name of the finished product. IB_02_Change in the name of the medicinal product	22/01/2010	n/a	SmPC, Annex II, Labelling and PL	
IA/0024	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	05/02/2009	n/a		
IA/0023	IA_25_b_02_Change to comply with Ph. - compliance with EU Ph. update - excipient	05/02/2009	n/a		
II/0021	The MAH applied for an additional site of manufacture for the active ingredient. Quality changes	22/01/2009	28/01/2009		
R/0018	Renewal of the marketing authorisation.	20/11/2008	13/01/2009	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 this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers that the benefit/risk profile of Emadine continues to be favourable. With this procedure the MAH also updated the product information. This update was based on the requirements in the 2005 Summary of Product Characteristics (SPC)

					Guidelines and QRD requirements. In detail this meant that the current section 4.8 (Undesirable effects) of the SPC, that was based upon 3 long-term studies, was updated to be based on all short-term, intermediate-term and long-term studies. All identified adverse events were therefore recoded into MedDRA preferred terms and the frequency classification for each adverse drug reaction (ADR) was identified. In addition, based on post-marketing adverse event data, the ADR "tachycardia" was included in section 4.8 of the SPC. Based upon the revision to section 4.8 of the SPC, section 4 of the PIL was subsequently updated.
IB/0022	IB_30_b_Change in supplier of packaging components - replacement/addition	04/09/2008	n/a		
IB/0020	IB_25_a_01_Change to comply with Ph. - compliance with EU Ph. - active substance	28/08/2008	n/a		
IB/0019	IB_30_b_Change in supplier of packaging components - replacement/addition	28/08/2008	n/a		
II/0017	Change(s) to the pharmaceutical documentation. Quality changes	15/11/2007	21/11/2007		
N/0016	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/02/2007	n/a	PL	
N/0015	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/11/2004	n/a	PL	
N/0014	Minor change in labelling or package leaflet not	09/07/2004	n/a	PL	

	connected with the SPC (Art. 61.3 Notification)				
R/0013	Renewal of the marketing authorisation.	17/12/2003	05/03/2004	SmPC, Annex II, Labelling and PL	
I/0012	20_Extension of shelf-life as foreseen at time of authorisation	24/07/2003	16/09/2003	SmPC	
II/0011	Update of Summary of Product Characteristics and Package Leaflet	20/02/2003	19/05/2003	SmPC, Labelling and PL	
I/0010	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	20/06/2002	25/06/2002		
X/0009	X-3-iv_Change or addition of a new pharmaceutical form	21/02/2002	30/05/2002	SmPC, Annex II, Labelling and PL	
I/0008	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	04/08/2000	04/08/2000		
I/0007	12_Minor change of manufacturing process of the active substance	04/08/2000	n/a		
I/0006	20a_Extension of shelf-life or retest period of the active substance	04/08/2000	n/a		
I/0005	24_Change in test procedure of active substance	04/08/2000	n/a		
I/0004	24_Change in test procedure of active substance	04/08/2000	n/a		

I/0003	24_Change in test procedure of active substance	04/08/2000	n/a		
I/0002	01_Change in or addition of manufacturing site(s) for part or all of the manufacturing process	24/03/2000	31/05/2000	Annex II and PL	
N/0001	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/02/1999	16/03/1999	Labelling and PL	