EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Altargo

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion / Notification issued on[1]	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
N/0030	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	09/11/2015		PL	
IB/0029	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/06/2015		SmPC, Annex II, Labelling and PL	
II/0027/G	This was an application for a group of variations. This was an application for a group of variations.	20/03/2014	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).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5520
Send a question via our website www.ema.europa.eu/contact

	To add alternate test procedures for reagents used in the manufacture of the active substance. To delete a test procedure for intermediate used in the manufacture of the active substance. To change a test procedure for the intermediate and active substance. To add sites responsible for quality control testing of active substance. To add an alternative site responsible for manufacture and testing of the active substance. 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.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.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				

	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 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 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.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.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier				
IB/0028/G	This was an application for a group of variations. B.I.a.4.c - Change to in-process tests or limits applied	04/12/2013	n/a		

	during the manufacture of the AS - Deletion of a non-significant in-process test B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation B.I.d.1.z - Stability of AS - Change in the re-test period/storage period or storage conditions - Other variation				
IG/0279	A.1 - Administrative change - Change in the name and/or address of the MAH	18/04/2013	27/03/2014	SmPC, Labelling and PL	
IG/0275	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	15/03/2013	n/a		
R/0023	Renewal of the marketing authorisation.	16/02/2012	20/04/2012	SmPC, Annex II, Labelling and PL	During the renewal period no major change to the manufacture of Altargo was implemented. No change in the efficacy of Altargo was observed in clinical trials conducted since initial marketing authorisation. No other new specific safety concern was raised in a number of clinical trials conducted with Altargo. The safety results provided in the PSURs since initial granting of the MAH do not indicate any other new safety signal or new adverse events, which are not covered in section 4.8 of the SmPC. 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 the benefit risk profile of Altargo continues to be favourable. Therefore, CHMP has recommended that the renewal can be granted with unlimited validity. The product information (PI) has been updated with minor changes proposed by the MAH and agreed by the CHMP; updates were also made according to the latest QRD template.
IG/0150/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV 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	05/04/2012	n/a		
IB/0021	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	19/09/2011	n/a		
II/0020	Update of section 5.1 of the Summary of Product Characteristics to include the results of a placebo controlled trial in secondary skin infections, according to FUM 14 and update of section 4.1. of the Summary of Product Characteristics with a cross-reference to section 5.1.	17/03/2011	20/04/2011	SmPC	Following the submission (as a follow-up measure) of the results of an additional study which intended to demonstrate superiority against placebo in the treatment of secondarily infected traumatic

	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				lesions (CIN) and which failed to meet its pre-defined primary endpoint, but showed numerical benefits for retapamulin in some populations and subgroups, the CHMP requested the MAH to submit this variation to update section 5.1 to include a summary of the study results and to update section 4.1 with a cross-reference to section 5.1
II/0019	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	20/01/2011	28/02/2011	SmPC and PL	
IG/0034/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 in the contact details of the QPPV C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the main contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD C.I.9.g - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the site undertaking pharmacovigilance activities C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS	06/01/2011	n/a	Annex II	

	that does not impact on the operation of the pharmacovigilance system 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 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				
II/0018	Update of section 4.4 of the SmPC to include the possible risk of epistaxis when using Altargo intra-nasally as requested by he CHMP after the assessment of PSUR 4th and 5th. Section 3 of the PL was updated accordingly. 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	22/07/2010	01/09/2010	SmPC and PL	Following PSUR 4th and 5th the CHMP requested the MAH to submit a variation to update section 4.4 to include the risk of epistaxis when retapamulin is applied intra-nasally. Conclusions were based on one post-marketing report of epistaxis following intra-nasal use of retapamulin and referred also to a clinical trial in healthy volunteers (ALB110247) where epistaxis occurred more commonly in subjects who received retapamulin compared to placebo. Therefore this type II variation has been submitted to update section 4.4 of the SPC and section 3 of the PIL accordingly. The CHMP agreed that the changes proposed by the MAH in the SPC and PL were appropriate to the risks identified.
II/0016	To update section 5.1 of the SmPC with new information on the mechanism of resistance to retapamulin and the potential for cross resistance with other drugs. The MAH took this opportunity to update contact details of the	18/03/2010	27/04/2010	SmPC	At the time of initial approval of retapamulin in the EU two mechanisms that cause reduced susceptibility to retapamulin in vitro had been identified.

	Slovakian local representative in the PL. Update of Summary of Product Characteristics				More recently, a third mechanism of resistance has been described for retapamulin. This variation has been submitted to update section 5.1 with new information on the mechanism of resistance to retapamulin and also the potential for cross-resistance to occur with drugs in other classes.
II/0012	To update sections 4.5 and 5.2 of the SPC to reflect data from a paediatric pharmacokinetics study, following the assessment of FU2 002.1. Section 2 of the PL was updated accordingly. The MAH took the opportunity to update the contact details of the company representative in Cyprus. Update of Summary of Product Characteristics and Package Leaflet	21/01/2010	17/03/2010	SmPC and PL	The MAH has conducted a paediatric study to assess the pharmacokinetics of topical retapamulin. Results of this study have shown that in children aged from 9 months to 2 years it is possible that higher plasma concentrations may occasionally occur during treatment with retapamulin 1% ointment compared to older children and adults. Therefore caution is advised if retapamulin 1% ointment is administered to children in this age group who are also receiving CYP3A4 inhibitors, as further increase in systemic exposure to retapamulin may occur upon CYP3A4 inhibition.
II/0015	Update of the Detailed Description of the Pharmacovigilance System (DDPS) including change of the Qualified Person for Pharmacovigilance (QPPV). Consequently, Annex II has been updated with the new version number. Update of DDPS (Pharmacovigilance)	17/12/2009	25/01/2010	Annex II	The DDPS has been updated (version 7.2) to reflect the change of the QPPV as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS. The CHMP considers that the Pharmacovigilance System as described by

					the MAH fulfils the requirements.
II/0013	Update of Summary of Product Characteristics and Package Leaflet To update section 4.8 of the SPC to add the adverse reaction "application site irritation (including burning sensation)" folowing CHMP request after assessment of the PSUR. Section 4 of the PL was updated accordingly. Update of Summary of Product Characteristics and Package Leaflet	19/11/2009	21/12/2009	SmPC and PL	The review of 284 reports of application site reactions received since launch showed that in 257 cases patients experienced a burning sensation or burning following application of retapamulin. Taking into account the broad nature of application site reactions, the SPC and the PL were revised to add the term "burning sensation".
IB/0017	IB_33_Minor change in the manufacture of the finished product	10/11/2009	n/a		
IA/0014	IA_32_b_Change in batch size of the finished product - downscaling down to 10-fold	09/09/2009	n/a		
II/0010	Changes to QPPV Update of DDPS (Pharmacovigilance)	19/02/2009	02/04/2009	Annex II	The DDPS has been updated (version 6.2) to reflect the change of the Qualified Person for Pharmacovigilance (QPPV) as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS.
IA/0011	IA_01_Change in the name and/or address of the marketing authorisation holde	12/02/2009	n/a	SmPC, Labelling and PL	
IB/0009	IB_10_Minor change in the manufacturing process of the	06/01/2009	n/a		

	active substance				
IB/0007	IB_11_c_Change in batch size of active substance or intermediate - more than 10-fold	06/01/2009	n/a		
IB/0005	IB_11_c_Change in batch size of active substance or intermediate - more than 10-fold	06/01/2009	n/a		
IA/0008	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	17/12/2008	n/a		
IA/0006	IA_11_a_Change in batch size of active substance or intermediate - up to 10-fold	17/12/2008	n/a		
N/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	28/03/2008	n/a	Labelling	
N/0002	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/11/2007	n/a	Labelling and PL	
IB/0003	IB_33_Minor change in the manufacture of the finished product	08/11/2007	n/a		
IB/0001	IB_10_Minor change in the manufacturing process of the active substance	05/10/2007	n/a		