EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Regranex

Procedural steps taken and scientific information after the authorisation

No	Scope	Opinion/ Notification[1] issued on	Commission Decision Issued[2] / amended on	Product Information affected[3]	Summary
IB/0037/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 active substance- 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 active substance, starting material, reagent or intermediate used in the manufacture of the active substance	11/10/2010	n/a	Annex II	

[1] Notifications are issued for type I variations (unless part of a group or a worksharing application). Opinions are issued for all other procedures.
[2] No Commission Decision is issued for type IA and type IB variations or for type II variations and annual re-assessments that do not affect the annexes.
[3] SPC (Summary of Product Characteristics), Annex II, Labelling, PL (Package Leaflet).

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	Change in the manufacturer of the active substance.				
A20/0033	Article 20 Review	24/06/2010	01/09/2010		
II/0036	12_Minor change of manufacturing process of the active substance Addition of an in-process control (IPC) applied during the manufacture of the active substance.	24/06/2010	30/06/2010		
II/0034	Update of Summary of Product Characteristics, Labelling and Package Leaflet	22/10/2009	20/11/2009	SPC, Labelling, PL	
II/0032	Change(s) to the manufacturing process for the active substance Changes to the manufacturing process for the active substance.	19/03/2009	24/03/2009		
R/0031	Renewal of the Marketing Authorisation	22/01/2009	19/03/2009	SPC, Annex II, Labelling, PL	Based upon the data that have become available since the last renewal, the CHMP considers that the benefit-risk balance of Regranex remains positive, but considers that its safety profile is to be closely monitored for the following reasons: The efficacy of Regranex over the placebo is modest and there are concerns over the possible risk of cancer. More specifically, the CHMP

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					is concerned over the data collected from an extension to the cohort study, investigating the risk of neoplasms both local to the application site and distant. In the CHMP's view, it is unclear whether there is a possibility of an increased risk of cancer from using Regranex. This safety concern should be continuously monitored in the coming years. Further information is expected to be provided by the Marketing Authorisation Holder (MAH), to allow this issue to be evaluated in more depth. Therefore, based upon the safety profile of Regranex the CHMP concluded that the MAH should submit one additional renewal application in 5 years time.
IB/0029	38_b_Change in test procedure of finished product - minor change, biol. active subst./excipient, 31_b_Change to in-process tests/limits during manufacture - addition of new tests/limits	24/07/2008	n/a		
IA/0030	04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	15/07/2008	n/a	Annex II	
IA/0028	04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	10/06/2008	n/a	Annex II	

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N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/12/2007	n/a	PL	
N/0025	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	03/08/2007	n/a	PL	
N/0024	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/08/2006	n/a	PL	
II/0020	Change(s) to the manufacturing process for the active substance	28/06/2006	03/07/2006		
IA/0023	08_a_Change in BR/QC testing - repl./add. of batch control/testing site	22/06/2006	n/a		
IA/0021	31_a_Change to in-process tests/limits during manufacture - tightening of in-process limits	11/04/2006	n/a		
IA/0022	12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	11/04/2006	n/a		
N/0019	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/03/2006	n/a	PL	
II/0018	Update of Summary of Product Characteristics and Package Leaflet	17/11/2005	23/12/2005	SPC, PL	After the evaluation of the 8th Periodic Safety Update Report (PSUR), the CHMP recommended to the MAH that the advice regarding not to

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	This variation relates to an update of the Summary of Product Characteristics (SPC) in order to move a warning regarding infected ulcers from section 4.4 of the SPC to 4.3 (as a contraindication) and to include "osteomyelitis" and "cellulitis" in section 4.8, as requested by the CHMP following the assessment of the 8th PSUR and a clinical study performed as a post-approval commitment. Relevant sections of the Package Leaflet (PL) were updated.				use Regranex in the presence of infection should be included in Section 4.3 of the SPC (as a contraindication) rather than as a special warning under Section 4.4. The MAH conducted an analysis of the ADR reports of infections and a characterisation of the frequency of these reactions. The conclusion was that the proper diagnosis and treatment of lower extremity infections was complicated and a delay in the treatment with antibiotics might result in serious complications. Additionally, as a result of the number of case reports on osteomyelitis and cellulitis received in the PSURs, the CHMP, after the evaluation of the 8th PSUR, requested that "osteomyelitis" and "cellulitis" should be added to Section 4.8 of the SPC in order to supplement and specify the term "infections". The Package Leaflet was also updated to reflect the above.
N/0017	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	13/09/2005	n/a	PL	
II/0015	Change(s) to the test method(s) and/or specifications for the finished product	28/07/2005	10/08/2005		
II/0016	Change(s) to the test method(s) and/or specifications for the active substance	28/07/2005	10/08/2005		
R/0014		21/01/2004	31/03/2004	SPC, Annex II, Labelling, PL	

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	Renewal of the marketing authorisation				
II/0013	Update of or change(s) to the pharmaceutical documentation	25/09/2003	02/10/2003		
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/07/2003	23/07/2003	PL	
II/0011	Change(s) to the test method(s) and/or specifications for the finished product	25/04/2003	02/05/2003		
I/0008	15a_Change in in-process controls applied during the manufacture of the product	16/08/2002	10/09/2002		
I/0010	08_Change in the qualitative composition of immediate packaging material	16/08/2002	10/09/2002		
I/0009	17_Change in specification of the medicinal product	16/08/2002	10/09/2002		
II/0007	Update of Summary of Product Characteristics	25/04/2002	22/08/2002	SPC	
I/0006	20a_Extension of shelf-life or retest period of the active substance	15/02/2002	15/02/2002		
II/0005	Change(s) to the test method(s) and/or specifications for the finished product,	27/06/2001	04/07/2001		

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	Change(s) to the manufacturing process for the active substance				
II/0004	Update of or change(s) to the pharmaceutical documentation	25/01/2001	13/03/2001		