EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Removab

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/0020/G	This was an application for a group of variations. A.1 - Administrative change - Change in the name and/or address of the MAH A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	19/12/2013		SmPC, Annex II, 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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R/0019	Renewal of the marketing authorisation.	24/10/2013	18/12/2013	SmPC, Annex II, Labelling and PL	
II/0016/G	This was an application for a group of variations. Update of section 4.8 of the SmPC to include new information from an integrated safety analysis based on data from study IP-CAT-AC-03, and update of section 5.1 of the SmPC with new clinical information from Studies IP-AT-AC-03 and -04. Additionally, information on liver enzyme increase following the assessment report of PSUR-4 has been reinserted in section 4.8 of the SmPC Furthermore, the MAH proposed this opportunity to bring the PI in line with the latest QRD template version 8 rev 2 and to implement minor editorial changes. The requested group of variations proposed amendments to the SmPC, Annex II, Labelling and Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	13/12/2012	18/12/2013	SmPC, Annex II, Labelling and PL	An updated integrated safety analysis from the clinical study IP-CAT-AC-03 comprised of 728 patients was submitted as part of the current variation. The safety profile was considered comparable to the well-known safety profile of catumaxumab. The efficacy results in terms of puncture-free survival , puncture-free time and overall survival were comparable to the outcome of the pivotal trial. In Study 03, premedication with prednisolone did not improve safety and did not negatively affect efficacy. This information was been included in sections 4.8 and 5.1 of the SmPC respectively. The results of the clinical study IP-CAT-AC-04, were also submitted as part of the current variation. These data demonstrate that despite the presence of anti-drug antibodies, a safety profile comparable in terms of nature but less severe compared to the first i.p. treatment cycle is observed. Furthermore patients benefit in terms of puncture-free survival, puncture-free time and overall survival. This information has been included in section 5.1 of the SmPC. Information on liver enzyme increase following the assessment report of PSUR-4 has been reinserted in section 4.8 of the SmPC.
IB/0017	B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place	12/11/2012	n/a		

IB/0015/G	This was an application for a group of variations. B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes place 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	15/08/2012	n/a		
II/0014	Change in a release and stability specification parameter for drug product. The corresponding specification of the active substance is revised accordingly. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	21/06/2012	21/06/2012		
II/0013/G	This was an application for a group of variations. Relocation of storage site for MCB and WCB and minor changes to no critical parameters. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	19/04/2012	19/04/2012		

	material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IAIN/0012/G	This was an application for a group of variations. C.I.9.a - Changes to an existing pharmacovigilance system as described in the DDPS - Change in 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	18/11/2011	n/a		
II/0011	Change the release and stability specification for a parameter outside the approved specification limit range for the finished product and active substance. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	17/11/2011	17/11/2011		
II/0009	Reduction of infusion time from 6 hours to 3 hours in section 4.2 of the SmPC following the assessment of PSUR 02, substantiated by new additional data. Sections 4.8 undesirable effects and section 6.6 method of administration of the SmPC have also been amended in line with this proposed change. Minor changes to the SmPC following PSUR 2 and PSUR 3 have been included. The Package Leaflet has also been amended in line with the changes proposed to the SmPC The Applicant has also taken the opportunity to	21/07/2011	05/09/2011	SmPC, Annex II and PL	The MAH proposed to reduce the duration of infusion with catumaxomab from 6 to 3 hours, based on pooled data sets from studies investigating both infusion times. Overall, an increased frequency of some adverse reactions was seen in relation to the 3-hour administration, which required an update of the frequency of adverse events in the SmPC. The benefit attributed to a reduced infusion time is reduced time spent at hospital, which was considered acceptable on a case by case basis. In more fragile patients, it was recommended that the 6h option for the first infusion be

	adapt the SmPC in line with the QRD template version 7.3.1. Annex II.B has also been updated with the latest wording as per October 2010 CHMP procedural announcement. 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				used.
II/0010	Update of section 5.1 of the SmPC with new efficacy data on overall survival and benefit of HAMA positive patients, based on the analysis of study IP-REM-AC-01. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	21/07/2011	05/09/2011	SmPC	The MAH proposed to amend section 5.1 of the SmPC with new efficacy data regarding overall survival and benefit from HAMA-positive patients following additional analyses of the pivotal study IP-REM-AC-01. Survival data was therefore reported only according to the ITT principle, without censoring for cross-over in the control arm and only for the FAS. In addition to this, the immunogenicity section was updated to reflect that patients who developed HAMAs 8 days after catumaxomab treatment showed better clinical outcome, as measured by puncture-free survival and Overall Survival, compared with HAMA-negative patients.
IB/0008/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or addition of a site where batch control/testing takes	05/04/2011	n/a		

	place				
IB/0007	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/11/2010	n/a	SmPC and Labelling	Addition of a warning sticker inside the packaging of Removab to ensure intraperitoneal application. Modification of the SmPC, Annex I (section 6.6) and Annex IIIA Labelling to reflect this additional sticker.
IA/0006	B.II.e.3.a - Change in test procedure for the immediate packaging of the finished product - Minor changes to an approved test procedure	13/10/2010	n/a		
IA/0005	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	06/09/2010	n/a		
IA/0002/G	This was an application for a group of variations. B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	19/02/2010	n/a		
IB/0001	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	11/12/2009	n/a	SmPC	