Lemtrada

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
II/0025/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the	18/10/2018	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).

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	change requires an assessment of comparability B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.II.d.2.b - Change in test procedure for the finished product - Deletion of a test procedure if an alternative method is already authorised B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.e.6.b - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that does not affect the product information				
II/0023	Update of section 4.4 of the SmPC to add a new warning on acute acalculous cholecystitis following a cumulative review. The Package Leaflet is updated accordingly. This procedure also included an update of section 4.8 of the SmPC in order to update the table of frequencies of adverse reactions in accordance with the SmPC guideline following a request from the PRAC in procedure EMEA/H/C/PSUSA/00010055/201703. C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation	20/09/2018		SmPC and PL	LEMTRADA may increase the risk of acute acalculous cholecystitis. In controlled clinical studies, 0.2% of LEMTRADA-treated MS patients developed acute acalculous cholecystitis, compared to 0% of patients treated with INFB-1a. During postmarketing use, additional cases of acute acalculous cholecystitis have been reported in LEMTRADA-treated patients. Symptoms of acute acalculous cholecystitis include abdominal pain, abdominal tenderness, fever, nausea, and vomiting. Acute acalculous cholecystitis is a condition that may be associated with high morbidity and mortality rates if not diagnosed early and treated. If acute acalculous cholecystitis is suspected, evaluate and treat promptly.
T/0024	Transfer of Marketing Authorisation	17/07/2018	23/08/2018	SmPC, Labelling and	

				PL	
II/0021/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method B.II.d.1.f - Change in the specification parameters and/or limits of the finished product - Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product	19/07/2018	n/a		
R/0020	Renewal of the marketing authorisation.	26/04/2018	02/07/2018	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Lemtrada in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IB/0022	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	08/05/2018	n/a		
PSUSA/10055 /201709	Periodic Safety Update EU Single assessment - alemtuzumab	12/04/2018	n/a		PRAC Recommendation - maintenance
PSUSA/10055 /201703	Periodic Safety Update EU Single assessment - alemtuzumab	12/10/2017	08/12/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10055/201703.
II/0017	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in	12/10/2017	15/11/2017	SmPC, Annex	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in order

	order to update the safety and long term use information in the posology following final results from study CAMMS03409 - An Extension Protocol For Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab (ongoing at the time of the initial MAA) to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received alemtuzumab during previous company-sponsored studies. The RMP version 3.0 has also been submitted. The PL has been updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to bring the PI in line with the latest QRD template version 10.0 and to introduce editorial corrections in the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data			II, Labelling and PL	to update the safety and long term use information in the posology following final results from study CAMMS03409 - An Extension Protocol For Multiple Sclerosis Patients Who Participated in Genzyme-Sponsored Studies of Alemtuzumab (ongoing at the time of the initial MAA) to evaluate the long term safety and efficacy of alemtuzumab in MS patients who received additional treatment courses of alemtuzumab. The update in the posology includes the option for a third and fourth treatment course with alemtuzumab if needed. If an additional course is administered, safety-follow up should be continued until 48 months after the last infusion. Updated safety information on immune thrombocytopenic Purpura (ITP), thyroid disorders, infusion-associated reactions and infections has been included.
PSUSA/10055 /201609	Periodic Safety Update EU Single assessment - alemtuzumab	06/04/2017	n/a		PRAC Recommendation - maintenance
IB/0016/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	01/03/2017	n/a		

	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
PSUSA/10055 /201603	Periodic Safety Update EU Single assessment - alemtuzumab	29/09/2016	n/a		PRAC Recommendation - maintenance
II/0014	Update of the Risk Management Plan to version 2.0 to include Progressive Multifocal Leucoencephalopathy (PML) as important potential risk, to describe the pharmacovigilance activities associated to PML and to include a standarize case definition for the diagnosis of PML. C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of change(s) which require to be further substantiated by new additional data to be submitted by the MAH where significant assessment is required	15/09/2016	n/a		
PSUSA/10055 /201509	Periodic Safety Update EU Single assessment - alemtuzumab	28/04/2016	21/06/2016	SmPC and PL	Please refer to Lemtrada PSUSA-10055-201509 EPAR: Scientific conclusions and grounds recommending the variation to the terms of the marketing authorisation.
IB/0012	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	10/05/2016	n/a		
PSUSA/10055 /201503	Periodic Safety Update EU Single assessment - alemtuzumab	08/10/2015	n/a		PRAC Recommendation - maintenance

II/0010	B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	24/09/2015	n/a		
PSUSA/10055 /201409	Periodic Safety Update EU Single assessment - alemtuzumab	10/04/2015	n/a		PRAC Recommendation - maintenance
PSUV/0005	Periodic Safety Update	09/10/2014	n/a		PRAC Recommendation - maintenance
IB/0007	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	22/07/2014	n/a		
IB/0006	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	22/07/2014	n/a		
IB/0004	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	28/05/2014	n/a		
IG/0418	C.I.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	11/04/2014	n/a		
IA/0002	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	17/12/2013	15/12/2014	SmPC	

IA/0001	B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer	15/11/2013	n/a		