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
IA/0050	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	10/04/2024		SmPC	
IB/0049	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	04/01/2024		Annex II 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).

N/0046	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	27/10/2023		PL	
PSUSA/10055 /202209	Periodic Safety Update EU Single assessment - alemtuzumab	26/04/2023	07/07/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10055/202209.
IB/0045/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	06/04/2023	n/a		
IB/0043	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	07/09/2022	07/07/2023	SmPC	
II/0041	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	07/07/2022	n/a		
PSUSA/10055 /202109	Periodic Safety Update EU Single assessment - alemtuzumab	22/04/2022	21/06/2022	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10055/202109.

IAIN/0042	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	07/06/2022	07/07/2023	SmPC and PL	
II/0038	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/01/2022	21/06/2022	SmPC and PL	
N/0040	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	22/12/2021	21/06/2022	PL	
IA/0036	A.7 - Administrative change - Deletion of manufacturing sites	27/08/2021	n/a		
IAIN/0035	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	02/08/2021	21/06/2022	SmPC and PL	
PSUSA/10055 /202009	Periodic Safety Update EU Single assessment - alemtuzumab	22/04/2021	21/06/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10055/202009.
IA/0034	A.7 - Administrative change - Deletion of manufacturing sites	26/04/2021	21/06/2022	Annex II and PL	
II/0032	To update sections 4.4 and 4.8 of the SmPC to amend the existing warning and adverse drug reactions on Epstein-Barr virus (EBV) infections and EBV associated hepatitis, following safety evaluation report (SER). The package leaflet is updated accordingly. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	03/09/2020	21/06/2021	SmPC and PL	Not applicable

	data				
II/0031	Submission of an update the RMP (version 7.2) incorporating all amendments and additional activities defined in the Article 20 referral procedure (EMEA/H/A-20/1483/C/3718/0028). 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	09/07/2020	n/a		
PSUSA/10055 /201909	Periodic Safety Update EU Single assessment - alemtuzumab	30/04/2020	03/07/2020	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10055/201909.
II/0029/G	This was an application for a group of variations. 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 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 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.d.2.d - Change in test procedure for the finished	23/01/2020	n/a		

	product - Other changes to a test procedure (including replacement or addition)				
A20/0028	Pursuant to Article 20 of Regulation (EC) No 726/2004, the European Commission requested on 10 April 2019 the opinion of the European Medicines Agency further to new emerging and serious concerns related to fatal cases, cardiovascular adverse events in close temporal association with Lemtrada infusion and immune-mediated diseases. The PRAC was requested to assess the impact thereof on the benefit-risk balance of Lemtrada and to give its recommendation whether the marketing authorisation of this product should be maintained, varied, suspended or revoked.	14/11/2019	16/01/2020	SmPC, Annex II and PL	Please refer to the assessment report: Lemtrada EMEA/H/A-31/1483/C/3718/0028
PSUSA/10055 /201809	Periodic Safety Update EU Single assessment - alemtuzumab	26/04/2019	29/04/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10055/201809.
IAIN/0026	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	22/11/2018	16/01/2020	SmPC and PL	
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	18/10/2018	n/a		

	the finished or intermediate product - The product is a biological/immunological medicinal product and the 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	16/01/2020	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	Periodic Safety Update EU Single assessment -	12/10/2017	08/12/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending

/201703	alemtuzumab				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 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	12/10/2017	15/11/2017	SmPC, Annex II, Labelling and PL	Update of sections 4.2, 4.4, 4.8 and 5.1 of the SmPC in 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 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	01/03/2017	n/a		

	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.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		