Gazyvaro

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
IB/0027	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	21/05/2018	n/a		
II/0023	Update of section 4.8 and 5.1 of the SmPC in order to update the overall survival data based on final results from study BO21004/CLL11 listed as a category 3 study in the RMP; this is the pivotal study that evaluated the efficacy and safety of	17/05/2018		SmPC and PL	Section 4.8 and 5.1 of the SmPC were updated to amend the overall survival data based the final results from a study that evaluated the efficacy and safety of obinutuzumab as therapy for patients with previously

[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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	obinutuzumab as therapy for patients with previously untreated CLL with comorbidities; The RMP version 4.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity format the listing of "other side effects" and correct the term heart attack to heart failure in section 4 of the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				untreated CLL with comorbidities.
PSUSA/10279 /201710	Periodic Safety Update EU Single assessment - obinutuzumab	17/05/2018	n/a		PRAC Recommendation - maintenance
IB/0026/G	This was an application for a group of variations. B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	30/04/2018	n/a		
IB/0025	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	14/04/2018	n/a		
T/0024	Transfer of Marketing Authorisation	15/03/2018	06/04/2018	SmPC, Labelling and PL	

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	20/12/2017	n/a		
PSUSA/10279 /201704	Periodic Safety Update EU Single assessment - obinutuzumab	30/11/2017	n/a		PRAC Recommendation - maintenance
II/0020	Update of section 4.4 of the SmPC to revise the safety information on delayed hypersensitivity reactions based on a review of relevant cases by the Marketing authorisation holder (MAH). In addition, the MAH took the opportunity to introduce editorial changes to the SmPC and package leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	26/10/2017	06/04/2018	SmPC and PL	Hypersensitivity reactions with immediate (e.g. anaphylaxis) and delayed onset (e.g. serum sickness) have been reported in patients treated with Gazyvaro. Hypersensitivity may be difficult to clinically distinguish from infusion related reactions. Hypersensitivity symptoms can occur after previous exposure and very rarely with the first infusion. If a hypersensitivity reaction is suspected during or after an infusion, the infusion must be stopped and treatment permanently discontinued. Patients with known hypersensitivity to obinutuzumab must not be treated.
II/0016	Extension of Indication to include a new indication for Gazyvaro in combination with chemotherapy, followed by Gazyvaro maintenance therapy in patients achieving a response, for the treatment of patients with previously untreated advanced follicular lymphoma; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet and the RMP are updated in accordance. In addition, the due date for provision of the final clinical study report of study BO21223/GALLIUM listed in the Gazyvaro RMP as Category 3 has been updated. Furthermore, the	20/07/2017	18/09/2017	SmPC, Annex II and PL	Please refer to the published Assessment Report Gazyvaro H-2799-II-016.

	Annex II is brought in line with the latest QRD template (version 10). In addition, clarification or editorial changes to the SmPC are proposed for accuracy and clarity. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
PSUSA/10279 /201610	Periodic Safety Update EU Single assessment - obinutuzumab	09/06/2017	n/a		PRAC Recommendation - maintenance
II/0013/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.g.1.a - Introduction of a new design space or extension of an approved design space for the finished product - One or more unit operations in the manuf. process of the FP including the resulting IPCs and/or test procedures	15/12/2016	n/a		
PSUSA/10279 /201604	Periodic Safety Update EU Single assessment - obinutuzumab	01/12/2016	n/a		PRAC Recommendation - maintenance
IB/0015/G	This was an application for a group of variations.	17/11/2016	n/a		

	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				
IB/0017	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	10/11/2016	n/a		
IB/0014	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	20/10/2016	n/a		
IB/0012	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	10/08/2016	n/a		
II/0007	Extension of indication to add the treatment of patients with follicular lymphoma based on the results of the pivotal study GAO4753g. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC have been updated. The Package Leaflet has been updated accordingly. Furthermore, the MAH took the opportunity to make editorial changes to sections 4.4, 4.6, 5.3 and 6.6 of the SmPC.	28/04/2016	13/06/2016	SmPC and PL	Please refer to the scientific discussion for Gazyvaro EMEA/H/C/002799/II/0007

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0010	B.I.a.2.b - Changes in the manufacturing process of the AS - Substantial change to the manufacturing process of the AS which may have a significant impact on the quality, safety or efficacy of the medicinal product	26/05/2016	n/a		
PSUSA/10279 /201510	Periodic Safety Update EU Single assessment - obinutuzumab	13/05/2016	n/a		PRAC Recommendation - maintenance
II/0009	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	01/04/2016	20/05/2016	Annex II and Labelling	
PSUSA/10279 /201504	Periodic Safety Update EU Single assessment - obinutuzumab	06/11/2015	n/a		PRAC Recommendation - maintenance
IB/0005	B.I.b.z - Change in control of the AS - Other variation	22/07/2015	n/a		
IG/0573	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	01/07/2015	n/a		

II/0003	Update of the SmPC sections 4.2 and 4.4 to revise the wording related to tumour lysis syndrome (TLS) in order to emphasize the importance of pre-medication and careful monitoring of patients at risk of TLS. In addition, text relating to batch number has been included in section 4.4 of the SmPC to improve the traceability of biological medicinal products. 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 data	21/05/2015	20/05/2016	SmPC and PL	
PSUSA/10279 /201410	Periodic Safety Update EU Single assessment - obinutuzumab	07/05/2015	n/a		PRAC Recommendation - maintenance
IG/0497	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	18/11/2014	n/a		