Calquence

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/0028	Extension of indication to include CALQUENCE in combination with venetoclax with or without obinutuzumab for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL), based on interim results from study AMPLIFY (D8221C00001); this is a randomised,	25/04/2025	02/06/2025	SmPC and PL	Please refer to Scientific Discussion "Calquence-EMEA/H/C/005299/II/28'

[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).

	multicentre, open-label, phase 3 study of acalabrutinib in combination with venetoclax with and without obinutuzumab compared to investigator's choice of chemoimmunotherapy in subjects with previously untreated CLL without del(17p) or TP53 Mutation. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 8.2 of the RMP was also submitted. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0026	Extension of indication to include CALQUENCE as monotherapy for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy based on final results from study ACE-LY-004 (D8225C00002); this is an open-label, phase 2 study of ACP-196 in subjects with Mantle Cell Lymphoma. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 7.2 of the RMP has also been submitted. In addition, the MAH took the opportunity to introduce minor editorial and formatting changes to the PI. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	27/02/2025	02/05/2025	SmPC and PL	Please refer to Scientific Discussion 'Calquence-EMEA/H/C/005299/II/0026'

II/0025	Extension of indication to include Calquence in combination with bendamustine and rituximab (BR) as treatment of adult patients with previously untreated mantle cell lymphoma (MCL) who are not eligible for autologous stem cell transplant (ASCT) based on interim results from study ACE-LY-308 (ECHO, D8220C00004); this is a Phase III, randomized, double-blind, placebo-controlled, multicenter study of BR alone versus in combination with acalabrutinib (ACP-196) in subjects with previously untreated MCL. As a consequence, sections 4.1, 4.2, 4.4, 4.8, and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 6, succession 2 of the RMP has also been submitted. In addition, the MAH took the opportunity to implement editorial changes to the SmPC. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	27/03/2025	02/05/2025	SmPC and PL	Please refer to Scientific Discussion ‘‘Calquence-EMEA/H/C/005299/II/25’
IB/0027/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.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	31/10/2024	n/a		

	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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation				
IB/0024/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.1.e - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch-release, batch control, primary and secondary packaging, for non-sterile medicinal products	14/06/2024	n/a		
PSUSA/10887 /202310	Periodic Safety Update EU Single assessment - acalabrutinib	16/05/2024	n/a		PRAC Recommendation - maintenance
IB/0023	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	14/05/2024	n/a		
N/0022	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	16/02/2024	02/05/2025	PL	
PSUSA/10887 /202210	Periodic Safety Update EU Single assessment - acalabrutinib	22/06/2023	16/08/2023		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for

					PSUSA/10887/202210.
IB/0019	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	21/06/2023	n/a		
IB/0020	B.II.f.1.b.1 - Stability of FP - Extension of the shelf life of the finished product - As packaged for sale (supported by real time data)	14/06/2023	16/08/2023	SmPC	
IA/0018	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	26/05/2023	n/a		
II/0015	Update of section 5.1 of the SmPC based on the interim report of study ACE-CL-007; a randomized, multicenter, open-Label, 3-arm phase 3 study of obinutuzumab in combination with chlorambucil, ACP-196 in combination with obinutuzumab, and ACP-196 monotherapy in subjects with previously untreated chronic lymphocytic leukemia. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/05/2023	16/08/2023	SmPC	For more information, please refer to the Summary of Product Characteristics.
IAIN/0017	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	03/05/2023	16/08/2023	Annex II and PL	
X/0009/G	This was an application for a group of variations.	15/12/2022	20/02/2023	SmPC,	

	Annex I_2.(d) Change or addition of a new pharmaceutical form A.6 - Administrative change - Change in ATC Code/ATC Vet Code			Labelling and PL	
II/0013	Update of section 5.1 of the SmPC in order to update efficacy and safety information based on final results from study ACE-CL-309 (A Phase 3 randomized open-label active-control study investigating Calquence for the Treatment of Subjects With Relapsed or Refractory Chronic Lymphocytic Leukaemia) listed as a category 3 study in the RMP. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/01/2023	16/08/2023	SmPC	For more information, please refer to the Summary of Product Characteristics.
PSUSA/10887 /202204	Periodic Safety Update EU Single assessment - acalabrutinib	01/12/2022	n/a		PRAC Recommendation - maintenance
PSUSA/10887 /202110	Periodic Safety Update EU Single assessment - acalabrutinib	10/06/2022	n/a		PRAC Recommendation - maintenance
II/0011	Submission of an updated RMP version 3 in order to add hepatotoxicity as an important potential risk to the safety concerns. 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	13/01/2022	n/a		Not applicable.

	by new additional data to be submitted by the MAH where significant assessment is required				
PSUSA/10887 /202104	Periodic Safety Update EU Single assessment - acalabrutinib	02/12/2021	n/a		PRAC Recommendation - maintenance
II/0004	Submission of the final report of the nonclinical Study 20266648 (5336BV) (Acalabrutinib: Neutral Red Uptake Phototoxicity Assay in BALB/c 3T3 Mouse Fibroblasts), in response to the CHMP recommendation to submit results from a modified 3T3 NRU phototoxicity study with adjusted wavelengths. SmPC sections 4.4 and 5.3 were updated accordingly. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	11/11/2021	08/07/2022	SmPC	For more information, please refer to the Summary of Product Characteristics.
IA/0010	A.4 - Administrative change - Change in the name and/or address of a manufacturer or an ASMF holder or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS or manufacturer of a novel excipient	21/10/2021	n/a		
II/0007	Update of section 4.5 of the SmPC following submission of the final report from ACE-HV-114, an open-label, fixed sequence study in healthy subjects to assess the pharmacokinetics of acalabrutinib and its active metabolite, ACP-5862, when administered alone and in combination with moderate CYP3A4 inhibitors fluconazole or isavuconazole.	30/09/2021	08/07/2022	SmPC	Small increases in acalabrutinib maximum concentration (Cmax) and Area Under the Curve (AUC) and decreases of the Cmax and AUC of its active metabolite ACP-5862 were obserevd when acalabrutinib was co-administed with moderate CYP3A inhibitors in helathy subjects. No dose adjustment of acalabrutinib is required when used in combination with moderate CYP3A inhibitors but patients

	In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				should be monitored closely for adverse reactions.
II/0006	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	30/09/2021	n/a		
II/0005	Submission of the final report from study XS-1468 to further characterise the plasma protein binding of acalabrutinib and its metabolite ACP-5862 in different species. Section 5.2 of the SmPC is updated accordingly to reflect the new plasma protein binding data. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	24/06/2021	08/07/2022	SmPC	
IAIN/0003	C.I.11.a - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Implementation of wording agreed by the competent authority	18/02/2021	n/a		
IA/0002	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	07/01/2021	n/a		

IAIN/0001	B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer	21/12/2020	n/a		