# 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 |
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| N/0022 | Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification) | 16/02/2024 | | 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 |

[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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| | | | | | 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.<br><br>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 | |

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| X/0009/G | This was an application for a group of variations.<br><br>Annex I_2.(d) Change or addition of a new pharmaceutical form<br>A.6 - Administrative change - Change in ATC Code/ATC Vet Code | 15/12/2022 | 20/02/2023 | SmPC, 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.<br><br>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.<br><br>C.I.11.b - Introduction of, or change(s) to, the obligations and conditions of a marketing | 13/01/2022 | n/a | | Not applicable. |

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| | 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 | | | | |
| 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.<br><br>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 | 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 |

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| | its active metabolite, ACP-5862, when administered alone and in combination with moderate CYP3A4 inhibitors fluconazole or isavuconazole.<br>In addition, the MAH took the opportunity to bring the PI in line with the latest QRD template version 10.2.<br><br>C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority | | | | moderate CYP3A inhibitors in helathy subjects. No dose adjustment of acalabrutinib is required when used in combination with moderate CYP3A inhibitors but patients 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.<br>Section 5.2 of the SmPC is updated accordingly to reflect the new plasma protein binding data.<br><br>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 | | |

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| 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 | | |