Brukinsa

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
X/0023	Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form	19/06/2025	14/08/2025	SmPC, Labelling and PL	
II/0026/G	This was an application for a group of variations.	27/03/2025	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).

	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 B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier B.I.a.1.g - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Introduction of a new manufacturer of the AS that is not supported by an ASMF and requires significant update to the relevant AS section in the dossier				
PSUSA/10960 /202405	Periodic Safety Update EU Single assessment - zanubrutinib	28/11/2024	n/a		PRAC Recommendation - maintenance
IB/0025	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	18/09/2024	14/08/2025	Annex II	
PSUSA/10960 /202311	Periodic Safety Update EU Single assessment - zanubrutinib	13/06/2024	n/a		PRAC Recommendation - maintenance

IB/0022/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	29/05/2024	n/a		
IB/0021/G	This was an application for a group of variations. B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.z - Quality change - Active substance - Other variation	18/03/2024	n/a		
IA/0019/G	This was an application for a group of variations. B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the originally approved batch size B.II.e.1.b.3 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Deletion of an immediate packaging container without a complete deletion of a strength or pharmaceutical form B.I.b.2.a - Change in test procedure for AS or	04/01/2024	n/a		

	starting material/reagent/intermediate - Minor changes to an approved test procedure				
PSUSA/10960 /202305	Periodic Safety Update EU Single assessment - zanubrutinib	30/11/2023	n/a		PRAC Recommendation - maintenance
II/0014	Extension of indication to include in combination with obinutuzumab treatment of adult patients with relapsed or refractory follicular lymphoma who have received at least two prior systemic treatments for BRUKINSA; based on results from studies BGB-3111-212 and BGB-3111-GA101-001. BGB-3111-212 is an ongoing international, Phase 2, open-label, randomized (2:1), active control study of zanubrutinib plus obinutuzumab (Arm A) versus obinutuzumab monotherapy (Arm B) in patients with R/R FL. The primary efficacy endpoint is overall response rate (ORR); while BGB-3111-GA101-001 is a Phase 1b Study to Assess Safety, Tolerability and Antitumor Activity of the Combination of BGB-3111 with Obinutuzumab in Subjects with B-Cell Lymphoid Malignancies. As a consequence, sections 4.1, 4.4, 4.8 and 5.1 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 5.0 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	12/10/2023	15/11/2023	SmPC and PL	Please refer to Scientific Discussion 'Brukinsa-EMEA/H/C/004978/II/0014'

IAIN/0017	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	28/09/2023	15/11/2023	Annex II and PL	
PSUSA/10960 /202211	Periodic Safety Update EU Single assessment - zanubrutinib	08/06/2023	n/a		PRAC Recommendation - maintenance
II/0013	Update of section 5.1 of the SmPC in order to update efficacy information based on final efficacy results of 'progression-free survival' (PFS) analysis from study BGB-3111-305; this is a Phase III, randomized study of Zanubrutinib compared with Ibrutinib in patients with Relapsed/Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma. In addition, the MAH took the opportunity to update section 4.4 of the SmPC in order to align the wording with the approved Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	25/05/2023	15/11/2023	SmPC	The SmPC is revised based on the results from the final study report from study 305 – at 205 PFS events at an additional 7 months since the final analysis for ORR. As of the data cutoff date (08 August 2022), the median PFS follow-up time was 31.4 months in the zanubrutinib arm and 27.8 months in the ibrutinib arm by investigator, and 32.9 months in the zanubrutinib arm and 28.1 months in the ibrutinib arm by IRC. Updated ORR data were also presented as the final ORR analysis had been performed with a DCO on Dec. 1, 2021: ORR assessed by investigator were 83.5% (95% CI, 79.0, 87.3) for the zanubrutinib arm and 74.2% (95% CI, 69.0, 78.8) for the ibrutinib arm; ORR assessed by ICR were 86.2% (95% CI, 82.0, 89.8) for the zanubrutinib arm and 75.7 % (95% CI, 70.7, 80.3) for the ibrutinib arm. For more information, please refer to the Summary of Product Characteristics.
II/0009	Submission of the final report from study BGB-3111-113 - A Drug-Drug Interaction Study of Zanubrutinib with Moderate and Strong CYP3A Inhibitors in Patients With B-Cell Malignancies, listed as a category 3 study in the RMP.	25/05/2023	15/11/2023	SmPC	SmPC new text The paragraph on Strong CYP3A inhibitors under section 4.5 was amended to reflect that the coadministration of multiple doses of itraconazole (strong CYP3A inhibitor) in healthy volunteers increased the Cmax of zanubrutinib by

	The RMP version 3.0 has also been submitted. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				2.6-fold and AUC by 3.8-fold . The coadministration of multiple doses of strong CYP3A inhibitors voriconazole and clarithromycin in patients with B-cell malignancies resulted in increased zanubrutinib exposures by 3.30-fold and 1.92-fold for dose-normalized AUC0-24h and 3.29-fold and 2.01-fold for dose-normalized Cmax, respectively. Further, in relation to moderate CYP3A inhibitors it was revised to state that he coadministration of multiple doses of moderate CYP3A inhibitors fluconazole and diltiazem in patients with B-cell malignancies resulted in increased zanubrutinib exposures by 1.88-fold and 1.62-fold for dose-normalized AUC0-24h and 1.81-fold and 1.62-fold for dose-normalized Cmax, respectively. For more information, please refer to the Summary of Product Characteristics.
IB/0015/G	This was an application for a group of variations. B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	23/05/2023	n/a		
IB/0012/G	This was an application for a group of variations. B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other	29/03/2023	n/a		

	variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size				
II/0008	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	16/03/2023	n/a		
IB/0010	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	13/02/2023	n/a		
PSUSA/10960 /202205	Periodic Safety Update EU Single assessment - zanubrutinib	15/12/2022	09/02/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10960/202205.
IA/0007/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol 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	15/12/2022	n/a		

	B.II.e.4.a - Change in shape or dimensions of the container or closure (immediate packaging) - Non-sterile medicinal products B.I.a.3.a - Change in batch size (including batch size ranges) of AS or intermediate - Up to 10-fold increase compared to the originally approved batch size 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.II.b.5.c - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of a non-significant in-process test B.II.e.2.c - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IB/0006	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	18/11/2022	n/a		
II/0003	Extension of indication to include treatment of adult patients with chronic lymphocytic leukaemia (CLL) for Brukinsa; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 1.3 of the RMP has also been submitted.	13/10/2022	15/11/2022	SmPC and PL	Please refer to Scientific Discussion 'Brukinsa-EMEA/H/C/004978/II/0003

	The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0002	Extension of indication to include treatment of adult patients with marginal zone lymphoma (MZL) who have received at least one-prior anti-CD20-based therapy, based on data from 88 patients with R/R MZL from 2 ongoing pivotal studies; Study BGB-3111-214: A Phase 2, open-label, single-arm study designed to evaluate the safety and efficacy of zanubrutinib in patients with R/R MZL, and Study BGB-3111-AU-003: A first-in-human, Phase 1/2, dose-escalation and selection, PK/pharmacodynamic, safety, and efficacy study in adult patients with R/R or treatment-naive B-cell malignancies. As a consequence, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated, and the Package Leaflet is updated in accordance. Version 1.1 of the RMP has also been submitted. In addition, the one additional year of market protection requested by the MAH has been granted. The variation leads to amendments to the Summary of Product Characteristics and Package Leaflet and to the Risk Management Plan (RMP). C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or	15/09/2022	28/10/2022	SmPC and PL	Please refer to Scientific Discussion 'Brukinsa-H-C-004978-II-0002'

	modification of an approved one				
IAIN/0004	B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	29/04/2022	28/10/2022	Annex II and PL	
IAIN/0001/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites B.II.b.2.c.1 - Change to importer, batch release arrangements and quality control testing of the FP - Replacement or addition of a manufacturer responsible for importation and/or batch release - Not including batch control/testing	21/12/2021	28/10/2022	Annex II and PL	