Tremfya

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/0043/G	This was an application for a group of variations. Extension application to add a new pharmaceutical form (concentrate for solution for infusion), a new strength (200 mg) and a new route of administration (intravenous use) and to add a new strength of 200 mg for solution for injection (in pre-filled syringe / pre-filled pen) for subcutaneous use in the treatment	27/02/2025	23/04/2025	SmPC, Labelling and PL	Please refer to Scientific Discussion EMEA/H/C/004271/X/0043/G

[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).

	of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy, or a biologic treatment. This application is grouped with a type II variation (C.I.6.a) to include the treatment of adult patients with moderately to severely active ulcerative colitis (UC) who have had an inadequate response, lost response, or were intolerant to either conventional therapy, or a biologic treatment. As a consequence, sections 4.1, 4.2, 4.5, 4.6, 4.8, 5.1, 5.2 and 5.3 of the SmPC of the existing form 100 mg solution for injection are updated. The Package Leaflet and Labelling are updated in accordance. Version 10.4 of the RMP is adopted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet, to align the PI with QRD template version 10.4 and to introduce editorial changes to the PI. Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form Annex I_2.(e) Change or addition of a new route of administration C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one Annex I_2.(c) Change or addition of a new strength/potency				

II/0044	Extension of indication to include treatment of adult patients with moderately to severely active Crohn's disease (CD) who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biologic treatment, based on results from GALAXI Phase 2/3 programme and the GRAVITI Phase 3 study. GALAXI is a Phase 2/3, randomized, double-blind, placebo- and active-controlled, parallel-group, multicenter protocol to evaluate the efficacy and safety of guselkumab in participants with moderately to severely active CD who have demonstrated an inadequate response or failure to tolerate previous conventional or biologic therapy. GRAVITI is a Phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate the efficacy and safety of guselkumab SC induction therapy in participants with moderately to severely active CD. As a consequence, sections 4.1, 4.2, 4.5, 4.8, 4.9, 5.1, and 5.2 of the SmPC are updated. The Package Leaflet is updated in accordance. Version 11.2 of the RMP is agreed. 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 EMEA/H/C/004271/II/0044
PSUSA/10652 /202407	Periodic Safety Update EU Single assessment - guselkumab	13/02/2025	n/a		PRAC Recommendation - maintenance
IB/0047/G	This was an application for a group of variations.	29/01/2025	n/a		

	B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.I.d.1.c - Stability of AS - Change in the re-test period/storage period or storage conditions - Change to an approved stability protocol 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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
IB/0045	B.I.c.1.z - Change in immediate packaging of the AS - Other variation	09/07/2024	n/a		
N/0042	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	21/06/2024	23/04/2025	Labelling and PL	
PSUSA/10652 /202307	Periodic Safety Update EU Single assessment - guselkumab	08/02/2024	n/a		PRAC Recommendation - maintenance
IB/0041/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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.2.c - Change in test procedure for AS or	30/01/2024	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
IA/0040	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	08/11/2023	n/a		
IA/0039/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	08/11/2023	n/a		
IB/0037	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	19/05/2023	n/a		
PSUSA/10652 /202207	Periodic Safety Update EU Single assessment - guselkumab	09/02/2023	n/a		PRAC Recommendation - maintenance
IB/0036/G	This was an application for a group of variations. 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)	07/12/2022	n/a		

	B.II.b.z - Change in manufacture of the Finished Product - Other variation				
II/0034/G	This was an application for a group of variations. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product 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 A.7 - Administrative change - Deletion of manufacturing sites	17/11/2022	n/a		
R/0033	Renewal of the marketing authorisation.	19/05/2022	15/07/2022	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Tremfya in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10652 /202107	Periodic Safety Update EU Single assessment - guselkumab	10/02/2022	n/a		PRAC Recommendation - maintenance
II/0031	C.I.4 Update of sections 4.8 and 5.1 of the SmPC based on the 2-year data from the psoriatic arthritis Phase 3 clinical study CNTO1959PSA3002 and to remove this study as an additional Pharmacovigilance activity from the Risk	13/01/2022	13/04/2022	SmPC	Long-term efficacy and safety data of guselkumab in adult patients with active psoriatic arthritis (PsA) was obtained with the completion of the Phase 3 clinical study CNTO1959PSA3002; a multicenter, randomized, double-blind, placebo-controlled, 3-arm study of guselkumab in

	Management Plan (RMP). The RMP version 8.2 is accepted. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				subjects with active PsA who had inadequate response to standard therapies (e.g., non-biologic DMARDs, apremilast, or NSAIDs). This submission focuses on efficacy and safety data from Week 52 to Week 112. Overall, clinical efficacy assessed across endpoints of signs and symptoms, physical function, and health related quality of life was maintained up to Week 100. The safety profile through Week 100 was consistent with the known safety profile previously described for guselkumab, including the frequency of transaminases increase.
II/0028	Update of sections 4.8 and 5.1 of the SmPC in order to revise the safety and efficacy profile in the EU product information based on 5 years data from the final study reports of pivotal psoriasis studies PSO3001 and PSO3002 listed as additional PV activities (category 3 studies) in the RMP; these are randomized, double-blind, multicenter, placebo- and active comparator-controlled studies through 48 weeks of treatment. In the long-term extension part of these studies subjects received open-label guselkumab q8w, starting at Week 52 in PSO3001 and at Week 76 in PSO3002, with the last dose at Week 252 and the last safety follow-up visit at Week 264. The RMP version 8.1 is accepted. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	30/09/2021	13/04/2022	SmPC and PL	Psoriasis improvement over time (Psoriasis Area and Severity Index [PASI] response and Investigator's Global Assessment [IGA] scores) and patient reported outcomes (Dermatology Life Quality Index [DLQI] and Psoriasis Symptom and Sign Diary [PSSD] scores) demonstrated maintenance of clinical efficacy of guselkumab through 5 years of treatment and were rather consistent between studies PSO3001 and PSO3002. Approximately 5% of patients who developed antidrug antibodies had neutralizing antibodies (0.76% of all treated patients), which was not associated with a reduction of clinical efficacy. The safety profile through 5 years was consistent with the known safety profile previously described for guselkumab. Data from individual and pooled PSO3001 and PSO3002 studies revealed that through 1 year, the frequency of transaminase increases (alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) for the guselkumab q8w dose was similar to that observed for the guselkumab q8w dose in the psoriatic arthritis clinical studies. Through 5 years, the incidence of transaminase elevation did not

					increase by year of guselkumab treatment. Most transaminase increases were ≤ 3 x upper limit of normal. In most cases, the increase in transaminases was transient and did not lead to the discontinuation of treatment. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10652 /202101	Periodic Safety Update EU Single assessment - guselkumab	02/09/2021	n/a		PRAC Recommendation - maintenance
IB/0030/G	This was an application for a group of variations. 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 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.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition) B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier B.I.c.2.c - Change in the specification parameters and/or limits of the immediate packaging of the AS - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	02/08/2021	n/a		
II/0029/G	This was an application for a group of variations.	22/07/2021	n/a		

	B.I.a.4.c - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of a non-significant in-process test B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product				
II/0026	Update of sections 4.8 and 5.1 of the SmPC in order to implement 1-year psoriatic arthritis clinical data from the pivotal Phase 3 studies CNTO1959PSA3001 and CNTO1959PSA3002. In addition, the MAH took the opportunity to make editorial changes to the product information. Furthermore, the MAH updated the list of local representatives. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	11/02/2021	13/04/2022	SmPC and PL	52-week data obtained from Phase 3 psoriatic arthritis (PsA) studies PSA3001 (completed) and PSA3002 (ongoing) show that response to guselkumab treatment was maintained or even increased on all clinical efficacy endpoints (ACR, DAS28-related endpoint, skin and soft tissue-related endpoints, QoL endpoints and joint structure-related endpoints) through Week 52. The safety profile remained consistent when compared with the Week 24 data, in adult patients with active PsA. For more information, please refer to the Summary of Product Characteristics.
II/0025	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	11/02/2021	n/a		
PSUSA/10652 /202007	Periodic Safety Update EU Single assessment - guselkumab	11/02/2021	n/a		PRAC Recommendation - maintenance

II/0017	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	15/10/2020	20/11/2020	SmPC, Annex II and PL	Please refer to Scientific Discussion 'Tremfya-H-C-004271-II-0017'
IB/0023/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.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	23/09/2020	n/a		
PSUSA/10652 /202001	Periodic Safety Update EU Single assessment - guselkumab	03/09/2020	n/a		PRAC Recommendation - maintenance
IB/0022	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	01/09/2020	n/a		
II/0020	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/05/2020	15/09/2020	SmPC and PL	
PSUSA/10652 /201907	Periodic Safety Update EU Single assessment - guselkumab	13/02/2020	n/a		PRAC Recommendation - maintenance

IB/0019	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	03/02/2020	n/a		
IAIN/0018	B.II.e.5.a.1 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change within the range of the currently approved pack sizes	06/12/2019	15/09/2020	SmPC, Labelling and PL	
II/0013	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	19/09/2019	15/09/2020	SmPC	Reports from the literature indicate that the risk of guselkumab transmission by lactation exposure can be considered theoretically very low. Although no specific data on investigation of concentration of guselkumab in breast milk is available, based on this analysis, it justified to remove the safety concern "exposure during lactation" as missing information in the RMP. The section 4.6 of the SmPC is also updated to reflect current scientific knowledge as follows. It is unknown whether guselkumab is excreted in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, and decrease to low concentrations soon afterwards; consequently, a risk to the breast-fed infant during this period cannot be excluded. A decision should be made whether to discontinue, or abstain from initiating treatment with Tremfya, taking into account the benefit of breast-feeding to the child and the benefit of Tremfya therapy to the woman.
II/0015	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	12/09/2019	n/a		
II/0014	C.I.4 - Change(s) in the SPC, Labelling or PL due to	12/09/2019	15/09/2020	SmPC and PL	In study CNTO1959PSO3009, patients were randomised to

	new quality, preclinical, clinical or pharmacovigilance data				receive guselkumab (N=534; 100 mg at Week 0, 4 and q8w thereafter), or secukinumab (N=514; 300 mg at Week 0, 1, 2, 3, 4, and q4w thereafter). The last dose was at week 44 for both treatment groups. Baseline disease characteristics were consistent with a population of moderate to severe plaque psoriasis with a median BSA of 20%, a median PASI score of 18, and an IGA score of severe for 24% of patients. Results showed that guselkumab was superior to secukinumab as measured by the primary endpoint of PASI 90 response at Week 48 (84.5% versus 70.0%, $p < 0.001$). Comparative PASI response rates are presented in tabulated format in the SmPC. The overall incidence of antibodies to guselkumab is consistent with the incidence rates reported in the pivotal guselkumab Phase 3 studies in subjects with psoriasis. The development of antibodies to guselkumab did not affect clinical responses. None of the subjects who were positive for antibodies to guselkumab had ISRs after developing the antibodies to guselkumab. The results of the PSO3009 study support the conclusion that guselkumab is well tolerated at the approved dose regimen of 100 mg, administered SC at Weeks 0, 4, and then q8w, in adult patients with moderate to severe plaque psoriasis. The available data from this study are consistent with the safety profile of guselkumab established to date, and no new safety concerns were identified.
II/0010	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	12/09/2019	15/09/2020	SmPC	The applicant submitted updated safety and efficacy data up to three years data from the 2 Phase-3 studies PSO3001 and PSO3002 submitted for registration. These studies PSO3001 and PSO3002 are currently ongoing and are in

					the open-label treatment phase which started at Week 52 in study PSO3001 and Week 76 in study PSO3002. The data submitted focuses on longer-term efficacy and safety through 3 years (156 weeks) of guselkumab treatment in moderate to severe psoriasis subjects (PSO3001 and PSO3002) as well as retreatment data among those subjects who reinitiated therapy after withdrawal (PSO3002). In PSO3001, for patients receiving continuous guselkumab treatment, the PASI 90 response rate was maintained from Week 52 through Week 156. For patients randomised to adalimumab at Week 0 who crossed over to guselkumab at Week 52, the PASI 90 response rate increased from Week 52 through Week 76 and was then maintained through Week 156. In PSO3002, among 112 patients randomised to adalimumab who failed to achieve a PASI 90 response at Week 28, 66% and 76% achieved a PASI 90 response after 20 and 44 weeks of treatment with guselkumab, respectively. In addition, among 95 patients randomised to guselkumab who failed to achieve a PASI 90 response at Week 28, 36% and 41% achieved a PASI 90 response with an additional 20 and 44 weeks of continued treatment with guselkumab, respectively. Among patients who were withdrawn from treatment and subsequently re-initiated guselkumab, 80% regained a PASI 90 response when assessed 20 weeks after initiation of retreatment. The safety analyses presented showed that guselkumab is well tolerated through 3 years of treatment, and the safety profile remains consistent when compared to Week 48 data, at the approved dose regimen of 100 mg, administered SC at Weeks 0, 4, and then q8w. No new adverse events were identified. Based on the results of the

					studies updates were made to the SmPC section "Selected to the description of selected adverse reactions" for gastroenteritis, injection site reactions and Immunogenicity. Through Week 156, 4.9% of all Tremfya-treated patients reported gastroenteritis. Adverse reactions of gastroenteritis were non serious and did not lead to discontinuation of Tremfya through Week 156. Through Week 156, 0.5% of Tremfya injections were associated with injection site reactions. Adverse reactions of injection site erythema and injection site pain were generally mild to moderate in severity; none were serious, and none led to discontinuation of Tremfya. In the pooled phase III analyses, approximately 9% of patients treated with Tremfya developed antidrug antibodies in up to 156 weeks of treatment. Antidrug antibodies were not associated with lower efficacy or development of injection site reactions.
PSUSA/10652 /201901	Periodic Safety Update EU Single assessment - guselkumab	11/07/2019	n/a		PRAC Recommendation - maintenance
IB/0012	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	24/04/2019	n/a		
II/0009/G	This was an application for a group of variations. B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change	14/03/2019	n/a		

	requires assessment of the comparability of a biological/immunological medicinal product or a new bioequivalence study B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation				
II/0005	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/02/2019	08/07/2019	SmPC and PL	
PSUSA/10652 /201807	Periodic Safety Update EU Single assessment - guselkumab	14/02/2019	n/a		PRAC Recommendation - maintenance
IB/0007	B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	26/11/2018	08/07/2019	SmPC, Labelling and PL	
IB/0008	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	22/11/2018	n/a		
N/0006	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/10/2018	08/07/2019	PL	
PSUSA/10652 /201803	Periodic Safety Update EU Single assessment - guselkumab	04/10/2018	n/a		PRAC Recommendation - maintenance
II/0002/G	This was an application for a group of variations. Update of sections 1, 2, 3, 6.4, 6.5, 6.6, of the	12/07/2018	08/07/2019	SmPC, Labelling and	Data obtained in study PSO3006 demonstrate that the efficacy, pharmacokinetics, and immunogenicity of the identical guselkumab 100 mg prefilled syringe used in the

	SmPC with details of a new presentation: Tremfya 100 mg solution for injection in pre-filled pen, based on the results from study CNTO1959PSO3006; this is study is an open-label, randomized, study to assess the design features of an investigational pre-filled pen (PFS-FID) and the ability of subjects with rheumatoid arthritis or psoriasis to self-administer placebo with the PFS-FID. The Package Leaflet and Labelling are updated accordingly. The RMP version 2.0 has also been submitted. In addition, the Marketing authorisation holder (MAH) took the opportunity to update section 5.1 with the ATC code and to update the list of local representatives in the Package Leaflet. B.IV.1.c - Change of a measuring or administration device - Addition or replacement of a device which is an integrated part of the primary packaging C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data			PL	Phase 3 program, administered using the SelfDose device (prefiled pen), are comparable to that using the UltraSafe Plus (prefilled syringe) device used in the pivotal Phase 3 clinical program to support marketing authorization. Study PSO3006 also demonstrated that guselkumab can be satisfactorily self-administered by patients using the prefilled pen device based on the aggregate usability results and acceptability results from the Self-injection Assessment Questionnaire. The efficacy, safety, PK, and immunogenicity results from study PSO3006 demonstrate that the benefit-risk profile of guselkumab administered using the prefilled pen device is comparable to the established benefit-risk profile using the prefilled syringe device.
IB/0001	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	29/05/2018	n/a		