Skyrizi

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/0053	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	29/01/2025		SmPC and PL	
II/0050	Update of sections 4.8 and 5.1 of the SmPC in order to add information based on data of the final study report M15-997 (LIMMITLESS) listed as a category 3 study in the RMP. This is a multicenter, open label	23/01/2025		SmPC	The following text is updated in SmPC Section 4.8: Immunogenicity • For subjects exposed to long term treatment of risankizumab in the extension study, the immunogenicity

[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).

	study to assess the safety and efficacy of risankizumab for maintenance in moderate to severe plaque type psoriasis. In addition, the MAH took the opportunity to introduce minor editorial changes to the PI. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				profile observed up to 204 weeks of treatment was consistent compared to the first 52 weeks of treatment. The following text is added in SmPC Section 5.1: • Of the patients who received risankizumab in ULTIMMA-1 and ULTIMMA-2, 525 continued to receive risankizumab every 12 weeks in LIMMITLESS. Of these, 376 (71.6%) completed an additional 252 weeks of open-label treatment. Among subjects remaining in the study, improvements achieved with risankizumab in rates of PASI 90 and sPGA of clear or almost clear at week 52 were maintained through week 304. • Of the patients who received ustekinumab in ULTIMMA-1 and ULTIMMA-2, 172 received risankizumab every 12 weeks in LIMMITLESS. Of these, 116 (67.4%) completed the study, including 252 weeks of open-label risankizumab treatment and end of study follow-up. Among subjects remaining in the study, rates of PASI 90 and sPGA response of clear or almost clear increased from week 52 through week 76 and were then maintained through week 304. • Improvements in Dermatology Life Quality Index (DLQI 0 or 1) were maintained in patients receiving continuous risankizumab treatment through wWeek 304 in the open label extension study LIMMITLESS. For more information, please refer to the Summary of Product Characteristics.
PSUSA/10765 /202403	Periodic Safety Update EU Single assessment - risankizumab	14/11/2024	13/01/2025	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10765/202403.
IA/0055	A.7 - Administrative change - Deletion of manufacturing sites	19/12/2024	n/a		

IA/0051	A.7 - Administrative change - Deletion of manufacturing sites	02/10/2024	n/a		
II/0049/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.e.1.z - Change in immediate packaging of the finished product - Other variation 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.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.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.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	05/09/2024	n/a		
X/0043/G	This was an application for a group of variations. Extension application to introduce a new strength of	30/05/2024	24/07/2024	SmPC, Annex II, Labelling	Please refer to the scientific discussion: EMEA/H/C/004759/X/0043/G

	180 mg of risankizumab (solution for injection in cartridge), grouped with a type II variation extension of indication (C.I.6.a) to add a new indication (treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy). As a consequence of the extension of indication, sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3, 6.5 and 6.6 of the SmPC are updated. The Annex II, Labelling and Package Leaflets are updated in accordance. In addition, the marketing authorisation holder has taken the opportunity to update the list of local representatives in the PL. The RMP version 5.3 is adopted. Annex I_2.(c) Change or addition of a new strength/potency C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one			and PL	
II/0046/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.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	18/04/2024	24/07/2024	Annex II and Labelling	Annex II is modified to reflect the inclusion of AbbVie Biotechnology Ltd., Road Number 2, Km 59.2, Barceloneta, Puerto Rico 00617, USA as an alternative site responsible for manufacture of the risankizumab 150 mg/mL active substance. In addition, the MAH took the opportunity to include editorial changes to Annex IIIA (inclusion of information on acceptance of justification regarding Braille).

	the AS -replacement or addition of a site where batch control/testing takes place B.I.a.3.c - Change in batch size (including batch size ranges) of AS or intermediate - The change requires assessment of the comparability of a biological/immunological AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS 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				
IB/0047/G	This was an application for a group of variations. B.I.z - Quality change - Active substance - Other variation B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.f - Change in the batch size (including batch size ranges) of the finished product - The scale for a biological/immunological medicinal product is increased/decreased without process change (e.g. duplication of line)	14/03/2024	24/07/2024	Annex II	
R/0039	Renewal of the marketing authorisation.	09/11/2023	05/01/2024	SmPC and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Skyrizi in the approved indication remains favourable and therefore recommended the renewal of the marketing

					authorisation with unlimited validity.
X/0033	Annex I_2.(c) Change or addition of a new strength/potency	09/11/2023	05/01/2024	SmPC, Annex II, Labelling and PL	
IB/0045	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	30/11/2023	n/a		
PSUSA/10765 /202303	Periodic Safety Update EU Single assessment - risankizumab	26/10/2023	n/a		PRAC Recommendation - maintenance
IAIN/0044	A.z - Administrative change - Other variation	17/10/2023	n/a		
II/0035	Update of sections 4.8 and 5.1 of the SmPC for 150 mg solution for injection in pre-filled pen and pre-filled syringe and 75 mg solution for injection in pre-filled syringe based on final results from study M15-997; this is a is a Phase 3, single-arm, multicenter, open label study to assess the safety and efficacy of risankizumab for maintenance in moderate to severe plaque type psoriasis. In addition, the MAH took the opportunity to implement editorial changes to the SmPC for all strengths / pharmaceutical forms. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	21/09/2023	05/01/2024	SmPC	In study M15-997 (LIMMITLESS), response rates among subjects who completed ULTIMMA-1 and ULTIMMA-2 and continued risankizumab treatment were maintained through week 160, with 88% (460/525) achieving PASI 90 and 88% (462/525) achieving sPGA response of clear or almost clear. For subjects exposed to long term treatment of risankizumab (up to 204 weeks in the extension study), the immunogenicity profile observed was consistent compared to the first 52 weeks of treatment. The safety profile of risankizumab with more than 5 years of exposure was consistent with the profile observed up to 16 weeks. For more information, please refer to the Summary of Product Characteristics.
II/0042	B.II.f.1.c - Stability of FP - Change in storage conditions for biological medicinal products, when the	14/09/2023	05/01/2024	SmPC and PL	Section 6.4 of the SmPC is modified to include optional storage out of the refrigerator (up to a maximum of 25°C)

	stability studies have not been performed in accordance with an approved stability protocol				for up to 24 hours. Package leaflet has been updated accordingly.
IB/0041/G	This was an application for a group of variations. B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product B.II.z - Quality change - Finished product - Other variation	25/08/2023	05/01/2024	SmPC and PL	
IB/0038/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.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	06/07/2023	n/a		
IB/0037	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	16/06/2023	n/a		
IA/0036	A.7 - Administrative change - Deletion of manufacturing sites	16/05/2023	n/a		
IB/0034	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	04/05/2023	n/a		

IB/0031/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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	28/03/2023	n/a		
IB/0030/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.II.d.1.z - Change in the specification parameters and/or limits of the finished product - Other variation	27/02/2023	n/a		
II/0028	Update of section 4.8 of the SmPC in order to add rash and urticaria to the list of adverse drug reactions (ADRs) based on a thorough evaluation of all events of rash and urticaria, including clinical trial and post-marketing data from the global safety database; 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	23/02/2023	05/01/2024	SmPC and PL	Based on the cumulative review of cases of rash and urticaria observed in clinical trial data and reported in post-marketing setting, an association between risankizumab and the adverse effects rash and urticaria is considered a possibility. Therefore rash and urticaria are added as new undesirable effects under section 4.8 of the SmPC with a frequency of "common" and "uncommon" respectively, based on pooled clinical trial and post-marketing data. For more information, please refer to the Summary of Product Characteristics.
IA/0032/G	This was an application for a group of variations.	21/02/2023	n/a		

	B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer B.III.1.b.2 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New certificate for a starting material/reagent/intermediate/or excipient from a new or an already approved manufacturer				
II/0029/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.4.c - Change in the batch size (including batch size ranges) of the finished product - The change requires assessment of the comparability of a biological/immunological medicinal product or a new bioequivalence study	02/02/2023	n/a		
PSUSA/10765/202203	Periodic Safety Update EU Single assessment - risankizumab	10/11/2022	10/01/2023	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10765/202203.
X/0020/G	Extension application to: - introduce a new pharmaceutical form (concentrate for solution for infusion), a new strength (600 mg) and a new route of administration (intravenous use) - add a new strength of 360 mg for risankizumab solution for injection (in cartridge) for subcutaneous	15/09/2022	21/11/2022	SmPC, Labelling and PL	Please refer to Scientific Discussion Skyrizi-H-C-4759-X-20

	use The above new presentations are indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response to, lost response to, or were intolerant to conventional therapy or a biologic therapy. The RMP (version 4.5) is updated in accordance. 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 Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(c) Change or addition of a new strength/potency				
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/08/2022	14/10/2022	PL	
IB/0026	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	01/08/2022	n/a		
IB/0021	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	13/06/2022	n/a		
IB/0023	B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS -	08/06/2022	n/a		

	Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place				
IB/0024/G	This was an application for a group of variations. B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	02/06/2022	n/a		
II/0019/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS 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	03/02/2022	n/a		
II/0014	New therapeutic indication for the treatment of active psoriatic arthritis in adults. Consequently sections 4.1, 4.2, 4.8, 5.1 and 5.2 to the SmPC have been updated. The Package leaflet is updated accordingly. Minor update of Annex II is also introduced.	14/10/2021	15/11/2021	SmPC, Annex II, Labelling and PL	Please refer to Scientific Discussion Skyrizi-H-C-4759-II-14

	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0017/G	This was an application for a group of variations. 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.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 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.c.3.b - Change in test procedure for the immediate packaging of the AS - Other changes to a test procedure (including replacement or addition) 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	28/10/2021	14/10/2022	Annex II	

	the AS -replacement or addition of a site where batch control/testing takes place B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
PSUSA/10765 /202103	Periodic Safety Update EU Single assessment - risankizumab	28/10/2021	n/a		PRAC Recommendation - maintenance
II/0018	B.II.f.1.c - Stability of FP - Change in storage conditions for biological medicinal products, when the stability studies have not been performed in accordance with an approved stability protocol	14/10/2021	15/11/2021	SmPC and PL	
II/0015/G	This was an application for a group of variations. B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation	15/07/2021	n/a		
X/0012	Annex I_2.(c) Change or addition of a new strength/potency	25/03/2021	21/05/2021	SmPC, Annex II, Labelling and PL	
PSUSA/10765 /202009	Periodic Safety Update EU Single assessment - risankizumab	09/04/2021	n/a		PRAC Recommendation - maintenance
PSUSA/10765 /202003	Periodic Safety Update EU Single assessment - risankizumab	29/10/2020	n/a		PRAC Recommendation - maintenance

II/0010/G	This was an application for a group of variations. A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release) 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.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.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	15/10/2020	21/05/2021	Annex II	

	B.I.a.1.j - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Replacement or addition of a site where batch control/testing takes place and any of the test method at the site is a biol/immunol method 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.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.c.1.c - Change in immediate packaging of the AS - Liquid ASs (non sterile) 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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process				
PSUSA/10765 /201909	Periodic Safety Update EU Single assessment - risankizumab	17/04/2020	n/a		PRAC Recommendation - maintenance
II/0008	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	17/04/2020	27/08/2020	SmPC	This variation is based on data previously submitted during the initial marketing authorisation and regarding the IMMhance study (M15-992): Risankizumab versus placebo in a multicenter randomised double-blind study in patients with moderate to severe chronic plaque psoriasis evaluating the efficacy and safety with randomised withdrawal and re-

					treatment. No new clinical data are submitted with this application. The change pertains to the addition of information on retreatment after withdrawal of risankizumab to the summary of the IMMhance clinical study for completeness. The new paragraph introduced is described below: “Among subjects who achieved a static Physician Global Assessment (sPGA) of clear or almost clear at week 28 and relapsed to sPGA of moderate or severe following withdrawal from risankizumab, 83.7% (128/153) regained sPGA of clear or almost clear after 16 weeks of retreatment. Loss of sPGA of clear or almost clear as early as 12 weeks after withdrawal from risankizumab (one missed dose). Of those subjects who were re-randomised to withdraw from treatment, 80.9% (182/225) relapsed and the median time to relapse was 295 days. No characteristics were identified to predict the time to loss of response or likelihood of regaining response at the individual patient level." In addition, a clarification on the duration of the IMMHANCE study after re-randomization is introduced.
N/0007	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	29/01/2020	27/08/2020	PL	
II/0002/G	This was an application for a group of variations. B.I.b.1.f - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Change outside the approved specifications limits range for the AS B.I.b.2.e - Change in test procedure for AS or	12/09/2019	n/a		

	starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
IA/0006	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	30/08/2019	27/08/2020	SmPC	
IB/0003/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.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier 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.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	22/08/2019	n/a		

IB/0005/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.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)	19/08/2019	n/a		
IA/0004	A.5.b - Administrative change - Change in the name and/or address of a manufacturer/importer of the finished product, including quality control sites (excluding manufacturer for batch release)	04/06/2019	n/a		
IA/0001/G	This was an application for a group of variations. 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 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.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	29/05/2019	n/a		