Fasenra

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/0054	Submission of the final report from study D3250R00042 listed as a category 3 study in the RMP. This is a noninterventional, descriptive post authorisation safety study of the incidence of malignancy in severe asthma patients receiving benralizumab and other therapies. The RMP version	13/02/2025	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).

	7.1 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				
II/0052	Extension of indication to include add-on treatment for adult patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis, based results from study D3253C00001 (Mandara); this was a randomised, double-blind, multicentre, parallel group, active-controlled, non-inferiority study that evaluated the efficacy and safety of benralizumab compared with mepolizumab in treatment of patients with EGPA on corticosteroid therapy with or without stable immunosuppressive therapy. 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 6.2 of the RMP has been agreed. In addition, the MAH took this opportunity to introduce editorial changes. The variation leads to amendments to the Summary of Product Characteristics, Package Leaflet and to the RMP. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	19/09/2024	24/10/2024	SmPC and PL	Please refer to Scientific Discussion Fasenra - H/C/4433/II/0052
IB/0053	B.II.b.1.z - Replacement or addition of a manufacturing site for the FP - Other variation	11/07/2024	n/a		

N/0051	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/11/2023	06/06/2024	PL	
II/0049/G	This was an application for a group of variations. Due to the recruitment challenges presented by the MAH, the discontinuation of the Pregnancy Registry Study D3250R00026 and the removal of the subsequent commitment to conduct additional pharmacovigilance activities are accepted. Use in pregnant and lactating women remains as missing information and will continue to be monitored as part of routine pharmacovigilance processes. Considering the cumulative data presented, serious infections are removed from the list of 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 by new additional data to be submitted by the MAH where significant assessment is required 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	28/09/2023	n/a		
II/0047	The results of the paediatric study D3250C00025 (TATE) were submitted. This was an open-label study to evaluate the pharmacokinetics and	20/07/2023	06/06/2024	SmPC	

	pharmacodynamics and long-term safety of benralizumab administered subcutaneously in children ages 6-11 years old with severe eosinophilic asthma. Comparison of the observed paediatric Population PK model to projections from the existing population PK model in adult and adolescent asthma patients treated with benralizumab demonstrated similarity between the two populations. The expected PD effect of near-complete eosinophil depletion was seen in both weight cohorts from the first time point (Week 4) and was maintained throughout the treatment period. The incidence of ADA was consistent with that seen in previous asthma studies with benralizumab. Treatment with benralizumab was generally safe and well tolerated, with no unexpected safety findings, and the safety data were consistent with the known safety profile of benralizumab. TATE was designed as an open-label study, with no control arm, small sample size and therefore uncertainties on the interpretation of results cannot be excluded. Considering the identified study limitations, the submitted results can be considered as preliminary evidence for the pharmacokinetic and pharmacodynamic characteristics of benralizumab for the treatment of paediatric patients with severe eosinophilic asthma. For more information, please refer to the Summary of Product Characteristics. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance				

	data				
IAIN/0050/G	This was an application for a group of variations. A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release 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)	16/06/2023	06/06/2024	Annex II and PL	
PSUSA/10661 /202211	Periodic Safety Update EU Single assessment - benralizumab	08/06/2023	n/a		PRAC Recommendation - maintenance
IA/0048/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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)	22/03/2023	n/a		
IA/0046/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.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	27/02/2023	n/a		

R/0044	Renewal of the marketing authorisation.	21/07/2022	15/09/2022	SmPC, Annex II, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Fasenra in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
PSUSA/10661 /202111	Periodic Safety Update EU Single assessment - benralizumab	10/06/2022	n/a		PRAC Recommendation - maintenance
II/0041	Update of section 5.1 of the SmPC in order to include efficacy information based on the final results from study D3250C00065 (PONENTE); this is a multicenter, open-label, Phase IIIb efficacy and safety study of benralizumab 30 mg administered subcutaneously to reduce oral corticosteroid use in adult patients with severe eosinophilic asthma on high-dose inhaled corticosteroid plus long-acting β2 agonist and chronic oral corticosteroid therapy. 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	19/05/2022	08/08/2022	SmPC and PL	The single arm, open-label study PONENTE (Trial 6), evaluated the efficacy of benralizumab for maintaining asthma control during rapid oral corticosteroid (OCS) tapering in adult patients with severe asthma (blood eosinophil count ≥150 cells/µL at entry or ≥300 cells/µL in the past 12 months if study entry count was <150 cells/µL) who were OCS-dependent. The proportion of patients who eliminated OCS while maintaining asthma control was 62.9%. The proportion of patients who achieved a final OCS dose less or equal to 5 mg while maintaining asthma control and not limited by adrenal function was 81.9%. Effects on OCS reduction were similar irrespective of blood eosinophil count at study entry and maintained over an additional period of 24 to 32 weeks. The annualized exacerbation rate in Trial 6 was comparable to that reported in previous trials. For more information, please refer to the Summary of Product Characteristics.
II/0038/G	This was an application for a group of variations. B.II.b.1.c - Replacement or addition of a manufacturing site for the FP - Site where any	27/01/2022	n/a		

	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 B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site				
II/0040	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	16/12/2021	n/a		
IB/0042	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	09/12/2021	n/a		
II/0039	Update of section 5.1 in order to include information on the maintenance of long-term safety based on the results from study D3250C00037 (MELTEMI) listed as a category 3 study in the RMP. This is a multicenter, open-label safety extension study to evaluate the safety and tolerability of a fixed 30 mg dose of benralizumab in adults with severe asthma. In addition, the MAH took the opportunity to update the	09/12/2021	08/08/2022	SmPC, Annex II and PL	The open-label safety extension study MELTEMI (D3250C00037, Trial 5) aimed to evaluate the long-term safety and efficacy of a fixed-dose of benralizumab administered subcutaneously to severe asthma adult patients on inhaled corticosteroids (ICS)/long-acting β-agonists (LABA) therapy with or without chronic oral corticosteroids and/or other asthma controllers. The annualised asthma exacerbation rate in patients receiving

	list of local representatives in the Package Leaflet and to bring the Product information in line with the latest QRD template version 10.2. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				30 mg benralizumab every 8 weeks spanning a median total follow-up of 3.4 years was comparable (0.47) to that reported in predecessor Trials (0.48 and 0.65). For more information, please refer to the Summary of Product Characteristics.
II/0036	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	30/09/2021	n/a		Update of the list of safety concerns of the Risk Managmenet Plan (RMP) following the finalisation of a category 3 long-term safety and tolerability extension study (D3250C00021, BORA) and an open label safety extension study (MELTEMI). Benralizumab was well tolerated with no unexpected safety findings over the on-treatment and post-treatment periods. As a consequence, the long-term use of benralizumab, serious hypersensibibility, loss/reduction of long-term efficacy due to persistent neutralizing anti-drug antibodies were no longer included in the RMP as safety concerns. Furthermore, the categorisation of helminth infection was changed from important identified risk to important potential risk.
II/0031	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	08/07/2021	08/08/2022	SmPC	
PSUSA/10661 /202011	Periodic Safety Update EU Single assessment - benralizumab	10/06/2021	n/a		PRAC Recommendation - maintenance
IAIN/0035	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	08/04/2021	25/01/2022	Annex II and PL	

IB/0033	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	06/01/2021	n/a		
IB/0032	B.II.f.1.e - Stability of FP - Change to an approved stability protocol	06/01/2021	n/a		
PSUSA/10661 /202005	Periodic Safety Update EU Single assessment - benralizumab	26/11/2020	n/a		PRAC Recommendation - maintenance
II/0029/G	This was an application for a group of variations. B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation B.I.a.4.d - Change to in-process tests or limits applied during the manufacture of the AS - Widening of the approved in-process test limits, which may have a significant effect on the overall quality of the AS	23/07/2020	n/a		
II/0028/G	This was an application for a group of variations. 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.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	16/07/2020	n/a		

	change requires an assessment of comparability				
IB/0027	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	16/07/2020	25/01/2022	PL	
PSUSA/10661 /201911	Periodic Safety Update EU Single assessment - benralizumab	11/06/2020	n/a		PRAC Recommendation - maintenance
II/0025/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 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)	30/01/2020	n/a		
PSUSA/10661 /201905	Periodic Safety Update EU Single assessment - benralizumab	28/11/2019	n/a		PRAC Recommendation - maintenance
IAIN/0024	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	13/11/2019	n/a		

IB/0022	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	24/10/2019	n/a		
IB/0023	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	27/09/2019	n/a		
IB/0020/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 variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	15/08/2019	n/a		
II/0014/G	This was an application for a group of variations. 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	27/06/2019	06/02/2020	SmPC, Labelling and PL	
IA/0019	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	14/06/2019	n/a		

II/0013	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	29/05/2019	06/02/2020	SmPC	
PSUSA/10661 /201811	Periodic Safety Update EU Single assessment - benralizumab	11/04/2019	n/a		PRAC Recommendation - maintenance
IAIN/0018	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	28/03/2019	06/02/2020	Annex II and PL	
II/0017	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	14/03/2019	06/02/2020	SmPC and PL	
IB/0016	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	14/03/2019	n/a		
II/0012	Update of sections 4.5 and 5.2 of the SmPC to reflect the outcome of the ALIZE study: a randomized, double-blind, parallel-group, placebo-controlled study designed to investigate the efficacy, safety, pharmacokinetics, and immunogenicity of a fixed dose of benralizumab (30 mg) administered subcutaneously on the humoral immune response following seasonal influenza virus vaccination in patients 12 to 21 years of age with severe asthma. C.I.4 - Change(s) in the SPC, Labelling or PL due to	14/02/2019	06/02/2020	SmPC	In the randomized, double blind parallel group ALIZE study of 103 patients aged between 12 and 21 years with severe asthma, the humoral antibody responses induced by seasonal influenza virus vaccination do not appear to be affected by benralizumab treatment.

	new quality, preclinical, clinical or pharmacovigilance data				
II/0010	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	24/01/2019	n/a		
II/0008	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	13/12/2018	n/a		
IB/0011	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	12/12/2018	n/a		
PSUSA/10661 /201805	Periodic Safety Update EU Single assessment - benralizumab	29/11/2018	n/a		PRAC Recommendation - maintenance
IB/0009	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	14/11/2018	n/a		
IB/0007	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	10/09/2018	n/a		
IA/0005	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)	03/08/2018	n/a		
IB/0004	B.II.z - Quality change - Finished product - Other variation	30/05/2018	n/a		

IB/0003	B.I.z - Quality change - Active substance - Other variation	24/05/2018	n/a		
IB/0002/G	This was an application for a group of variations. B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	01/03/2018	n/a		
IAIN/0001	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/02/2018	25/02/2019	SmPC	