Nucala

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/0051	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	11/10/2022		SmPC and PL	
II/0048	Submission of an updated RMP version 11 to reflect the proposal to stop the enrolment and to close the pregnancy registry "Mepolizumab Pregnancy	07/07/2022	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).

	Exposure Study 200870: a phase IV, prospective, observational, exposure cohort study of pregnancy outcomes in women (category 3 post authorisation measure in the RMP)" in 2024. The application also includes details of the proposed enhanced data collection for all pregnancies reported as an alternative. 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				
X/0042	Annex I_2.(c) Change or addition of a new strength/potency	24/02/2022	29/04/2022	SmPC, Labelling and PL	
II/0049	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	07/04/2022	n/a		
PSUSA/10456 /202109	Periodic Safety Update EU Single assessment - mepolizumab	07/04/2022	n/a		PRAC Recommendation - maintenance
IB/0046/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	02/12/2021	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				
II/0037	Extension of indication to include hypereosinophilic syndrome (HES) for Nucala (mepolizumab); as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2. In addition, section 6.6 of the SmPC (for the powder for solution for injection only) has been updated to introduce minor clarifications. The Package Leaflet is updated in accordance. Version 7.2. of the RMP has also been adopted. 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	16/09/2021	12/11/2021	SmPC and PL	Please refer to Scientific Discussion Nucala-H-C-3860-II-37
II/0036/G	This was an application for a group of variations. Variation C.1.6.a : Extension of indication to include Eosinophilic Granulomatosis with Polyangiitis (EGPA) to Nucala (mepolizumab); 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 7.2 of the RMP has also been approved.	16/09/2021	12/11/2021	SmPC, Labelling and PL	Please refer to Scientific Discussion Nucala-H-C-3860-II-36-G

	2 Variations type I B.11.e.5.a.2: Addition of a new pack size of 9x100mg/ml multipack for pre-filled pens for Nucala 100 mg/ml solution for injection and another pack size of 9x100mg/ml multipack for pre-filled syringes for Nucala 100 mg/ml solution for injection. As a consequence, sections 6.5 and 8 of SmPC and section 6 of the PL are updated accordingly. Annex IIIA is also being updated to include information relating to the new pack sizes. The group of variations leads to amendments to the Summary of Product Characteristics, Labelling, Package Leaflet and Annex A and to the Risk Management Plan (RMP). 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 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 C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
II/0035	Extension of indication to include Chronic Rhinosinusitis with Nasal Polyps (CRSwNP) for Nucala (mepolizumab). As a consequence of this new indication, sections 4.1, 4.2, 4.8 and 5.1 of the	16/09/2021	12/11/2021	SmPC and PL	Please refer to Scientific Discussion Nucala-H-C-3860-II-35

	SmPC have been updated. The Package Leaflet has been updated accordingly. Editorial changes have also been introduced in section 5.2, 6.1 and in Annex II. Version 7.2 of the RMP has also been adopted. In addition, the Marketing authorisation holder took the opportunity to update local representative information in the package leaflet. The variation leads to amendments to the Summary of Product Characteristics, Annex II 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/0043	B.III.1.b.5 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - New/updated certificate from an already approved/new manufacturer using materials of human/animal origin for which a risk assessment on potential contamination with adventitious agents is required	15/07/2021	n/a		
IB/0045/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.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	16/06/2021	n/a		

	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation				
IB/0044/G	This was an application for a group of variations. B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.e - Stability of FP - Change to an approved stability protocol B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Biological/immunological medicinal product in accordance with an approved stability protocol	15/06/2021	12/11/2021	SmPC and PL	
PSUSA/10456 /202009	Periodic Safety Update EU Single assessment - mepolizumab	09/04/2021	n/a		PRAC Recommendation - maintenance
IA/0041/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites A.7 - Administrative change - Deletion of manufacturing sites	10/02/2021	12/11/2021	Annex II and PL	
IA/0040	A.7 - Administrative change - Deletion of manufacturing sites	08/02/2021	n/a		
II/0038	B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial changes to a manufacturing process that may have a	21/01/2021	n/a		

	significant impact on the quality, safety and efficacy of the medicinal product				
II/0033	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	22/10/2020	n/a		
IB/0034/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.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	05/10/2020	n/a		
R/0031	Renewal of the marketing authorisation.	28/05/2020	10/08/2020	SmPC, Labelling and PL	Based on the review of data on quality, safety and efficacy, the CHMP considered that the benefit-risk balance of Nucala in the approved indication remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
IAIN/0032	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	02/06/2020	n/a		

PSUSA/10456 /201909	Periodic Safety Update EU Single assessment - mepolizumab	17/04/2020	n/a		PRAC Recommendation - maintenance
IAIN/0029	A.1 - Administrative change - Change in the name and/or address of the MAH	12/12/2019	10/08/2020	SmPC, Annex II, Labelling and PL	
N/0027	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/10/2019	10/08/2020	Labelling and PL	
IA/0028	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	10/10/2019	n/a		
II/0026/G	This was an application for a group of variations. B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)	19/09/2019	n/a		

II/0025	B.I.a.2.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological substance which may have a significant impact on the medicinal product and is not related to a protocol	19/09/2019	n/a		
X/0018	Annex I_2.(d) Change or addition of a new pharmaceutical form	29/05/2019	31/07/2019	SmPC, Labelling and PL	
IB/0022/G	This was an application for a group of variations. 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) 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 B.II.b.5.b - Change to in-process tests or limits applied during the manufacture of the finished product - Addition of a new test(s) and limits B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	14/06/2019	n/a		
IB/0024/G	This was an application for a group of variations. B.I.a.1.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other	06/06/2019	n/a		

	variation B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter) B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0021	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	16/05/2019	31/07/2019	SmPC	
II/0023	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP -	26/04/2019	n/a		

	Replacement/addition of a site where batch control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method				
PSUSA/10456 /201809	Periodic Safety Update EU Single assessment - mepolizumab	11/04/2019	n/a		PRAC Recommendation - maintenance
IB/0020	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	01/02/2019	n/a		
PSUSA/10456 /201803	Periodic Safety Update EU Single assessment - mepolizumab	04/10/2018	n/a		PRAC Recommendation - maintenance
IB/0016/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.4.b - Change to in-process tests or limits applied during the manufacture of the AS - Addition of a new in-process test and limits B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	14/09/2018	31/07/2019	Annex II	
II/0013/G	This was an application for a group of variations.	26/07/2018	27/08/2018	SmPC and PL	Nucala is indicated as an add-on treatment for severe refractory eosinophilic asthma in adults, adolescents and

	Type II-C.I.6-Extension of Indication to include children and adolescents aged 6 to 17 years for Nucala; as a consequence, Sections 4.1, 4.2, 4.5, 4.8, 5.1, 5.2 and 6.6 of the SmPC and the Package Leaflet are updated accordingly. In addition, Section 4.4 of the SmPC and package leaflet are updated in order to reflect that the name and batch number of the administered product should be clearly recorded in the patient file. Type IB-B.II.d.2.z- Change to the justification of specifications for the finished product to include a dose dependent calculation in support of the approved specifications. To change the dose dependent controls for raw material clearance and exposure. Type IB B.I.b.2.z –Change to the justification of specifications for the active substance to include a dose dependent calculation in support of the approved specifications. To change the dose dependent controls for raw material clearance and exposure. In addition, editorial changes are introduced in section P.5.5 of Module 3. B.I.b.2.z - Change in test procedure for AS or starting material/reagent/intermediate - Other variation B.II.d.2.z - Change in test procedure for the finished product - Other variation C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				children aged 6 years and older. Adults and adolescents aged 12 years and older: The recommended dose of mepolizumab is 100 mg administered subcutaneously once every 4 weeks. Children aged 6 to 11 years old: The recommended dose of mepolizumab is 40 mg administered subcutaneously once every 4 weeks. The posology of Nucala in children and adolescents aged between 6 to 17 years old with severe refractory eosinophilic asthma has been determined by limited efficacy, pharmacokinetic and pharmacodynamic studies and supported by modelling and simulation data.

IB/0015/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.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure 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)	01/06/2018	27/08/2018	SmPC	
PSUSA/10456 /201709	Periodic Safety Update EU Single assessment - mepolizumab	12/04/2018	n/a		PRAC Recommendation - maintenance
II/0012	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	01/02/2018	n/a		
II/0011	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	25/01/2018	n/a		
PSUSA/10456 /201703	Periodic Safety Update EU Single assessment - mepolizumab	26/10/2017	n/a		PRAC Recommendation - maintenance
II/0007	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	22/06/2017	n/a		

PSUSA/10456 /201609	Periodic Safety Update EU Single assessment - mepolizumab	06/04/2017	n/a		PRAC Recommendation - maintenance
IA/0009/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method 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 B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	17/03/2017	n/a		
IB/0008	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)	28/02/2017	19/02/2018	SmPC	
II/0005	Update of sections 4.4 and 4.8 of the SmPC in order to include "anaphylaxis" as an adverse reaction. The Package Leaflet is updated accordingly. Minor amendments to section 6.6 of the SmPC and to the Instructions for use and handling, reconstitution, and administration for the HCP are also introduced. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives in the Package Leaflet and to bring the PI (Product Information) in line with the latest	27/10/2016	16/02/2017	SmPC, Labelling and PL	

	QRD template version 10. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10456 /201603	Periodic Safety Update EU Single assessment - mepolizumab	29/09/2016	n/a		PRAC Recommendation - maintenance
IB/0004	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	26/08/2016	n/a		
IAIN/0002	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	02/06/2016	n/a		
IA/0001	A.6 - Administrative change - Change in ATC Code/ATC Vet Code	25/02/2016	16/02/2017	SmPC	