Entyvio

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/0081	Update of section 4.6 of the SmPC in order to update information on pregnancy based on final results from study Vedolizumab-5001 (OTIS Entyvio Pregnancy Exposure Registry); this is a non-interventional study to monitor planned and unplanned pregnancies in female patients with ulcerative colitis or Crohn's	07/03/2024		SmPC and PL	In a small prospective observational study the rate of major birth defects was 7.4% in 99 women with ulcerative colitis or Crohn's disease treated with vedolizumab and 5.6% in 76 women with ulcerative colitis or Crohn's disease treated with other biologic agents (adjusted relative risk (RR) 1.07, 95% Confidence Interval (CI): 0.33, 3.52).

[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).

	disease. In addition, the MAH took the opportunity to introduce minor changes and corrections to the PI and bring it in line with the latest QRD template. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
X/0075	Annex I_1.(d) Modification of the vector used to produce the antigen or the source material, including a new master cell bank from a different source	14/12/2023	16/02/2024		Please refer to Scientific Discussion Entyvio-H-C-002782-X/0075
II/0079/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	14/12/2023	n/a		
IB/0080	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	15/11/2023	n/a		
IB/0078/G	This was an application for a group of variations. B.I.a.2.a - Changes in the manufacturing process of	25/07/2023	n/a		

	the AS - Minor change in the manufacturing process of the 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.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS				
II/0073	Submission of the final report from study MLN0002_401 listed as a category 3 study in the RMP in order to fulfil MEA/001.2; this is an international observational prospective cohort study comparing vedolizumab to other biologic agents in patients with ulcerative colitis or Crohn's disease. The RMP version 8.0 has also been submitted. Update of the SmPC sections 4.2, 4.4, 4.8 and Annex II (removal of additional risk minimisation measures based on data from this study. The package leaflet has been updated in accordance. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	06/07/2023	16/02/2024	SmPC, Annex II and PL	Following review of study MLN0002_401 SmPC 4.8 was updated to include Clostridoides diffiicle infection to 4.8 of the SmPC with a frequency "common". Furthermore, frequencies on herpes zoster, infusion site reaction (including: infusion site pain and infusion site irritation), and infusion related reaction, pneumonia and blurred vision were updated in 4.8 of the SmPC. No cases of PML were reported in the study and the study did not suggest an increased risk of malignancies. Patient alert card and Physician's Educational material was removed from Annex II of the MA. The package leaflet was updated in accordance. For more information, please refer to the Summary of Product Characteristics.

IB/0077	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	30/05/2023	n/a		
IB/0076/G	This was an application for a group of variations. C.z - Safety, Efficacy, Pharmacovigilance changes - Other variation 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 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	24/04/2023	16/02/2024	SmPC, Labelling and PL	
IB/0074	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	15/02/2023	n/a		
II/0070/G	This was an application for a group of variations. 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.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The	29/09/2022	17/03/2023	Annex II	The Annex II has been updated as follows: Name and address of the manufacturers of the biological active substance Takeda Pharmaceuticals U.S.A. Inc. 9450 Winnetka Avenue North Minneapolis MN 55445 USA

	change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product 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				
IA/0072	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	07/06/2022	n/a		
IB/0071/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.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 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	02/06/2022	n/a		
IB/0068/G	This was an application for a group of variations.	31/03/2022	n/a		

	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.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 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - 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 B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - 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 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.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
IA/0069	A.7 - Administrative change - Deletion of manufacturing sites	28/03/2022	17/03/2023	Annex II and PL	
IB/0067	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	16/03/2022	n/a		
II/0061	Extension of indication to include treatment of adult patients with moderately to severely active chronic pouchitis, who have undergone proctocolectomy and ileal pouch anal anastomosis for ulcerative colitis, and have had an inadequate response with or lost response to antibiotic therapy for Entyvio; as a consequence, sections 4.1, 4.2, 4.5, 4.8, 5.1 and 5.2 of the SmPC for Entyvio 300 mg are updated. The Package Leaflet is updated accordingly. The RMP is updated to version 7. 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) -	16/12/2021	31/01/2022	SmPC and PL	Please refer to Scientific Discussion Entyvio-H-C-002782-II-0061

	Addition of a new therapeutic indication or modification of an approved one				
IB/0065	B.II.z - Quality change - Finished product - Other variation	06/01/2022	n/a		
II/0063/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.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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the 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.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	09/12/2021	n/a		
IA/0066/G	This was an application for a group of variations. B.II.d.2.a - Change in test procedure for the finished	06/12/2021	n/a		

	product - Minor changes to an approved test procedure 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 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) 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)				
PSUSA/10186 /202105	Periodic Safety Update EU Single assessment - vedolizumab	02/12/2021	n/a		PRAC Recommendation - maintenance
II/0059/G	This was an application for a group of variations. C.I.4 Update of section 4.6 of the Summary of Products Characteristics (SmPC) and the section 2 of the Package Leaflet (PL) in order to implement information on lactation based on study Vedolizumab-4001 (An Open-Label, Multicenter and Open Enrollment Model, Postmarketing, Milk-Only Lactation Study to Assess Concentration of Vedolizumab in Breast Milk of Lactating Women With Active Ulcerative Colitis or Crohn's Disease Who Are	14/10/2021	31/01/2022	SmPC and PL	Study MLN0002-4001(open-label, multicenter and open enrollment model, postmarketing, milk-only lactation study to assess concentration of vedolizumab in breast milk of lactating women with active ulcerative colitis or crohn's disease who are receiving vedolizumab therapeutically) was designed to detect the presence of vedolizumab in breast milk but the effect of this medicine on infants remains unknown. Therefore, the use of vedolizumab in lactating women should continue to take into account the benefit of therapy to the mother and potential risks to the infant. In order to inform Health Care Providers (HCP) when making prescribing decisions, it is proposed to update section 4.6

	Receiving Vedolizumab Therapeutically), including the concentration of vedolizumab in human breast milk and the estimated average daily dose of vedolizumab ingested by the infant. C.I.4 Update of section 5.2 of the SmPC in order to adjust the values for clearance (CL) and serum half-life of vedolizumab IV and SC in subjects with ulcerative colitis and Crohn's disease. The updated pop PK dataset consists of pooled data across 4 phase 3 studies (C13006, C13007, MLN0002SC-3027, MLN0002SC-3031) and 1 open-label extension study (MLN0002SC-3030). The data on intravenous and subcutaneous CL changed from 0.169 L/day to 0.162 L/h and half-life changed from 24 to 26 days. In addition, the MAH took the opportunity to update the local representatives and contacts of Malta and United kingdom in the Package Leaflet, to correct minor typographical errors and to bring the Product Information in line with the latest QRD template version 10.2 rev. 1. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				of the Summary of Products Characteristics (SmPC) and the section 2 of the Package Leaflet (PL) to add the new data obtained from the study MLN0002-4001, including the concentration of vedolizumab in human breast milk and the estimated average daily dose of vedolizumab ingested by the infant. In the mentioned study, the concentration of vedolizumab obtained was approximately 0.4% to 2.2% of the maternal serum concentration obtained from historical studies of vedolizumab. The estimated average daily dose of vedolizumab ingested by the infant was 0.02 mg/kg/day, (which is approximately 21% of the body weight-adjusted average maternal daily dose. New pharmacokinetic data based on intravenous and subcutaneous analyses indicated that the clearance of vedolizumab is approximately 0. 162 L/day (through linear elimination pathway) and the serum half life is 26 days. Taking in consideration this data, the previous values of clearance and half-life in the section 5.2 of the SmPC were updated. In addition, the MAH took the opportunity to update the local representatives and contacts of Malta and United kingdom in the PL, to correct minor typographical errors and to bring the Product Information in line with the latest QRD template version 10.2 rev. 1. For more information, please refer to the Summary of Product Characteristics.

IB/0064	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	23/09/2021	n/a		
IA/0060/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	09/04/2021	n/a		
II/0058	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 significant impact on the quality, safety and efficacy of the medicinal product	25/03/2021	n/a		
PSUSA/10186 /202005	Periodic Safety Update EU Single assessment - vedolizumab	28/01/2021	22/03/2021	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10186/202005.
IB/0057	A.7 - Administrative change - Deletion of manufacturing sites	27/01/2021	n/a		
IB/0056	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	22/12/2020	n/a		
IAIN/0055	A.1 - Administrative change - Change in the name and/or address of the MAH	05/11/2020	22/03/2021	SmPC, Labelling and	

				PL	
IB/0054/G	This was an application for a group of variations. 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 B.II.f.1.e - Stability of FP - Change to an approved stability protocol	25/09/2020	22/03/2021	SmPC	
II/0053	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	04/09/2020	n/a		n/a
II/0050	Update of the RMP with regards to the measures to evaluate effectiveness of additional risk minimization measures (educational material) and addition of the completion date of the interim report for the post approval safety study (PASS) MLN00020401. 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	09/07/2020	n/a		The applicant amended the RMP in order to add a comparison of the cumulative incidence rate of opportunistic infections and PML from the Entyvio PASS study (MLN-0002-401) between the vedolizumab and 'other biologic' treatment arms to the criteria to evaluate effectiveness of additional risk minimisation measures. Furthermore, the RMP the completion date of the interim report for the post approval safety study (PASS) MLN00020401 was added to the RMP.
IB/0051/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor	02/06/2020	n/a		

	changes to an approved test procedure 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				
II/0049	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	28/05/2020	n/a		
X/0040	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	27/02/2020	28/04/2020	SmPC, Annex II, Labelling and PL	
II/0048	B.II.b.2.b - Change to importer, batch release arrangements and quality control testing of the FP - 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	23/04/2020	n/a		
IB/0047	B.II.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	14/02/2020	n/a		
IB/0046	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	12/02/2020	n/a		

IB/0045/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.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	20/12/2019	n/a		
PSUSA/10186 /201905	Periodic Safety Update EU Single assessment - vedolizumab	28/11/2019		SmPC	PRAC Recommendation - maintenance
IB/0042	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	29/07/2019	n/a		
IB/0041	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	02/07/2019	n/a		
II/0039	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	26/04/2019	n/a		
II/0038/G	This was an application for a group of variations.	14/03/2019	n/a		

	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.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				
PSUSA/10186 /201805	Periodic Safety Update EU Single assessment - vedolizumab	13/12/2018	20/02/2019	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10186/201805.
II/0036/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.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.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	13/12/2018	20/02/2019	Annex II	

	starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB B.III.1.b.3 - Submission of a new/updated or deletion of Ph. Eur. TSE Certificate of Suitability - Updated certificate from an already approved manufacturer				
II/0035	Update of sections 4.6 and 5.3 of the SmPC concerning the information on breast-feeding based on findings from published literature. The Package Leaflet is updated accordingly. In addition, section 4.2 was updated for consistency amongst both approved indications with regards to discontinuing treatment when no therapeutic benefit is observed. Section 4.4 is updated to remove that no cases of PML were reported in clinical trials. Editorial changes were also made in sections 4.4 and 5.1 of the SmPC. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	13/12/2018	20/02/2019	SmPC and PL	Vedolizumab has been detected in human milk. The effect of vedolizumab on infants is unknown. The use of vedolizumab in lactating women should take into account the benefit of therapy to the mother and potential risks to the infant. For consistency and clarity purposes amongst both approved indications of ulcerative colitis and Crohn's disease wordings were aligned with regards to discontinuing vedolizumab treatment when no therapeutic benefit is observed. A single case of progressive multifocal leukoencephalopathy (PML) was reported in post-marketing in a patient treated with vedolizumab with no causal relationship established with vedolizumab. In order to minimise possible misleading interpretation the CHMP agreed on the removal of the statement indicating that no cases of PML were reported in clinical studies of vedolizumab.
R/0032	Renewal of the marketing authorisation.	18/10/2018	12/12/2018	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 Entyvio in the approved indications remains favourable and therefore recommended the renewal of the marketing authorisation with unlimited validity.
II/0037	B.II.b.2.b - Change to importer, batch release	29/11/2018	n/a		

	arrangements and quality control testing of the FP - 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				
II/0034	Please refer to the Recommendations section above. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	29/11/2018	20/02/2019	SmPC	Final results from study C13008 showed that the benefits of vedolizumab treatment, as assessed by partial Mayo score, clinical remission, and clinical response were shown for up to 196 weeks. Immunogenicity data showed that during vedolizumab treatment antibodies to vedolizumab may develop, most of which are neutralising. The formation of anti-vedolizumab antibodies is associated with increased clearance of vedolizumab and lower rates of clinical remission. Infusion related reactions after vedolizumab infusion are reported in subjects with anti-vedolizumab antibodies.
II/0029	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	25/10/2018	n/a		
PSUSA/10186 /201711	Periodic Safety Update EU Single assessment - vedolizumab	28/06/2018	23/08/2018		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10186/201711.
IB/0030	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the	26/05/2018	23/08/2018	SmPC and PL	

	diluted/reconstituted product				
IB/0031	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	23/04/2018	n/a		
IB/0027/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.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.z - Change in the specification parameters and/or limits of the finished product - Other variation	14/02/2018	n/a		
PSUSA/10186 /201705	Periodic Safety Update EU Single assessment - vedolizumab	14/12/2017	09/02/2018		Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10186/201705.
N/0026	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/09/2017	09/02/2018	Labelling and PL	
PSUSA/10186 /201611	Periodic Safety Update EU Single assessment - vedolizumab	09/06/2017	n/a		PRAC Recommendation - maintenance
IB/0024/G	This was an application for a group of variations. B.I.b.2.a - Change in test procedure for AS or	24/04/2017	n/a		

	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 B.II.d.2.e - Change in test procedure for the finished product - Update of the test procedure to comply with the updated general monograph in the Ph. Eur.				
IB/0023	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	14/03/2017	n/a		
IB/0020/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	06/02/2017	n/a		
N/0021	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	08/12/2016	09/02/2018	PL	
PSUSA/10186 /201605	Periodic Safety Update EU Single assessment - vedolizumab	01/12/2016	n/a		PRAC Recommendation - maintenance
IAIN/0019	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	14/11/2016	19/12/2016	Annex II and PL	

IB/0018	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	08/11/2016	n/a		
II/0016/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.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.5.d - Change to in-process tests or limits applied during the manufacture of the finished product - Deletion of an in-process test which may have a significant effect on the overall quality of the finished product B.II.b.5.e - Change to in-process tests or limits applied during the manufacture of the finished product - Widening of the approved IPC limits, which may have a significant effect on overall quality of the finished product	21/07/2016	n/a		
PSUSA/10186 /201511	Periodic Safety Update EU Single assessment - vedolizumab	09/06/2016	n/a		PRAC Recommendation - maintenance
II/0012/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	12/05/2016	19/12/2016	Annex II	

	material [-] used in the manufacture of a biological/immunological product 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.2.z - Changes in the manufacturing process of the AS - Other variation 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.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.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.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation				
IB/0015	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	06/04/2016	n/a		
N/0014	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	04/04/2016	19/12/2016	PL	

IB/0013/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.g.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	22/03/2016	n/a		
IG/0652	C.I.8.a - Introduction of or changes to a summary of Pharmacovigilance system - Changes in QPPV (including contact details) and/or changes in the PSMF location	22/01/2016	n/a		
IAIN/0009	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	14/12/2015	19/12/2016	Annex II and PL	
II/0008	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	03/12/2015	n/a		
PSUSA/10186 /201505	Periodic Safety Update EU Single assessment - vedolizumab	03/12/2015	n/a		PRAC Recommendation - maintenance
IB/0007	B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	02/10/2015	n/a		

PSUSA/10186 /201411	Periodic Safety Update EU Single assessment - vedolizumab	25/06/2015	20/08/2015	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10186/201411.
N/0005	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	10/07/2015	19/12/2016	PL	
IAIN/0003	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	22/04/2015	n/a		
N/0004	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	15/04/2015	20/08/2015	PL	
IA/0001	A.7 - Administrative change - Deletion of manufacturing sites	19/01/2015	n/a		