Stelara

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/0059/G	This was an application for a group of variations. B.II.z - Quality change - Finished product - Other variation B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	09/12/2017		SmPC and PL	

[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).

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II/0058	Update of section 4.8 of the SmPC in order to include Lower Respiratory Tract Infection as an Adverse Drug Reaction based on a comprehensive evaluation of safety information from the STELARA clinical studies database and post-marketing database, as well as available literature. 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	14/09/2017		SmPC and PL	Update of section 4.8 of the SmPC in order to include Lower Respiratory Tract Infection as an Adverse Drug Reaction based on a evaluation of safety information from the ustekinumab clinical studies database and post-marketing database, as well as available literature. The Package Leaflet has been updated accordingly to prompt patients or carers to inform the doctor straight away if signs of infection. These may be signs of infections such as chest infections, or skin infections or shingles that could have serious complications
PSUSA/3085/ 201612	Periodic Safety Update EU Single assessment - ustekinumab	06/07/2017	n/a		PRAC Recommendation - maintenance
IA/0057	B.III.2.a.2 - Change of specification(s) of a former non EU Pharmacopoeial substance to fully comply with the Ph. Eur. or with a national pharmacopoeia of a Member State - Excipient/AS starting material	03/05/2017	n/a		
IA/0056/G	This was an application for a group of variations. B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	30/03/2017	n/a		
IB/0054	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	30/03/2017		SmPC	

	stability protocol				
IA/0053/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 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)	24/02/2017		Annex II	
IA/0052	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	08/02/2017	n/a		
II/0051/G	This was an application for a group of variations. B.II.b.3.c - Change in the manufacturing process of the finished or intermediate product - The product is a biological/immunological medicinal product and the change requires an assessment of comparability B.II.b.4.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)	24/11/2016	n/a		
X/0049/G	This was an application for a group of variations.	15/09/2016	11/11/2016	SmPC, Labelling and	

	Annex I_2.(c) Change or addition of a new strength/potency Annex I_2.(d) Change or addition of a new pharmaceutical form Annex I_2.(e) Change or addition of a new route of administration C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one			PL	
PSUSA/3085/ 201512	Periodic Safety Update EU Single assessment - ustekinumab	07/07/2016	n/a		PRAC Recommendation - maintenance
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	07/07/2016	n/a		
IA/0047/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.II.b.5.a - Change to in-process tests or limits applied during the manufacture of the finished product - Tightening of in-process limits	28/07/2015	15/07/2016	Annex II	

PSUSA/3085/ 201412	Periodic Safety Update EU Single assessment - ustekinumab	09/07/2015	n/a		PRAC Recommendation - maintenance
II/0042	Extension of Indication to add treatment of moderate to severe plaque psoriasis in paediatric patients from the age of 12 years and older, who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies. As a consequence SmPC sections 4.1, 4.2, 4.8, 5.1, 5.2, 6.1 and 6.6 have been updated and the Package Leaflet has been updated accordingly. A revised RMP version 12.1 was agreed during the procedure. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	21/05/2015	22/06/2015	SmPC and PL	Please refer to the Scientific Discussion 'Stelara-H-C-958-II-42'.
IG/0531	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	05/03/2015	n/a		
II/0044/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.II.d.2.c - Change in test procedure for the finished product - Substantial change to or replacement of a biol/immunol/immunochemical test method or a	26/02/2015	n/a		

	method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol				
II/0041	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/10/2014	21/11/2014	SmPC and PL	
IA/0043/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 A.7 - Administrative change - Deletion of manufacturing sites 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.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	30/10/2014	22/06/2015	Annex II	
PSUV/0040	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
II/0036	Update to section 5.1 of the SmPC with data showing that ustekinumab reduces the rate of progression of peripheral joint damage. The package leaflet has been updated accordingly. Section 4.8 of the SmPC has been updated with data from the phase 3 studies of ustekinumab in psoriatic arthritis (PsA).	20/03/2014	21/11/2014	SmPC and PL	Please refer to the scientific discussion Stelara EMEA/H/C/000958/II/0036 for further information.

	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
II/0037	Extension of indication to include the treatment of moderate to severe plaque psoriasis in adults who failed to respond to, or who have a contraindication to, or are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or PUVA (psoralen and ultraviolet A). Section 1 of the Package Leaflet has been updated accordingly C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	23/01/2014	21/02/2014	SmPC and PL	Please refer to the scientific discussion Stelara EMEA/H/C/000958/II/0037 for further information.
IB/0039/G	This was an application for a group of variations. B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	15/01/2014	n/a		
N/0038	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	12/12/2013	21/02/2014	PL	
R/0034	Renewal of the marketing authorisation.	25/07/2013	19/09/2013	SmPC, Annex II	Based on the CHMP review of the available information and on the basis of a re-evaluation of the benefit risk balance, the

				and PL	CHMP is of the opinion that the quality, safety and efficacy of Stelara continues to be adequately and sufficiently demonstrated and therefore considered that the benefit risk profile of Stelara continues to be favourable.
II/0029	Extension of indication to include the treatment of psoriatic arthritis. As a consequence of this new indication, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC have been updated. The Package leaflet has been updated accordingly. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	25/07/2013	19/09/2013	SmPC and PL	Please refer to the scientific discussion Stelara EMEA/H/C/000958/II/0029 for further information.
IG/0341	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	31/07/2013	n/a		
II/0033	Addition of pustular psoriasis as an adverse drug reaction in section 4.8 of the SmPC and in section 4 of the package leaflet, based on safety information from Stelara clinical trial and post-marketing data. The MAH took the opportunity to update the list of local representatives in the package leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	25/07/2013	19/09/2013	SmPC and PL	Following a cumulative review of ustekinumab in association with pustular psoriasis including assessment of cases derived from clinical studies and post-marketing experience, the MAH identified 15 cases of rash pustular and 6 cases of pustular psoriasis in a pool of psoriasis phase 2 and 3 studies. In terms of post-marketing experience the MAH identified no serious cases of pustular psoriasis with ustekinumab in the PSOLAR database and 2 non-serious events of possible pustular psoriasis which are not considered significant evidence for this variation. A total of 61 cases of pustular psoriasis/rash pustular were identified in the SCEPTRE database. Forty (40) cases were assessed as de novo pustular psoriasis, 10 cases concerned patients with a known history of pustular psoriasis, 8 cases

					reported the indication of ustekinumab as some type of pustular psoriasis and the remaining 3 cases reported patients who had pustular disease when ustekinumab was initiated but did not clearly state pustular psoriasis as the indication. Therefore, “pustular psoriasis” is added as an adverse drug reaction in section 4.8 of the SmPC with category uncommon and in section 4 of the package leaflet.
II/0030/G	This was an application for a group of variations. To add a post approval change management protocols to introduce new manufacturing sites for the drug substance B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS B.I.e.2 - Design Space - Introduction of a post approval change management protocol related to the AS	25/04/2013	n/a		
IB/0031	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	22/02/2013	19/09/2013	SmPC	
IA/0032	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	01/02/2013	n/a		

II/0028	Update of section 4.4 and 4.8 of the SmPC regarding the need to monitor the appearance of non-melanoma skin cancer in all patients. Update of section 4.4 and 5.1 of the SmPC regarding the lack of suppression of humoral immune response to pneumococcal polysaccharide or tetanus vaccines after long term treatment with Stelara. Exposure numbers in section 4.8 have also been updated in accordance with the 5-year safety update for studies C0743T08 and C0743T09. Section 4.9 of the SmPC has also been amended with the updated single IV dose of Stelara at which no direct toxic effect is observed. Section 2 of the package leaflet has been updated with a wording regarding the need to tell the doctor before taking Stelara in case the patient has ever had an allergic reaction to Stelara (or if the patient is not sure about it) or if the patient has any new or changing lesions within psoriasis areas or on normal skin. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/01/2013	19/09/2013	SmPC and PL	Results with up to 5 years of treatment with ustekinumab in subjects with moderate to severe psoriasis and updated information on potential overdosing of ustekinumab have provided additional information on safety, efficacy, pharmacokinetic, and immunogenicity. The overall safety database has increased and no major changes in the known safety profile for Stelara have emerged. No cumulative safety signals have been seen over 5 years follow-up and the rates of AEs and SAEs are consistent with year 3 and year 4 data. With the larger safety data base, six (6) cases of melanoma (one with invasive melanoma) were identified. There is no evidence of a dose-response with ustekinumab for the development of melanoma. However, the event of melanoma has been added in section 4.8 of the SmPC and will continue to be monitored. Information from the literature identified 2 patients older than 60 years of age, who developed multiple cutaneous squamous cell carcinomas (SCCs) after each receiving 2 doses of ustekinumab. Therefore, a warning regarding the need to monitor all patients for the appearance of non-melanoma skin cancer has been added in the SmPC. New data has been provided on vaccination responses to tetanus and pneumococcal vaccination. The results show no impairment of antibody responses to these vaccinations in subjects who have received Stelara for at least 3.5 years. The above information has been included in sections 4.4 and 5.1 of the SmPC and is considered by the CHMP to be in line with the 5-year clinical trial update and the results from the vaccine substudy. In addition the maximum dose given without safety signals is now 6mg/kg since intravenous dosing up to 6 mg/kg was

					evaluated in the C0743T26 Phase 2b trial of ustekinumab in Crohn's disease. Section 4.9 of the SmPC has been updated accordingly. Moreover, the exposure numbers in the SmPC have been updated in line with the 5-year clinical update for studies C0743T08 and C0743T09. Information regarding the presence of neutralizing antibodies has been included in section 4.8 of the SmPC as approximately 75% of ADA positive subjects had Nab. The benefit/risk balance for Stelara in the treatment of psoriasis is positive and a further key benefit has been provided in the data for this variation; namely the demonstration that after at least 3.5 years treatment with Stelara vaccination responses to tetanus and to pneumococcus are not impaired compared with subjects who have not received Stelara.
IB/0027	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	24/09/2012	n/a		
IG/0213	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	28/08/2012	n/a		
IB/0025	B.II.f.1.b.5 - Stability of FP - Extension of the shelf life of the finished product - Extension of storage period of a biological/immunological medicinal product in accordance with an approved stability protocol	05/06/2012	29/10/2012	SmPC	
IB/0024	B.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits	03/04/2012	n/a		

II/0022/G	This was an application for a group of variations. Addition of an alternative testing site for Active substance. Introduction of additional assays for active substance testing. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Change (replacement) to 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	15/03/2012	15/03/2012		
II/0021	Update of section 4.8 of the SmPC to include facial palsy and arthralgia as adverse drug reactions, and update of the PL accordingly, further to post-marketing and clinical trials data from PSUR 4. Additionally, the product information was updated according to the latest QRD template. C.I.3.z - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under A 45/46, or amendments to reflect a Core SPC - Other variation	19/01/2012	21/02/2012	SmPC, Annex II, Labelling and PL	Both facial palsy and arthralgia have been observed in the post-marketing setting as well as in clinical trials. In accordance with the European Commission Guideline on Summary of Product Characteristics (September 2009), the MAH has calculated the frequency of these ADRs based on clinical trial data. In order to be consistent with the rates already described in the ADR table of the SmPC, the incidence rate of facial palsy is based on 2 cases in 2,266 (0.09%) subjects exposed to Stelara in psoriasis clinical studies and the assigned frequency category is “rare”. Similarly, the incidence rate of arthralgia is based on 159 cases in 2,266 (7.02%) subjects exposed to Stelara in psoriasis clinical studies and the assigned frequency category

					is “common”.
II/0018	Update of sections 4.8 and 5.1 of the Summary of Product Characteristics (SmPC) with longer-term efficacy and safety information of continuous ustekinumab administration based on up to 4 year clinical trial data. The Package Leaflet (PL) is updated in accordance. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the PI is being brought in line with the latest QRD template version 7.3.1. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data	17/11/2011	13/01/2012	SmPC and PL	The currently approved product information for Stelara provides efficacy data on the maintenance of clinical response with q12 week dosing up to 52 weeks and safety data reflecting exposure to ustekinumab in 2266 psoriasis subjects (2251 patient-years of exposure), including 1970 exposed for at least 6 months, 1285 exposed for at least one year, and 373 exposed for at least 18 months. With this variation, the product information of Stelara is updated with information on the long-term maintenance of efficacy and safety information of continuous ustekinumab administration based on up to 4 year clinical trial data.
IB/0023	B.II.b.3.z - Change in the manufacturing process of the finished product - Other variation	16/12/2011	n/a		
II/0017/G	This was an application for a group of variations. Additional site for the manufacture of the finished product. 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, batch control, and secondary packaging, for biological/immunological medicinal products. B.II.b.2.a - Change to batch release arrangements and quality control testing of the FP - Replacement or	17/11/2011	17/11/2011		

	addition of a site where batch control/testing takes place				
IA/0016/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	29/07/2011	n/a	Annex II	
II/0015/G	This was an application for a group of variations. This was an application for a group of variations: Update of sections 4.5 and 5.2 of the SmPC regarding the potential for interleukin IL-12 and IL-23 (separate and in combination) to alter the functional activity and mRNA expression of various CYP450 isoforms. Update of section 5.2 of the SmPC regarding pharmacokinetic findings in Asian patients of the C0743T25 study, as requested by the CHMP. C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article	23/06/2011	26/07/2011	SmPC	The effects of IL 12 or IL 23 on the regulation of CYP450 enzymes were evaluated in an in vitro study using human hepatocytes, which showed that IL 12 and/or IL 23 at levels of 10 ng/mL did not alter human CYP450 enzyme activities (CYP1A2, 2B6, 2C9, 2C19, 2D6, or 3A4). This information is now reflected in sections 4.5 and 5.2 of the SmPC. Additionally, it was observed that the pharmacokinetics of ustekinumab from study C0743T25 (a phase 3 study in Korean and Taiwanese subjects) were generally comparable between Asian and non-Asian subjects with psoriasis, with some numerical differences in serum ustekinumab concentrations which might be attributed to cross-study comparisons, inter-subject variability, and most likely, the difference in body weight between the 2 populations. Section

	45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				5.2 of the SmPC has been updated to reflect this information.
IG/0090/G	This was an application for a group of variations. C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV C.I.9.h - Changes to an existing pharmacovigilance system as described in the DDPS - Other change(s) to the DDPS that does not impact on the operation of the pharmacovigilance system	08/07/2011	n/a		
IB/0014	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	17/05/2011	n/a		
IB/0013/G	This was an application for a group of variations. 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.II.d.1.a - Change in the specification parameters and/or limits of the finished product - Tightening of specification limits B.II.d.1.d - Change in the specification parameters and/or limits of the finished product - Deletion of a	31/03/2011	n/a		

	non-significant specification parameter (e.g. deletion of an obsolete parameter B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
IA/0012/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 supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.4 - Administrative change - Change in the name and/or address of a manufacturer or supplier of the AS, starting material, reagent or intermediate used in the manufacture of the AS A.5.a - Administrative change - Change in the name and/or address of a manufacturer responsible for batch release A.5.b - Administrative change - Change in the name and/or address of a manufacturer of the finished product, including quality control sites (excluding manufacturer for batch release)	15/02/2011	n/a	Annex II and PL	
IA/0011	C.I.9.i - Changes to an existing pharmacovigilance system as described in the DDPS - Change(s) to a DDPS following the assessment of the same DDPS in relation to another medicinal product of the same MAH	06/01/2011	n/a		
II/0008/G	This was an application for a group of variations. To add new manufacturing sites for active substance.	18/11/2010	20/12/2010	SmPC, Annex II and PL	

	To change the current approved manufacturing process. To add CBIL as a release and stability testing site of STELARA drug substance and the drug product Vials and Pre-filled Syringes. To change in IPC methods 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.c - Changes in the manufacturing process of the AS - The change refers to a [-] substance in the manufacture of a biological/immunological medicinal product and is not related to a protocol B.II.b.2.b.3 - Change to batch release arrangements and quality control testing of the FP - Including batch control/testing for a biol/immunol product and one of the test methods is a biol/immunol/immunochemical method 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.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure				
II/0007/G	This was an application for a group of variations.	22/07/2010	26/08/2010	SmPC, Annex II	The MAH conducted a cumulative review of hypersensitivity reactions reported in clinical trials and in the post-marketing

	This application was submitted for a group of variations consisting of two Type II variations. One type II variation is to update sections 4.4 and 4.8 of the SPC with information on hypersensitivity reactions further to the assessment of PSUR 1, and to update the relevant section of the PL and the educational materials accordingly. The other type II variation is to update section 4.4 of the SPC to state the lack of data on secondary transmission of live vaccines and the lack of evidence that Stelara affects allergy immunotherapy. Additionally, the MAH took this opportunity to include administrative changes in Annex IIB. C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data C.I.3.b - Implementation of change(s) requested following the assessment of an USR, class labelling, a PSUR, RMP, FUM/SO, data submitted under Article 45/46, or amendments to reflect a Core SPC - Change(s) with new additional data submitted by the MAH			and PL	setting in which 18 cases were identified (6 from clinical trials and 12 post-marketing). The majority of non-serious cases reported rash or urticaria; three serious post-marketing cases were reported (hypersensitivity, angioedema). The CHMP concluded that a warning about the possibility of delayed hypersensitivity should be added to section 4.4 of the SPC, and that the respective adverse drug reactions should be added to section 4.8. It is in general possible that secondary transmission of live vaccine viruses from individuals vaccinated with such vaccines to contacts of the vaccine recipients occurs. There are no data available on such secondary transmission of infection by live vaccines in patients receiving Stelara. Nevertheless the CHMP accepted the inclusion of such precautionary statement in section 4.4 of the SPC. Finally, there is a theoretical risk that that treatment of patients who have undergone allergy immunotherapy could alter the protection conferred by the allergy immunotherapy based on the mechanism of action of Stelara. Although there is no evidence that Stelara may affect allergy immunotherapy, the CHMP accepted to include such statement in section 4.4 of the SPC.
IB/0010	B.I.b.z - Change in control of the AS - Other variation	24/08/2010	n/a		
IA/0009	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	29/07/2010	n/a		

IG/0007	C.I.9.c - Changes to an existing pharmacovigilance system as described in the DDPS - Change of the back-up procedure of the QPPV	04/06/2010	n/a	Annex II	
II/0006	Update of the Detailed Description of the Pharmacovigilance System (DDPS) to version 005 to include non-QPPV related changes. Consequently, Annex II has been updated with the new version number of the DDPS. Update of DDPS (Pharmacovigilance)	18/02/2010	15/03/2010	Annex II	With this variation the MAH submitted a new version of the DDPS (version 005) in accordance with the current Pharmacovigilance guideline. After assessing the documentation the CHMP concluded that the submitted DDPS contained all required elements.
X/0002	Addition of a new pharmaceutical form Annex I_2.(d) Change or addition of a new pharmaceutical form	17/12/2009	11/03/2010	SmPC, Annex II, Labelling and PL	
II/0005	Extension of shelf life of drug substance intermediates. Change(s) to shelf-life or storage conditions	18/02/2010	01/03/2010		
II/0004	Changes related with the QC testing sites Change(s) to the manufacturing process for the active substance	17/12/2009	07/01/2010		
II/0001	Update of section 5.1 of the SPC with clinical data from the ACCEPT trial and weight-based response scores derived from the PHOENIX 1 and PHOENIX 2 studies. Further minor/administrative updates were applied to sections 2, 4.2, 4.4, 4.8, 5.1, 6.6, 8 and 9 of the SPC.	19/11/2009	22/12/2009	SmPC, Annex II, Labelling and PL	12-week data efficacy data from the ACCEPT trial, an active comparator study of ustekinumab versus etanercept in patients with moderate to severe plaque psoriasis, was included in section 5.1 of the SPC. Additionally, in order to provide further information regarding the currently

	The PL was updated accordingly. Annex II was updated with information regarding educational material and the Marketing Authorisation number for Stelara was included in the Labelling. Finally, the information regarding the local representatives in Germany and Greece was updated and the Instructions for Administration at the end of the PL were revised to improve clarity. Update of Summary of Product Characteristics, Labelling and Package Leaflet				recommended posology information based on a 2-tiered approach to dosing by weight, clinical efficacy data from the PHOENIX 1 and PHOENIX 2 studies was included in section 5.1.
IA/0003	IA_04_Change in name and/or address of a manuf. of the active substance (no Ph. Eur. cert. avail.)	01/10/2009	n/a		