Orencia

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
N/0157	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/06/2023		PL	
IB/0156	B.II.e.2.a - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Tightening of specification limits	18/04/2023	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).

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IA/0154	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	10/03/2023	n/a		
IB/0153	B.II.c.1.z - Change in the specification parameters and/or limits of an excipient - Other variation	04/01/2023	n/a		
IA/0151	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.	28/03/2022	n/a		
IAIN/0150/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.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	17/02/2022	03/02/2023	Annex II and PL	
IA/0149	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	23/11/2021	n/a		
N/0148	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	11/10/2021	03/02/2023	PL	

IB/0147/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.z - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Other variation B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB 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	27/07/2021	n/a		
II/0145/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.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	25/03/2021	n/a		

	biological AS				
IB/0146/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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	15/02/2021	n/a		
IB/0144	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	18/12/2020	n/a		
IB/0143/G	This was an application for a group of variations. B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place B.II.b.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	11/12/2020	n/a		
IA/0142/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	09/10/2020	n/a		

	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure				
II/0140/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.1.c - Replacement or addition of a manufacturing site for the FP - Site where any manufacturing operation(s) take place, except batch release/control, and secondary packaging, for biol/immunol medicinal products or pharmaceutical forms manufactured by complex manufacturing processes B.II.b.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch control/testing takes place 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.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.2.a - Change to importer, batch release arrangements and quality control testing of the FP - Replacement/addition of a site where batch	24/09/2020	n/a		

	control/testing takes place 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				
II/0137/G	This was an application for a group of variations. A.7 - Administrative change - Deletion of manufacturing sites 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.g - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Widening of the approved specs for starting mat./intermediates, which may have a significant effect on the quality of the AS and/or the FP B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.c.1.b - Change in immediate packaging of the AS - Qualitative and/or quantitative composition for sterile and non-frozen biological/immunological ASs B.II.b.3.b - Change in the manufacturing process of the finished or intermediate product - Substantial	24/09/2020	09/12/2020	Annex II, Labelling and PL	

	changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product				
PSUSA/13/20 1912	Periodic Safety Update EU Single assessment - abatacept	03/09/2020	n/a		PRAC Recommendation - maintenance
II/0139	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 method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	11/06/2020	n/a		
IAIN/0141	A.5.a - Administrative change - Change in the name and/or address of a manufacturer/importer responsible for batch release	11/05/2020	09/12/2020	Annex II and PL	
IB/0136	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	12/03/2020	n/a		
IG/1193	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	17/01/2020	n/a		
II/0134	As a result of the outcome of the Article P46 064, update of sections 4.8 and 5.1 of the SmPC for Orencia solution for injection in pre-filled syringe based on the final 24-month results from study IM101301; this was an open-label study to assess	12/12/2019	09/12/2020	SmPC, Annex II and PL	Please refer to Scientific Discussion Orencia EMEA/H/C/000701/II/0134

	pharmacokinetics, safety and efficacy of SC abatacept in pJIA with no formal hypothesis testing. Update of section 4.8 of the SmPC for Orencia powder for concentrate for solution for infusion based on the final 24-month results from study IM101301. The PL for Orencia solution for injection in pre-filled syringe has been updated to reflect the removal of the IFU booklet, as requested by the CHMP as part of the procedure EMEA/H/C/000701/X/0117/G. The RMP version 27.1 was updated with clinical trial exposure data from the 2-year data for 2 to 5 years old cohort in study IM101301. The presentation of identified and potential risks was updated with study IM101301 data on infections, injection reactions, malignancies and autoimmune symptoms in the 2 to 5 years old cohort and 6-17 years old cohort. In addition, the MAH took the opportunity to update the Annex II and to update section 4.4 of the SmPCs in line with the latest QRD template version 10.1 for all registered presentations. In addition, the list of local representatives in the PLs has been updated. C.I.3.z - Change(s) in the SPC, Labelling or PL intended to implement the outcome of a procedure concerning PSUR or PASS or the outcome of the assessment done under A 45/46 - Other variation				
IB/0133	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	29/10/2019	n/a		

	the AS -replacement or addition of a site where batch control/testing takes place				
IB/0132	B.II.e.1.z - Change in immediate packaging of the finished product - Other variation	04/09/2019	n/a		
IB/0131	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	11/07/2019	n/a		
IB/0130	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	11/07/2019	n/a		
II/0124/G	This was an application for a group of variations. Submission of the final reports from studies IM101125, IM101127, IM101211, IM101213 (four C.I.13 variations) and the interim report from study IM101121 listed as category 3 studies in the RMP. These are biologic registries and pharmacoepidemiology studies to assess the risk associated with the use of abatacept during post-marketing in geographically diverse populations and subgroups. The RMP (version 26.2) was updated to reflect the completion of the studies IM101125, IM101127, IM101211, and IM101213. Due to feasibility issues the study IM101121 has been removed from the RMP and "Adverse Pregnancy Outcomes" was removed	11/07/2019	n/a		Studies IM101125, IM101127, IM101211and IM101213 are part of the overall abatacept post-marketing epidemiology program. The program was specifically designed to enhance the understanding of the identified, potential, and unknown/missing risks that are outlined in the abatacept Risk Management Plan (RMP). ☐ IM101125, ARTIS: a nation-wide post-marketing study on safety and effectiveness of abatacept treatment in patients with rheumatic disease in Sweden: ☐ IM101127, RABBIT: long-term observation of treatment with biologics in rheumatoid arthritis in Germany: ☐ IM101213, British Columbia: post-marketing observational study assessing the long-term safety of abatacept using a population-based cohort of rheumatoid arthritis patients in the province of British Columbia

	from the RMP safety specification. Two additional epidemiological studies IM101803 and IM101816 aimed to gather more information on malignancies were added as category 3 studies in the RMP. Based on a cumulative search from Company Safety Database, the RMP was updated to remove the safety concern PML from the safety specifications. The following Missing Information items were also removed in the RMP safety specification: combination therapy, including biologic therapy, and elderly patients. Submission of final study report from study IM101488 "Post-marketing Study Assessing the Long-term Safety of Abatacept" (C.I.13 variation), a retrospective cohort study that was conducted separately among 3 existing administrative health care databases in the US. No changes were made to the PI or the RMP as results of the assessment of those data. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority				☐ IM101121 abatacept pregnancy exposure registry OTIS autoimmune diseases in pregnancy project Study IM101488 was to estimate and compare the risk of malignancies as well as the risk of infections among a cohort of RA patients who are prescribed abatacept and a cohort of patients who are prescribed other RA treatments. Overall, no increased risk of infections, overall malignancies, breast cancer, lymphoma and autoimmune diseases were identified in these studies. The incidence rates for death in the abatacept group were similar to those found in the csDMARDs and other bDMARD groups across the studies. No change to previously described risk/benefit analysis was seen considering infusion/injection reactions. The overall results from the post-marketing epidemiology studies confirmed the existing understanding on the safety profile of abatacept. The SmPC includes adequate information and risk minimisation measures to ensure that the risks of abatacept are being well mitigated. No changes were made to the PI as a result of the assessment. In addition, two additional epidemiological studies IM101803 and IM101816 aimed to gather more information on malignancies were added as category 3 studies in the RMP.

	C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
IA/0129/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 changes to an approved test procedure B.II.d.2.f - Change in test procedure for the finished product - To reflect compliance with the Ph. Eur. and remove reference to the outdated internal test method and test method number	21/06/2019	n/a		
II/0125	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	26/04/2019	n/a		
IB/0127	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	10/04/2019	n/a		
X/0117/G	This was an application for a group of variations. Annex I_2.(c) Change or addition of a new strength/potency	31/01/2019	08/04/2019	SmPC, Labelling and PL	

	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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation B.II.e.1.z - Change in immediate packaging of 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				
IAIN/0128	B.IV.1.a.1 - Change of a measuring or administration device - Addition or replacement of a device which is not an integrated part of the primary packaging - Device with CE marking	03/04/2019	n/a		
IG/1059	A.1 - Administrative change - Change in the name and/or address of the MAH	15/02/2019	15/04/2019	SmPC, Labelling and PL	
II/0122/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 changes to an approved test procedure 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	24/01/2019	n/a		

	control/testing takes place for a biol/immunol product and any of the test methods at the site is a biol/immunol method				
IB/0123	B.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS	20/12/2018	n/a		
II/0120/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.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	27/09/2018	n/a		
IB/0119	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	15/08/2018	n/a		
IA/0121	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	31/07/2018	n/a		

IB/0118	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	11/04/2018	n/a		
II/0116/G	This was an application for a group of variations. 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.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	11/01/2018	n/a		
IB/0115	B.IV.z - Quality change - Change in Medical Devices - Other variation	12/09/2017	n/a		
IB/0114	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	07/09/2017	n/a		
PSUSA/13/201612	Periodic Safety Update EU Single assessment - abatacept	01/09/2017	n/a		PRAC Recommendation - maintenance
IA/0113	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	28/07/2017	n/a		

	manufacturer of a novel excipient				
II/0105	C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one	22/06/2017	25/07/2017	SmPC and PL	Please refer to the Scientific Discussion Orencia EMEA/H/C/000701/II/0105.
IB/0112	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	03/07/2017	n/a		
IB/0111	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	23/06/2017	n/a		
IB/0110	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	12/05/2017	n/a		
II/0108/G	This was an application for a group of variations. C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority C.I.13 - Other variations not specifically covered elsewhere in this Annex which involve the submission of studies to the competent authority	05/05/2017	n/a		This Type II variation EMEA/H/C/000701/II/0108 concerns submission of Final Study Reports on two PASS studies IM101045A and IM101045B (Category 3 studies in the abatacept RMP) which were aimed to gather post-marketing data on safety of abatacept use. The epidemiological studies epidemiological studies IM101045A and IM101045B were registry studies conducted in the US. The data reported is in line with the previous understanding on the safety of abatacept, and no new major safety concerns were raised. The benefit-risk balance of Orencia

					remains positive.
II/0107	C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	05/05/2017	25/07/2017	SmPC and PL	The number of rheumatoid arthritis patients in controlled clinical trials of Orencia (abatacept) has risen since its approval. The MAH undertook an initiative to create an integrated clinical safety database for Orencia. The clinical safety database now integrates selected studies of subcutaneous and intravenous abatacept in rheumatoid arthritis through June 2016. With this variation, the SmPC and Risk Management Plan were updated with figures based on the relevant data generated from the integrated clinical safety database. In particular, Sections 4.4 and 4.8 of the SmPC were updated concerning new ADRs and frequencies of known ADRs. For more detailed information, please refer to the Summary of Product Characteristics.
II/0106/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.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	16/03/2017	n/a		

	product and is not related to a protocol 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.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				
II/0103/G	This was an application for a group of variations. To update test methods for the active substance and finished product. 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.1.d - Change in the specification parameters	10/11/2016	n/a		

	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 B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.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/0104/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.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 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.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	13/10/2016	n/a		
II/0097	Extension of Indication for Orencia in combination with methotrexate (MTX) in the treatment of adults with rheumatoid arthritis (RA) who have highly active disease not previously treated with MTX. As a	21/07/2016	25/08/2016	SmPC and PL	Please refer to the Scientific Discussion Orencia EMEA/H/C/000701/II/0097.

	consequence, sections 4.1 and 5.1 of the SmPC (for powder for concentrate for solution for infusion) and sections 4.1, 4.8 and 5.1 of the SmPC (for solution for injection in pre-filled syringe and solution for injection in pre-filled pen) are updated based on results from AVERT study (IM101226). The Package Leaflet is updated accordingly. Moreover, the updated RMP version 20.1 has been agreed. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one				
IB/0102	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	23/08/2016	n/a		
II/0099/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.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 B.II.b.2.c.3 - Change to importer, batch release arrangements and quality control testing of the FP -	09/06/2016	25/08/2016	Annex II and PL	

	Including batch control/testing for a biol/immunol product and any of the test methods is a biol/immunol/immunochemical method				
IB/0100	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	03/06/2016	n/a		
IB/0101/G	This was an application for a group of variations. B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	11/05/2016	n/a		
II/0094/G	This was an application for a group of variations. Type II variation Update of sections 4.8 and 5.1 of the Summary Product Characteristics (125 mg) in order to update the safety information with data from the long-term (LT) final Clinical Study Report for IM101174. In addition, the Product Information is being aligned to the QRD template, version 10.1 and the French local representatives updated. Type IB variation Update timelines for study IM101537, aimed at evaluating the effectiveness of risk minimization	01/04/2016	25/08/2016	SmPC, Annex II, Labelling and PL	Update the SmPC for the SC Orencia 125 mg solution for injection, in section 4.8 Undesirable effects and section 5.1 Pharmacodynamic properties, with the data from the long-term (LT) final Clinical Study Report for IM101174. This variation addresses the CHMP conclusions dated 26 November 2013 received after the assessment of the immunogenicity update and the response to the list of outstanding issues (MEA052.1). In addition, the MAH submitted an update of the timelines for study IM101537, aimed at evaluating the effectiveness of risk minimization measure (alert card).

	measure (alert card). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				
II/0096/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.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	28/01/2016	n/a		
IB/0098	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	05/01/2016	n/a		
II/0089	Update of sections 4.5 and 4.6 of the SmPC in order to amend the safety information on the risk of infection associated with live vaccination in infants	17/12/2015	25/08/2016	SmPC and PL	Update of sections 4.5 and 4.6 of the SmPC in order to amend the safety information on the risk of infection associated with live vaccination in infants born to women

	born to women treated with abatacept during pregnancy. The Package Leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to correct some typographical errors and propose editorial changes in the Product Information. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				treated with abatacept during pregnancy. Administration of live vaccines to infants exposed to abatacept in utero is not recommended for 14 weeks following the mother's last exposure to abatacept during pregnancy. The Package Leaflet is updated accordingly. In addition the MAH has updated the Risk Management Plan (RMP).
N/0095	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	26/10/2015	25/08/2016	PL	
II/0088/G	This was an application for a group of variations. 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 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 method using a biol. reagent or replacement of a biol. reference preparation not covered by an approved protocol	17/09/2015	n/a		
II/0090	B.I.a.4.d - Change to in-process tests or limits	06/08/2015	n/a		

	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				
IB/0092/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.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process B.II.e.3.b - Change in test procedure for the immediate packaging of the finished product - Other changes to a test procedure (including replacement or addition) B.II.e.7.a - Change in supplier of packaging components or devices (when mentioned in the dossier) - Deletion of a supplier	03/07/2015	n/a		
IB/0091	B.II.b.3.a - Change in the manufacturing process of the finished or intermediate product - Minor change in the manufacturing process	01/07/2015	n/a		
IB/0093	B.I.a.1.k - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - New storage site of MCB and/or WCB	25/06/2015	n/a		
II/0087/G	This was an application for a group of variations.	23/04/2015	08/10/2015	SmPC, Labelling and	Introduction of prefilled pen presentations for Orencia 125 mg solution for injection (pack sizes of 4 and 12 pre-filled

	B.II.e.1.b.2 - Change in immediate packaging of the finished product - Change in type/addition of a new container - Sterile medicinal products and biological/immunological medicinal products 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			PL	pens). The requested group of variations proposed amendments to the Annex A, Summary of Product Characteristics, Labelling and Package Leaflet and to the Risk Management Plan (RMP).
II/0083/G	This was an application for a group of variations. B.I.b.2.d - Change in test procedure for AS or starting material/reagent/intermediate - Substantial change to or replacement of a biological/immunological/immunochemical test method or a method using a biological reagent for a biological AS B.I.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	22/01/2015	n/a		
IB/0086	B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation	16/01/2015	n/a		
IB/0084/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	09/01/2015	n/a		

	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.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)				
IB/0085	C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	03/12/2014	n/a		
II/0082	B.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range	25/09/2014	n/a		
II/0081/G	This was an application for a group of variations. Grouping of 1 Type II variation: Update sections 4.4 and 4.8 of the SmPC regarding systemic injection reactions with the use of SC abatacept to harmonize the SmPC for SC abatacept with the SmPC for intravenous (IV) abatacept. The RMP is updated accordingly; 5 Type IB: Change the milestones for the core SC study protocols IM101063, IM101167, IM101173, IM101174 and IM101185. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance	25/09/2014	08/10/2015	SmPC and Annex II	On the basis of the post marketing data provided by the MAH, ADRs, which may be interpreted as systemic injection reactions, occur not only with the IV formulation, but also infrequently with the SC formulation of abatacept. A possible causal relationship is supported by the provided data. Furthermore, considering the potential life threatening consequences of the most serious of the reactions (anaphylactic reaction etc.) the CHMP endorsed the inclusion of the possibility of the occurrence of systemic injection reactions during SC abatacept therapy in the product information. The changes to the milestones for the core SC study protocols IM101063, IM101167, IM101173, IM101174 and

	data C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation				IM101185 study timelines were considered acceptable.
PSUV/0079	Periodic Safety Update	10/07/2014	n/a		PRAC Recommendation - maintenance
II/0077	Update of sections 4.2 and 5.1 of the SmPC with the results of study IM101235. The Package Leaflet is updated accordingly. 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. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/03/2014	28/04/2014	SmPC, Annex II and PL	The scope of this type II variation was to amend the product information with the results of study IM101235, a 2-year, Phase 3b, randomized, single (investigator)-blinded, active-controlled, head-to-head clinical study designed to compare the efficacy and safety of subcutaneous abatacept, without an IV loading dose, versus subcutaneous adalimumab, both with background methotrexate, in adult biologic-naïve RA patients, with moderate to severe active RA, who have responded inadequately to previous therapy with methotrexate. The study met the primary objective of demonstrating non-inferiority of SC abatacept without IV loading to

					adalimumab at 12 months on the primary efficacy end point ACR 20 with comparable and clinically meaningful response rates throughout the 24-months period. The safety data of study IM101235 did not reveal any new safety signals for abatacept. This study also provides further evidence, corroborating previous data that the safety of SC abatacept, administered without IV loading, appears for the most part, to be comparable to that of the IV formulation. Section 5.1 of the product information has been updated accordingly. The posology and method of administration section of Orencia 125 mg solution for injection has also been updated to mention that Orencia SC may be initiated with or without an intravenous (IV) loading dose and that if a single IV infusion is given to initiate treatment (IV loading dose before SC administration), the first 125 mg abatacept SC should be administered within a day of the IV infusion, followed by the weekly 125 mg abatacept SC injections.
IAIN/0080	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	04/04/2014	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 the AS - Minor change in the manufacturing process of the AS B.I.a.2.z - Changes in the manufacturing process of the AS - Other variation	27/11/2013	n/a		

II/0073/G	This was an application for a group of variations. Changes to the manufacturing process of the active substance at the Lonza site. 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 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.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits B.I.a.4.z - Change to in-process tests or limits applied during the manufacture of the AS - Other variation	19/09/2013	n/a		

IB/0076	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	18/07/2013	n/a		
IB/0075/G	This was an application for a group of variations. B.I.b.2.b - Change in test procedure for AS or starting material/reagent/intermediate - Deletion of a test procedure for the AS or a starting material/reagent/intermediate, if an alternative test procedure is already authorised 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.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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	07/06/2013	n/a		

	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.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 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.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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of				

	specification limits 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.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.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation 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.I.b.2.c - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure for a reagent, which does not have a significant effect on the overall quality of the AS				
II/0072	Update of section 4.5 of the SmPC with the data from the influenza vaccine substudy to protocol IM101174. Section 4.4 of the SmPC has been updated accordingly. In addition, the MAH took the opportunity to update the list of local representatives in the Package Leaflet. Furthermore, the Annex II is being brought in line with the latest QRD template version.	30/05/2013	03/12/2013	SmPC, Annex II and PL	The purpose of the influenza vaccine substudy to protocol IM101174 was to assess antibody response to the seasonal influenza trivalent virus vaccine in subjects with RA who were on a stable dose of SC abatacept and background disease modifying anti-rheumatic drug (DMARD) therapy, and without protective antibody levels to the influenza antigens at baseline. Results of the study showed that a majority of the subjects with long-term abatacept treatment were able to mount an immune response to the

	C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				vaccine. There were no unexpected safety findings related to the vaccination during concurrent SC abatacept therapy.
II/0070/G	This was an application for a group of variations. B.I.a.1.e - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The change relates to a biological AS or a starting material [-] used in the manufacture of a biological/immunological product B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.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.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.b.2.d - Change in test procedure for AS or	25/04/2013	03/12/2013	Annex II	

	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.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.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)				
II/0062/G	This was an application for a group of variations. Update of the warning in section 4.4 of the SmPC to include that cases of tuberculosis have been reported in patients receiving Orencia. Update of the warning in section 4.4 of the SmPC to include that cases of non-melanoma skin cancers have been reported in patients receiving Orencia. Update of section 4.5 of the SmPC to add additional information regarding pneumococcal vaccinations. Update of section 4.8 of the SmPC to include data from clinical trials, post-authorisation safety studies and post-marketing spontaneous reports. The Package Leaflet is updated accordingly. These changes have been requested by the CHMP following the assessment of PSUR 7 (covering the 1-	25/04/2013	03/12/2013	SmPC, Labelling and PL	Following assessment of Orencia's PSUR 7 (covering the 1-year period from 23 December 2010 to 22 December 2011), the CHMP adopted conclusions including a request for an SmPC update with the following information: Section 4.4: Change of text under "Infections" –section regarding tuberculosis; inclusion of a sentence on the post-marketing experience of cases with "Non-melanoma skin cancers" under the Malignancy section. Section 4.5: inclusion of information from the pneumococcal vaccination study under "Vaccinations". Section 4.8: replacement of the existing table under the 4.8 "undesirable effects"-section to include data from clinical trials, post-authorisation safety studies and post-marketing spontaneous reports. The MAH has implemented the changes requested by the CHMP in the Orencia PI. The MAH has also updated the information in the product

	year period from 23 December 2010 to 22 December 2011). Update of the warning in section 4.4 of the SmPC regarding allergic reactions and to include further recommendations on the permanent discontinuation of Orencia in case of serious allergic or anaphylactic reactions. The patient alert card has been updated accordingly to include information on the risk of systemic hypersensitivity reactions. In addition, the MAH has also taken the opportunity of this variation to make editorial changes to section 4.2 of the Orencia 125 mg solution for injection SmPC and to section 5.1 of the Orencia 250 mg powder for concentrate for solution for infusion SmPC. In addition, changes were also made to bring the ORENCIA IV PI in line with the approved Orencia SC PI. 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 C.I.4 - Variations related to significant modifications of the SPC due in particular to new quality, pre-clinical, clinical or pharmacovigilance data				information regarding fatal anaphylaxis and to include further recommendations on the discontinuation of Orencia in case of anaphylactic reactions. This was agreed by the CHMP.
II/0067/G	This was an application for a group of variations.	21/02/2013	n/a		

	This was an application for a group of variations to replace and add WCB testing sites. As a consequence some testing methods were updated. 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.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement or addition) for the AS or a starting material/intermediate B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same pharmaceutical group as the currently approved manufacturer B.I.a.1.a - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - The proposed manufacturer is part of the same				

	pharmaceutical group as the currently approved manufacturer				
IB/0071	B.II.b.5.z - Change to in-process tests or limits applied during the manufacture of the finished product - Other variation	05/02/2013	n/a		
II/0065	Update of sections 4.8 and 5.1 of the Orencia 250 mg powder for concentrate for solution for infusion to update the safety information with additional long-term follow-up paediatric data from study IM101033. In addition, the wording in section 6.6 of the SmPC has been updated regarding the use of a filter during the administration of the 250 mg strength presentation. Editorial changes have also been made to the ORENCIA 125 mg solution for injection package. Furthermore the Annex II is being brought in line with the latest QRD template. 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	17/01/2013	03/12/2013	SmPC, Annex II and PL	The final Study Report of IM101033 Period C has previously been submitted under Article 46 of Regulation (EC) No. 1901/2006 (P46 039 application). As requested in the CHMP conclusions on this procedure, the MAH has updated SmPC sections 4.8 and 5.1 with long-term efficacy and safety results of Study IM101033. The updated sections are approvable. The subheading 'Infusion-related reactions' under section 4.8 of the SmPC has been updated to reflect the change in frequency of infusion-related reactions during Period C from 3 to 4% and the on-treatment immunogenicity results. The response rates and the exposure to abatacept during Period C have been updated in section 5.1 of the SmPC. Furthermore, instructions regarding the use of a filter prior to administration of Orencia intravenously have been re-included in SmPC section 6.6.
II/0061/G	This was an application for a group of variations. to implement changes to the Tryptic Peptide Mapping test method used for Orencia active substance and drug product. As a consequence, the specification	17/01/2013	n/a		

	limits are changed. 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.II.d.1.e - Change in the specification parameters and/or limits of the finished product - Change outside the approved specifications limits range				
IG/0254	C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	17/12/2012	n/a		
IB/0066	B.II.b.5.f - Change to in-process tests or limits applied during the manufacture of the finished product - Addition or replacement of an in-process test as a result of a safety or quality issue	20/11/2012	n/a		
IAIN/0068	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	19/11/2012	03/12/2013	SmPC, Labelling and PL	
IB/0063	B.I.a.2.a - Changes in the manufacturing process of the AS - Minor change in the manufacturing process of the AS	13/11/2012	n/a		
II/0058/G	This was an application for a group of variations. to implement substantial changes to the drug	18/10/2012	n/a		

	product manufacturing process following addition of a new manufacturing area at the already authorised manufacturing site. As a consequence, the batch size is increased. These changes apply only to the new area. B.II.b.3.b - Change in the manufacturing process of the finished product - Substantial changes to a manufacturing process that may have a significant impact on the quality, safety and efficacy of the medicinal product B.II.b.4.a - Change in the batch size (including batch size ranges) of the finished product - Up to 10-fold compared to the currently approved batch size				
X/0054	Extension application: New pharmaceutical form (125 mg) and route of administration (SC) Annex I_2.(e) Change or addition of a new route of administration Annex I_2.(d) Change or addition of a new pharmaceutical form	19/07/2012	04/10/2012	SmPC, Labelling and PL	
IB/0060	B.I.b.1.z - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Other variation	10/09/2012	n/a		
IA/0057	B.I.b.2.a - Change in test procedure for AS or starting material/reagent/intermediate - Minor changes to an approved test procedure	24/05/2012	n/a		

R/0055	Renewal of the marketing authorisation.	19/01/2012	15/03/2012	SmPC, Annex II, Labelling and PL	Based on the review of the available information, the CHMP is of the opinion that the quality, the safety and the efficacy of this medicinal product continues to be adequately and sufficiently demonstrated and therefore considers the benefit/risk profile of Orencia continues to be favourable. The MAH should continue to submit yearly PSURs. The CHMP is also of the opinion that the renewal can be granted with unlimited validity.
IB/0056/G	This was an application for a group of variations. B.IV.z - Quality change - Change in Medical Devices - Other variation B.IV.z - Quality change - Change in Medical Devices - Other variation	03/02/2012	n/a		
IB/0053/G	This was an application for a group of variations. B.II.c.3.a.2 - Change in source of an excipient or reagent with TSE risk - From TSE risk material to vegetable or synthetic origin - For excipients or reagents USED in the manufacture of a biol/immunol AS or in a biol/immunol medicinal product B.II.c.3.a.2 - Change in source of an excipient or reagent with TSE risk - From TSE risk material to vegetable or synthetic origin - For excipients or reagents USED in the manufacture of a biol/immunol AS or in a biol/immunol medicinal product	27/10/2011	n/a		
IB/0052	B.I.b.2.e - Change in test procedure for AS or starting material/reagent/intermediate - Other changes to a test procedure (including replacement	08/09/2011	n/a		

	or addition) for the AS or a starting material/intermediate				
IA/0051	B.I.a.4.a - Change to in-process tests or limits applied during the manufacture of the AS - Tightening of in-process limits	27/07/2011	n/a		
II/0045	Change in the manufacturer of the active substance. 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	23/06/2011	23/06/2011		
II/0043	Update of section 5.1 of the SmPC with results of study IM101023. This variation application is submitted further to the request of the CHMP following assessment of FUM 13. Editorial changes have been made to section 4.4, 4.5, 4.8, 5.1 and 5.2 of the SmPC. C.I.z - Changes (Safety/Efficacy) of Human and Veterinary Medicinal Products - Other variation	23/06/2011	23/06/2011	SmPC	Information on the maintenance therapy of patients with RA who had achieved remission was proposed to be added to section 5.1 of the SmPC. The study, contributing to this evaluation, has previously been assessed by the CHMP. Its designs is deemed not optimal by the CHMP and the data overall limited, thus any conclusions from this study has uncertainties. Taking into account the available data and the quality of this data, the CHMP considers the text proposed by the MAH an accurate description.
IA/0050	B.I.b.1.b - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Tightening of specification limits	22/06/2011	n/a		
IA/0049	B.I.b.1.d - Change in the specification parameters	22/06/2011	n/a		

	and/or limits of an AS, starting material/intermediate/reagent - Deletion of a non-significant specification parameter (e.g. deletion of an obsolete parameter)				
IA/0048	B.II.e.6.a - Change in any part of the (primary) packaging material not in contact with the finished product formulation - Change that affects the product information	27/05/2011	n/a	SmPC, Labelling and PL	
IB/0047/G	This was an application for a group of variations. To improve the testing standards of the immediate packaging. B.II.e.2.z - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Other variation B.II.e.2.b - Change in the specification parameters and/or limits of the immediate packaging of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	13/05/2011	n/a		
IA/0046	C.I.9.e - Changes to an existing pharmacovigilance system as described in the DDPS - Changes in the major contractual arrangements with other persons or organisations involved in the fulfilment of pharmacovigilance obligations and described in the DD	26/04/2011	n/a	Annex II	

II/0041	Changes in the specification parameters of the drug substance B.I.b.1.e - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Deletion of a specification parameter which may have a significant effect on the overall quality of the AS and/or the FP	21/10/2010	27/10/2010		
II/0039	Change to in-process test or limits applied during the manufacture of the active substance - Widening of the approved in-process test limits, which may have a sigmificant effect on the overall quality of the active substance. 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	23/09/2010	29/09/2010		
IA/0042	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	03/09/2010	n/a	Annex II	
II/0040	Change to in-process test of the active substance B.I.a.4.e - Change to in-process tests or limits applied during the manufacture of the AS - Deletion of an in-process test which may have a significant	22/07/2010	19/08/2010		

	effect on the overall quality of the AS				
II/0033	Extension of the indication to the treatment of moderate to severe active rheumatoid arthritis in patients who have responded inadequately to previous therapy with one or more DMARDs including MTX or a TNF alfa inhibitor. Consequential changes have been made to section 4.1, 4.4, 4.6, 4.8, and 5.1 of the SmPC. The Package Leaflet has been updated accordingly. Annex II has also been corrected to include the following statement: "The MAH should provide a patient alert card in each pack, the text of which is included in Annex III". Extension of Indication Update of Package Leaflet	20/05/2010	01/07/2010	SmPC, Annex II and PL	Please refer to the Scientific Discussion "Orencia/H/C/000701/II/0033" for further information.
IA/0037/G	This was an application for a group of variations. C.I.9.b - Changes to an existing pharmacovigilance system as described in the DDPS - Change in the contact details 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	23/03/2010	n/a	Annex II	
II/0034	Changes to the manufacturing process of the active substance B.I.a.z - Change in manufacture of the AS - Other	20/01/2010	02/02/2010		

	variation				
II/0024	Extension of the therapeutic indication to include the treatment of moderate to severe active polyarticular juvenile idiopathic arthritis in paediatric patients 6 years of age and older who have had an insufficient response to other DMARDs including at least one TNF inhibitor. Consequential changes have been proposed to sections 4.1, 4.2, 4.4, 4.8, 5.1, 5.2, 5.3 and 6.6 of the SPC. The package leaflet has been updated accordingly. Moreover, Annex II is to be updated with the RMP standard text reflecting the latest agreed version number. Minor corrections have also been made to section 4.5 and 4.6 of the SPC. Paediatric Art. 8 - Changes to the product information	17/12/2009	20/01/2010	SmPC and PL	Please refer to the Scientific Discussion "Orencia/H/C/000701/II/0024" for further information.
IA/0036	IA_28_Change in any part of primary packaging material not in contact with finished product	15/01/2010	n/a		
IA/0035	IA_28_Change in any part of primary packaging material not in contact with finished product	15/01/2010	n/a		
II/0030	Changes in the transport of the drug substance Change(s) to the manufacturing process for the active substance	24/09/2009	30/09/2009		
II/0025	Replacement of the peptide mapping method in the release testing of drug substance and drug product.	24/09/2009	30/09/2009		

	Change(s) to the test method(s) and/or specifications for the active substance				
IA/0032	IA_09_Deletion of manufacturing site	17/09/2009	n/a		
N/0031	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	24/08/2009	n/a	PL	
II/0029	Changes in the shelf life of the drug substance Change(s) to shelf-life or storage conditions	23/07/2009	18/08/2009		
II/0028	Change in the specification of a media component used in the manufacture of abatacept Change to the test procedure and/or specification of a raw material	25/06/2009	03/07/2009		
II/0027	Changes in the manufacture of the drug substance Change(s) to the manufacturing process for the active substance	25/06/2009	03/07/2009		
II/0023	Update of the section 4.4 and 4.8 of the summary of product characteristics with safety information included in the last PSUR (Period covered: 23.12.07 - 22.06.08) as submitted in August 2008. Update of Summary of Product Characteristics	23/04/2009	29/05/2009	SmPC	Section 4.4 of the Orencia's SPC has been amended to reflect that some of the serious infections, including sepsis and pneumonia reported with abatacept have been fatal, as a cumulative search of the post-marketing safety database on 22 June 2008 identified 49 reports with a fatal outcome; of these 19 deaths were due to infection. Section 4.8 of the SPC was amended to reflect that

					hypersensitivity, anaphylaxis, and drug hypersensitivity reactions were rarely reported in patients treated with abatacept during controlled and open-label clinical trial. Section 4.8 was also amended to reflect that, based on additional exposure data in the current time period (4149 abatacept-treated patients during 10,365 patient-years), there does not appear to be an increased risk of malignancy with abatacept in humans.
IB/0026	IB_42_a_01_Change in shelf-life of finished product - as packaged for sale	19/03/2009	n/a	SmPC	
II/0022	Update of Detailed Description of the Pharmacovigilance System. Changes to QPPV Update of DDPS (Pharmacovigilance)	22/01/2009	25/02/2009	Annex II	The Detailed Description of the Pharmacovigilance System has been updated (Version 3.0) to reflect the change of the Qualified Person for Pharmacovigilance (QPPV) as well as to notify other changes to the DDPS performed since the last approved version. Consequently, Annex II has been updated using the standard text including the new version number of the agreed DDPS.
II/0021	Addition of alternate testing sites for some tests of abatacept drug sustance. Change(s) to the test method(s) and/or specifications for the active substance	19/02/2009	25/02/2009		
II/0020	Changes on a chromatography step used in the manufacture of abatacept drug substance. Change(s) to the test method(s) and/or specifications for the active substance	20/11/2008	26/11/2008		

II/0007	Change(s) to the manufacturing process for the active substance	23/10/2008	03/11/2008		
II/0019	Changes in the collection end point criterion of a chromatographic step used in the manufacture of the drug substance. Change(s) to the test method(s) and/or specifications for the active substance	25/09/2008	01/10/2008		
II/0014	Change(s) to the test method(s) and/or specifications for the active substance	25/09/2008	01/10/2008		
II/0010	Change(s) to the test method(s) and/or specifications for the active substance	24/07/2008	28/07/2008		
II/0011	Change(s) to the manufacturing process for the finished product	26/06/2008	03/07/2008		
II/0008	Change(s) to the manufacturing process for the active substance	30/05/2008	05/06/2008		
II/0013	Change(s) to the test method(s) and/or specifications for the active substance	24/04/2008	28/04/2008		
IB/0018	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	22/04/2008	n/a		
IB/0017	IB_12_b_02_Change in spec. of active subst./agent in manuf. of active subst. - test parameter	22/04/2008	n/a		

IA/0016	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	02/04/2008	n/a		
IA/0015	IA_12_a_Change in spec. of active subst./agent used in manuf. of active subst. - tightening of spec.	02/04/2008	n/a		
II/0009	Change(s) to the test method(s) and/or specifications for the finished product	19/03/2008	31/03/2008		
N/0012	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	01/02/2008	n/a	PL	
II/0006	Change(s) to the manufacturing process for the finished product	13/12/2007	19/12/2007		
II/0002	Change(s) to the test method(s) and/or specifications for the active substance	13/12/2007	19/12/2007		
II/0004	Change(s) to the manufacturing process for the active substance	15/11/2007	21/11/2007		
N/0003	Minor change in labelling or package leaflet not connected with the SPC (Art. 61.3 Notification)	14/09/2007	n/a	PL	