Cosentyx

Procedural steps taken and scientific information after the authorisation

Application number	Scope	Opinion / Notification [1] issued on	Commission Decision Issued [2] / amended on	Product Information affected [3]	Summary
II/0033/G	This was an application for a group of variations. Update of sections 4.2, 4.8, 5.1 and 5.2 of the SmPC in order to include information on dose up-titration for Psoriatic Arthritis (PsA) and update of the radiographic sub-section for Psoriatic Arthritis (PsA) based on results from the 24-week data from study CAIN457F2342, the pooled data from PsA Phase 3 studies, the pooled data from patients who up-titrated	20/09/2018	23/10/2018	SmPC and PL	In psoriatic arthritis patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Based on clinical response, the dose can be increased to 300 mg. For information from study CAIN457F2342 and from pooled analyses, please refer to the Summary of Product Characteristics.

[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).

	their secukinumab dose in studies CAIN457F2306E1, CAIN457F2312 and CAIN457F2318, and long-term study observations which demonstrate higher rates of discontinuation for patients on secukinumab 150 mg compared to patients on secukinumab 300 mg. The Package leaflet is updated accordingly. In addition, the Marketing authorisation holder (MAH) took the opportunity to update the list of local representatives for Bulgaria, Estonia, Lithuania, Latvia and Hungary in the Package Leaflet and to bring the Package leaflet in line with the latest approved SmPC as per procedure (EMEA/H/C/003729/IB/0028). The RMP (v.3.1) has also been updated including suicidal ideation and behaviour as an important potential risk in the RMP and including minor administrative/editorial changes (LEG 005.2). C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data				
PSUSA/10341 /201712	Periodic Safety Update EU Single assessment - secukinumab	26/07/2018	20/09/2018	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10341/201712.
IA/0040/G	This was an application for a group of variations. B.I.b.1.d - Change in the specification parameters and/or limits of an AS, starting	10/08/2018	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)				
IA/0039	B.II.d.2.a - Change in test procedure for the finished product - Minor changes to an approved test procedure	07/08/2018	n/a		
IA/0038	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	26/07/2018	n/a		
II/0031/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.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	07/06/2018	20/09/2018	Annex II	The Annex II has been updated to include the following additional manufacturer of the active substance: Sandoz GmbH, Business Unit Biologics Technical Development and Manufacturing Drug Substance Schaftenau (BTDM DSS), Biochemiestrasse 10, 6336 Langkampfen, Austria

II/0034	B.II.g.2 - Introduction of a post approval change management protocol related to the finished product	17/05/2018	n/a		
T/0036	Transfer of Marketing Authorisation	20/03/2018	26/04/2018	SmPC, Labelling and PL	
IA/0037	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	24/04/2018	n/a		
IB/0030/G	This was an application for a group of variations. B.II.b.3.z - Change in the manufacturing process of the finished or intermediate product - Other variation B.II.b.4.z - Change in the batch size (including batch size ranges) of the finished product - Other variation	14/11/2017	n/a		
II/0026	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	14/09/2017	n/a		
IB/0027/G	This was an application for a group of variations. B.I.a.1.f - Change in the manufacturer of AS or of a starting material/reagent/intermediate for AS - Changes to quality control testing arrangements for the AS -replacement or addition of a site where batch control/testing takes place B.I.e.5.c - Implementation of changes foreseen in an	16/08/2017	n/a		

	approved change management protocol - For a biological/immunological medicinal product				
IB/0028	B.II.f.1.d - Stability of FP - Change in storage conditions of the finished product or the diluted/reconstituted product	15/08/2017	26/04/2018	SmPC and PL	
IAIN/0029	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	03/08/2017	n/a		
II/0020	Update of section 4.5 of the SmPC in order to revise general information on CYP450/CYP3A4 as a result of data provided by the clinical drug-drug interaction study A2110. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	20/07/2017	26/04/2018	SmPC	In a study in subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).
II/0024	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	06/07/2017	n/a		
PSUSA/10341 /201612	Periodic Safety Update EU Single assessment - secukinumab	06/07/2017	n/a		PRAC Recommendation - maintenance
IB/0025/G	This was an application for a group of variations. 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	29/06/2017	n/a		

	B.II.d.2.d - Change in test procedure for the finished product - Other changes to a test procedure (including replacement or addition)				
II/0021/G	This was an application for a group of variations. Update of section 5.1 of the SmPC in order to add long term (52 week) data from the CLEAR study (CAIN457A2317) and to add new data from a scalp psoriasis study (CAIN457US01). In addition the MAH has taken the occasion to include a correction in section 4.2 of the SmPC to avoid medication errors -the Package Leaflet has been updated accordingly- and in section 5.1 of the SmPC to align the Psoriatic Arthritis Response Criteria (PsARC) definition to the relevant EMA guideline. The MAH has also implemented the latest QRD template version 10.0. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/06/2017	26/04/2018	SmPC, Annex II, Labelling and PL	Statistically significant improvements at Week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks. Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at Week 16 and Week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab. Statistically significant improvements (decreases) at Week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo. A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at Week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who

					continued treatment through to Week 24.
IAIN/0023	B.II.b.1.a - Replacement or addition of a manufacturing site for the FP - Secondary packaging site	24/04/2017	n/a		
PSUSA/10341 /201606	Periodic Safety Update EU Single assessment - secukinumab	26/01/2017	22/03/2017	SmPC and PL	Refer to Scientific conclusions and grounds recommending the variation to terms of the Marketing Authorisation(s)' for PSUSA/10341/201606.
II/0017	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	16/02/2017	n/a		
IB/0016	B.I.e.5.c - Implementation of changes foreseen in an approved change management protocol - For a biological/immunological medicinal product	09/11/2016	n/a		
II/0011	B.I.e.2.z - Design Space - Introduction of a post approval change management protocol related to the AS - Other variation	13/10/2016	n/a		
IA/0014	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	15/08/2016	n/a		
II/0012	B.I.e.2 - Introduction of a post approval change management protocol related to the AS	28/07/2016	n/a		

PSUSA/10341 /201512	Periodic Safety Update EU Single assessment - secukinumab	07/07/2016	n/a		PRAC Recommendation - maintenance
IA/0013	B.II.e.7.b - Change in supplier of packaging components or devices (when mentioned in the dossier) - Replacement or addition of a supplier	24/06/2016	n/a		
II/0008/G	This was an application for a group of variations. Update of section 5.1 of the SmPC in order to add new data from the “CLEAR” study CAIN457A2317 (head-to-head versus Stelara) in moderate to severe plaque psoriasis. Update of section 5.1 of the SmPC in order to add new data from the “TRANSFIGURE” study CAIN457A2312 in moderate to severe palmoplantar plaque psoriasis. Update of section 5.1 of the SmPC in order to add new data from the “GESTURE” study CAIN457A2313 in moderate to severe plaque psoriasis with nail involvement. In addition, section 4.8 of the SmPC was amended with updated exposure data from the 3 studies. C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data C.I.4 - Change(s) in the SPC, Labelling or PL due to new quality, preclinical, clinical or pharmacovigilance data	01/04/2016	22/03/2017	SmPC	The results of study A2317 confirmed the efficacy of secukinumab 300 mg in patients with moderate to severe plaque psoriasis. Superiority to ustekinumab was shown with respect to the results of the primary endpoint at Week 16 and the secondary endpoints available. The results of studies A2312, A2313 at Week 16 showed superior efficacy of secukinumab 300 mg compared to placebo in the treatment of moderate to severe plaque palmoplantar psoriasis and psoriasis with nail involvement, respectively. Disease-related quality of life was also improved in the secukinumab treated patients. The results from study A2313 relate mainly to disease of the fingernails as significant fingernail involvement was among the inclusion criteria and efficacy assessment at Week 16 was too early for toenails. Safety findings in studies A2317, A2312 and A2313 were consistent with the known safety profile of secukinumab.

II/0006	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	25/02/2016	n/a		
IB/0009	B.II.d.1.c - Change in the specification parameters and/or limits of the finished product - Addition of a new specification parameter to the specification with its corresponding test method	18/01/2016	n/a		
PSUSA/10341 /201506	Periodic Safety Update EU Single assessment - secukinumab	14/01/2016	n/a		PRAC Recommendation - maintenance
IB/0007	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	21/12/2015	n/a		
II/0002	Extension of indication to add new indication for Cosentyx in the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional therapy; consequently, SmPC sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 have been revised to include new efficacy and safety information. The Package Leaflet and RMP have 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	22/10/2015	19/11/2015	SmPC and PL	Please refer to the scientific discussion Cosentyx EMEA/H/C/003729/II/0002

II/0001/G	This was an application for a group of variations. Extension of Indication to include new indication for Cosentyx in the treatment alone or in combination with methotrexate (MTX) of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate; as a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, and 5.2 of the SmPC are updated in order to update the safety and efficacy information. The Package Leaflet and RMP have been updated accordingly. Furthermore, the due of the final report for the psoriasis registry in the RMP has been amended and minor editorial changes have been introduced throughout the PI. C.I.6.a - Change(s) to therapeutic indication(s) - Addition of a new therapeutic indication or modification of an approved one C.I.11.z - Introduction of, or change(s) to, the obligations and conditions of a marketing authorisation, including the RMP - Other variation	22/10/2015	19/11/2015	SmPC and PL	Please refer to the Scientific Discussion Cosentyx-H-C-3729-II-01 G
IB/0004/G	This was an application for a group of variations. B.I.b.1.c - Change in the specification parameters and/or limits of an AS, starting material/intermediate/reagent - Addition of a new specification parameter to the specification with its corresponding test method B.I.b.2.a - Change in test procedure for AS or starting	04/08/2015	n/a		

	material/reagent/intermediate - Minor changes to an approved test procedure				
IB/0003/G	This was an application for a group of variations. B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes B.II.e.5.a.2 - Change in pack size of the finished product - Change in the number of units (e.g. tablets, ampoules, etc.) in a pack - Change outside the range of the currently approved pack sizes	17/04/2015	19/11/2015	SmPC, Labelling and PL	