ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg powder for solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial of powder contains 150 mg secukinumab*. After reconstitution, 1 ml of solution contains 150 mg secukinumab.

*Secukinumab is a recombinant fully human monoclonal antibody selective for interleukin-17A. Secukinumab is of the IgG1/κ-class produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder for solution for injection

The powder is a white solid lyophilisate.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis.

Posology

The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at Weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at Week 4. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Consideration should be given to discontinuing treatment in patients who have shown no response up to 16 weeks of treatment. Some patients with initially partial response may subsequently improve with continued treatment beyond 16 weeks.

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children below the age of 18 years have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites. The powder for solution for injection must be reconstituted before use. For instructions on reconstitution of the medicinal product before administration, see section 6.6 and the Instructions for Use in the package leaflet.

4.3 Contraindications

Severe hypersensitivity reactions to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection (e.g. active tuberculosis; see section 4.4).

4.4 Special warnings and precautions for use

Infections

Cosentyx has the potential to increase the risk of infections. In clinical studies, infections have been observed in patients receiving Cosentyx (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of Cosentyx, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and Cosentyx should not be administered until the infection resolves.

No increased susceptibility to tuberculosis was reported from clinical studies. However, Cosentyx should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of Cosentyx in patients with latent tuberculosis.

Crohn's disease

Caution should be exercised when prescribing Cosentyx to patients with Crohn's disease as exacerbations of Crohn's disease, in some cases serious, were observed in clinical studies in both Cosentyx and placebo groups. Patients who are treated with Cosentyx and have Crohn's disease should be followed closely.

Hypersensitivity reactions

If an anaphylactic or other serious allergic reactions occur, administration of Cosentyx should be discontinued immediately and appropriate therapy initiated.

Vaccinations

Live vaccines should not be given concurrently with Cosentyx.

Patients receiving Cosentyx may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that Cosentyx does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of Cosentyx in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with Cosentyx (see also section 4.4).

No interaction studies have been performed in humans. There is no direct evidence for the role of IL-17A in the expression of CYP450 enzymes. The formation of some CYP450 enzymes is suppressed by increased levels of cytokines during chronic inflammation. Thus, anti-inflammatory treatments, such as with the IL-17A inhibitor secukinumab, may result in normalisation of CYP450 levels with accompanying lower exposure of CYP450-metabolised co-medications. Therefore, a clinically relevant effect on CYP450 substrates with a narrow therapeutic index, where the dose is individually adjusted (e.g. warfarin) cannot be excluded. On initiation of secukinumab therapy in patients being treated with these types of medicinal products, therapeutic monitoring should be considered.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx in pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of Cosentyx therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

A total of 4,498 patients have been treated with Cosentyx in blinded and open-label clinical studies in various indications (plaque psoriasis and other autoimmune conditions). Of these, 1,900 patients were exposed to Cosentyx for at least one year, representing 3,588 patient years of exposure.

Four placebo-controlled phase III studies in plaque psoriasis were pooled to evaluate the safety of Cosentyx in comparison to placebo up to 12 weeks after treatment initiation. In total, 2,076 patients were evaluated (692 patients on 150 mg, 690 patients on 300 mg and 694 patients on placebo).

The most frequently reported adverse drug reactions (ADRs) were upper respiratory tract infections (most frequently nasopharyngitis, rhinitis). Most of the reactions were mild or moderate in severity.

Tabulated list of adverse reactions

ADRs from clinical studies (Table 1) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Table 1 List of adverse reactions in clinical studies[1)]

System Organ Class		**Cosentyx**		**Placebo** (N=694) n (%)
		300 mg (N=690) n (%)	150 mg (N=692) n (%)	
Infections and infestations				
Very common	Upper respiratory tract infections	117 (17.0)	129 (18.6)	72 (10.4)
Common	Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)
Uncommon	Oral candidiasis	4 (0.6)	1 (0.1)	1 (0.1)
Uncommon	Tinea pedis	5 (0.7)	5 (0.7)	0 (0)
Uncommon	Otitis externa	5 (0.7)	3 (0.4)	0 (0)
Blood and lymphatic system disorders				
Uncommon	Neutropenia	2 (0.3)	1 (0.1)	0 (0)
Eye disorders				
Uncommon	Conjunctivitis	5 (0.7)	2 (0.3)	1 (0.1)
Respiratory, thoracic and mediastinal disorders				
Common	Rhinorrhoea	8 (1.2)	2 (0.3)	1 (0.1)
Gastrointestinal disorders				
Common	Diarrhoea	28 (4.1)	18 (2.6)	10 (1.4)
Skin and subcutaneous tissue disorders				
Common	Urticaria	4 (0.6)	8 (1.2)	1 (0.1)

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis patients exposed to 300 mg, 150 mg or placebo up to 12 weeks treatment duration
Note: A single case of anaphylactic reaction was observed in a non-psoriasis study as outlined below.

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with Cosentyx and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with Cosentyx compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with Cosentyx and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3,430 patients treated with Cosentyx for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with Cosentyx (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with Cosentyx (0.015 per patient-year of follow-up).

Neutropenia
Neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE Grade 3) was reported in 18 out of 3,430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of Cosentyx were reported in the remaining 3 cases.

Hypersensitivity reactions
In clinical studies, urticaria and one case of anaphylactic reaction to Cosentyx were observed (see also section 4.4).

Immunogenicity
Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No cases of overdose have been reported in clinical studies.

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Clinical efficacy and safety

The safety and efficacy of Cosentyx were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of Cosentyx 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a “retreatment as needed” regimen [SCULPTURE].

Of the 2,403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis Study 1 (ERASURE) evaluated 738 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Psoriasis Study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both Study 1 and Study 2, patients randomised to receive placebo who were non-responders at Week 12 then crossed over to receive Cosentyx (either 150 mg or 300 mg) at Weeks 12, 13, 14, and 15, followed by the same dose every month starting at Week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis Study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of Cosentyx self-administration via the pre-filled syringe. Psoriasis Study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of Cosentyx self-administration via the pre-filled pen. In both Study 3 and Study 4, patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Patients were also randomised to receive placebo at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4.

Psoriasis Study 5 (SCULPTURE) evaluated 966 patients. All patients received Cosentyx 150 mg or 300 mg doses at Weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at Week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at Week 12 (see Tables 2 and 3). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at Week 16, therefore this dose is recommended.

Table 2 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in Psoriasis Studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

		Week 12		Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-

Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 3 Summary of clinical response on Psoriasis Study 2 (FIXTURE)

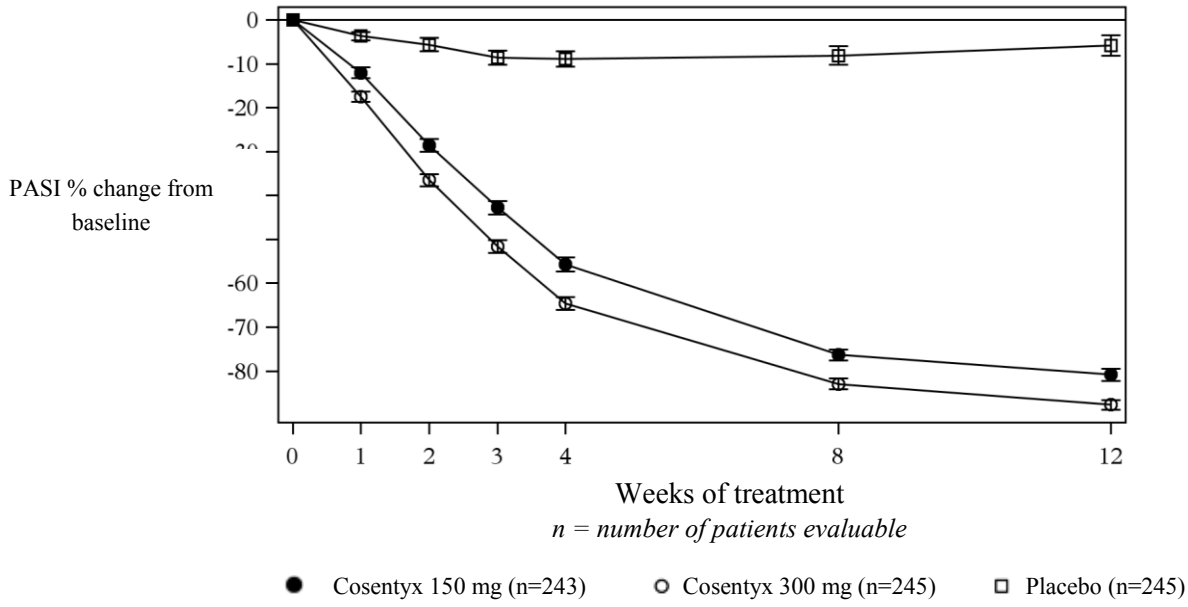
	Week 12				**Week 16**			**Week 52**		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 "clear" or "almost clear" response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p values versus etanercept: $p=0.0250$

Cosentyx was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Cosentyx was associated with a fast onset of efficacy with a 50% reduction in mean PASI by Week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in Study 1 (ERASURE)



Quality of life/patient-reported outcomes
Statistically significant improvements at Week 12 (Studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at Week 12. These improvements were maintained for 52 weeks (Studies 1 and 2).

Forty percent of the participants in Studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at Week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years (see section 4.2 for information on paediatric use).

The European Medicines Agency has deferred the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from 6 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Elderly patients

Of the 3,430 plaque psoriasis patients exposed to Cosentyx in clinical studies, a total of 230 were 65 years of age or older and 32 patients were 75 years of age or older.

Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment

No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact Cosentyx, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of Cosentyx.

5.3 Preclinical safety data

Non-clinical data revealed no special risks for humans based on tissue cross-reactivity testing, safety pharmacology, repeated dose and reproductive toxicity studies performed with secukinumab or a murine anti-murine IL-17A antibody.

Since secukinumab binds to cynomolgus monkey and human IL-17A, its safety was studied in the cynomolgus monkey. No undesirable effects of secukinumab were seen following subcutaneous administration to cynomolgus monkeys for up to 13 weeks and intravenous administration up to 26 weeks (including pharmacokinetic, pharmacodynamic, immunogenicity and immunotoxicity (e.g. T-cell dependent antibody response and NK cell activity) evaluations). The average serum concentrations observed in monkeys after 13 weekly subcutaneous doses of 150 mg/kg were considerably higher than the predicted average serum concentration expected in psoriatic patients at the highest clinical dose. Antibodies to secukinumab were detected in only one of the exposed animals. No non-specific tissue cross-reactivity was observed when secukinumab was applied to normal human tissue.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

In an embryofoetal development study in cynomolgus monkeys, secukinumab showed no maternal toxicity, embryotoxicity or teratogenicity when administered throughout organogenesis and late gestation.

No undesirable effects of a murine anti-murine IL-17A antibody were seen in fertility and early embryonic development and pre-and postnatal development studies in mice. The high dose used in these studies was in excess of the maximum effective dose in terms of IL-17A suppression and activity (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
L-histidine
L-histidine hydrochloride monohydrate
Polysorbate 80

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

3 years

After reconstitution

Chemical and physical in-use stability has been demonstrated for 24 hours at 2ºC to 8ºC.
From a microbiological point of view, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C).
For storage conditions after reconstitution of the medicinal product, see section 6.3

6.5 Nature and contents of container

Cosentyx is supplied in a colourless glass vial with a grey coated rubber stopper and aluminium cap with a white flip-off component containing 150 mg of secukinumab.

Cosentyx is available in packs containing one vial.

6.6 Special precautions for disposal and other handling

The single-use vial contains 150 mg secukinumab for reconstitution with sterile water for injections. The resulting solution should be clear and colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown. Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled syringe contains 150 mg secukinumab in 1 ml.

*Secukinumab is a recombinant fully human monoclonal antibody selective for interleukin-17A. Secukinumab is of the IgG1/κ-class produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe (injection)

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis.

Posology

The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at Weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at Week 4. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Consideration should be given to discontinuing treatment in patients who have shown no response up to 16 weeks of treatment. Some patients with initially partial response may subsequently improve with continued treatment beyond 16 weeks.

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children below the age of 18 years have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites.

After proper training in subcutaneous injection technique, patients may self-inject Cosentyx if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients should be instructed to inject the full amount of Cosentyx according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.

4.3 Contraindications

Severe hypersensitivity reactions to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection (e.g. active tuberculosis; see section 4.4).

4.4 Special warnings and precautions for use

Infections

Cosentyx has the potential to increase the risk of infections. In clinical studies, infections have been observed in patients receiving Cosentyx (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of Cosentyx, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and Cosentyx should not be administered until the infection resolves.

No increased susceptibility to tuberculosis was reported from clinical studies. However, Cosentyx should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of Cosentyx in patients with latent tuberculosis.

Crohn’s disease

Caution should be exercised when prescribing Cosentyx to patients with Crohn’s disease as exacerbations of Crohn’s disease, in some cases serious, were observed in clinical studies in both Cosentyx and placebo groups. Patients who are treated with Cosentyx and have Crohn’s disease should be followed closely.

Hypersensitivity reactions

If an anaphylactic or other serious allergic reactions occur, administration of Cosentyx should be discontinued immediately and appropriate therapy initiated.

Latex-sensitive individuals

The removable needle cap of the Cosentyx pre-filled syringe contains a derivative of natural rubber latex. No natural rubber latex has to date been detected in the removable needle cap. Nevertheless, the use of Cosentyx pre-filled syringes in latex-sensitive individuals has not been studied and there is therefore a potential risk of hypersensitivity reactions which cannot be completely ruled out.

Vaccinations

Live vaccines should not be given concurrently with Cosentyx.

Patients receiving Cosentyx may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that Cosentyx does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of Cosentyx in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with Cosentyx (see also section 4.4).

No interaction studies have been performed in humans. There is no direct evidence for the role of IL-17A in the expression of CYP450 enzymes. The formation of some CYP450 enzymes is suppressed by increased levels of cytokines during chronic inflammation. Thus, anti-inflammatory treatments, such as with the IL-17A inhibitor secukinumab, may result in normalisation of CYP450 levels with accompanying lower exposure of CYP450-metabolised co-medications. Therefore, a clinically relevant effect on CYP450 substrates with a narrow therapeutic index, where the dose is individually adjusted (e.g. warfarin) cannot be excluded. On initiation of secukinumab therapy in patients being treated with these types of medicinal products, therapeutic monitoring should be considered.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx in pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of Cosentyx therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

A total of 4,498 patients have been treated with Cosentyx in blinded and open-label clinical studies in various indications (plaque psoriasis and other autoimmune conditions). Of these, 1,900 patients were exposed to Cosentyx for at least one year, representing 3,588 patient years of exposure.

Four placebo-controlled phase III studies in plaque psoriasis were pooled to evaluate the safety of Cosentyx in comparison to placebo up to 12 weeks after treatment initiation. In total, 2,076 patients were evaluated (692 patients on 150 mg, 690 patients on 300 mg and 694 patients on placebo).

The most frequently reported adverse drug reactions (ADRs) were upper respiratory tract infections (most frequently nasopharyngitis, rhinitis). Most of the reactions were mild or moderate in severity.

Tabulated list of adverse reactions

ADRs from clinical studies (Table 1) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Table 1 List of adverse reactions in clinical studies[1)]

System Organ Class		**Cosentyx**		**Placebo** (N=694) n (%)
		300 mg (N=690) n (%)	150 mg (N=692) n (%)	
Infections and infestations				
Very common	Upper respiratory tract infections	117 (17.0)	129 (18.6)	72 (10.4)
Common	Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)
Uncommon	Oral candidiasis	4 (0.6)	1 (0.1)	1 (0.1)
Uncommon	Tinea pedis	5 (0.7)	5 (0.7)	0 (0)
Uncommon	Otitis externa	5 (0.7)	3 (0.4)	0 (0)
Blood and lymphatic system disorders				
Uncommon	Neutropenia	2 (0.3)	1 (0.1)	0 (0)
Eye disorders				
Uncommon	Conjunctivitis	5 (0.7)	2 (0.3)	1 (0.1)
Respiratory, thoracic and mediastinal disorders				
Common	Rhinorrhoea	8 (1.2)	2 (0.3)	1 (0.1)
Gastrointestinal disorders				
Common	Diarrhoea	28 (4.1)	18 (2.6)	10 (1.4)
Skin and subcutaneous tissue disorders				
Common	Urticaria	4 (0.6)	8 (1.2)	1 (0.1)

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis patients exposed to 300 mg, 150 mg or placebo up to 12 weeks treatment duration
Note: A single case of anaphylactic reaction was observed in a non-psoriasis study as outlined below.

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with Cosentyx and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with Cosentyx compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with Cosentyx and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3,430 patients treated with Cosentyx for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with Cosentyx (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with Cosentyx (0.015 per patient-year of follow-up).

Neutropenia
Neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE Grade 3) was reported in 18 out of 3,430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of Cosentyx were reported in the remaining 3 cases.

Hypersensitivity reactions
In clinical studies, urticaria and one case of anaphylactic reaction to Cosentyx were observed (see also section 4.4).

Immunogenicity
Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No cases of overdose have been reported in clinical studies.

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Clinical efficacy and safety

The safety and efficacy of Cosentyx were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of Cosentyx 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2,403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis Study 1 (ERASURE) evaluated 738 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Psoriasis Study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both Study 1 and Study 2, patients randomised to receive placebo who were non-responders at Week 12 then crossed over to receive Cosentyx (either 150 mg or 300 mg) at Weeks 12, 13, 14, and 15, followed by the same dose every month starting at Week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis Study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of Cosentyx self-administration via the pre-filled syringe. Psoriasis Study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of Cosentyx self-administration via the pre-filled pen. In both Study 3 and Study 4, patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Patients were also randomised to receive placebo at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4.

Psoriasis Study 5 (SCULPTURE) evaluated 966 patients. All patients received Cosentyx 150 mg or 300 mg doses at Weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at Week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at Week 12 (see Tables 2 and 3). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at Week 16, therefore this dose is recommended.

Table 2 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in Psoriasis Studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

	Week 12			Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 3 Summary of clinical response on Psoriasis Study 2 (FIXTURE)

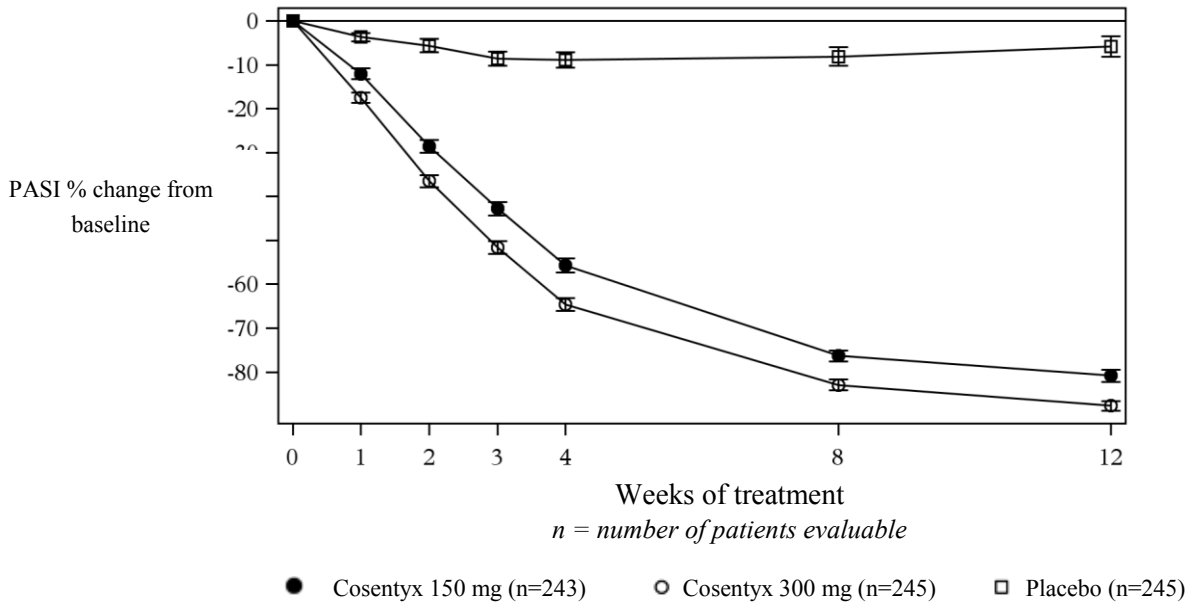
	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 “clear” or “almost clear” response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p values versus etanercept: p=0.0250

Cosentyx was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Cosentyx was associated with a fast onset of efficacy with a 50% reduction in mean PASI by Week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in Study 1 (ERASURE)



Quality of life/patient-reported outcomes
Statistically significant improvements at Week 12 (Studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at Week 12. These improvements were maintained for 52 weeks (Studies 1 and 2).

Forty percent of the participants in Studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at Week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years (see section 4.2 for information on paediatric use).

The European Medicines Agency has deferred the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from 6 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Elderly patients

Of the 3,430 plaque psoriasis patients exposed to Cosentyx in clinical studies, a total of 230 were 65 years of age or older and 32 patients were 75 years of age or older.

Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment

No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact Cosentyx, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of Cosentyx.

5.3 Preclinical safety data

Non-clinical data revealed no special risks for humans based on tissue cross-reactivity testing, safety pharmacology, repeated dose and reproductive toxicity studies performed with secukinumab or a murine anti-murine IL-17A antibody.

Since secukinumab binds to cynomolgus monkey and human IL-17A, its safety was studied in the cynomolgus monkey. No undesirable effects of secukinumab were seen following subcutaneous administration to cynomolgus monkeys for up to 13 weeks and intravenous administration up to 26 weeks (including pharmacokinetic, pharmacodynamic, immunogenicity and immunotoxicity (e.g. T-cell dependent antibody response and NK cell activity) evaluations). The average serum concentrations observed in monkeys after 13 weekly subcutaneous doses of 150 mg/kg were

considerably higher than the predicted average serum concentration expected in psoriatic patients at the highest clinical dose. Antibodies to secukinumab were detected in only one of the exposed animals. No non-specific tissue cross-reactivity was observed when secukinumab was applied to normal human tissue.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

In an embryofoetal development study in cynomolgus monkeys, secukinumab showed no maternal toxicity, embryotoxicity or teratogenicity when administered throughout organogenesis and late gestation.

No undesirable effects of a murine anti-murine IL-17A antibody were seen in fertility and early embryonic development and pre-and postnatal development studies in mice. The high dose used in these studies was in excess of the maximum effective dose in terms of IL-17A suppression and activity (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trehalose dihydrate
L-histidine
L-histidine hydrochloride monohydrate
L-methionine
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Store the syringes in the original package in order to protect from light.

6.5 Nature and contents of container

Cosentyx is supplied in a pre-filled 1 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber assembled in a passive safety device of polycarbonate.

Cosentyx is available in packs containing 1 or 2 pre-filled syringes.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled syringe for individual use. Do not shake or freeze the syringe. The syringe should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Prior to use, a visual inspection of the pre-filled syringe is recommended. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/002
EU/1/14/980/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each pre-filled pen contains 150 mg secukinumab in 1 ml.

*Secukinumab is a recombinant fully human monoclonal antibody selective for interleukin-17A. Secukinumab is of the IgG1/κ-class produced in Chinese Hamster Ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection in pre-filled pen (SensoReady pen)

The solution is clear and colourless to slightly yellow.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy.

4.2 Posology and method of administration

Cosentyx is intended for use under the guidance and supervision of a physician experienced in the diagnosis and treatment of psoriasis.

Posology

The recommended dose is 300 mg of secukinumab by subcutaneous injection with initial dosing at Weeks 0, 1, 2 and 3, followed by monthly maintenance dosing starting at Week 4. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

Consideration should be given to discontinuing treatment in patients who have shown no response up to 16 weeks of treatment. Some patients with initially partial response may subsequently improve with continued treatment beyond 16 weeks.

Elderly patients (aged 65 years and over)
No dose adjustment is required (see section 5.2).

Renal impairment / hepatic impairment
Cosentyx has not been studied in these patient populations. No dose recommendations can be made.

Paediatric population
The safety and efficacy of Cosentyx in children below the age of 18 years have not yet been established. No data are available.

Method of administration

Cosentyx is to be administered by subcutaneous injection. If possible, areas of the skin that show psoriasis should be avoided as injection sites.

After proper training in subcutaneous injection technique, patients may self-inject Cosentyx if a physician determines that this is appropriate. However, the physician should ensure appropriate follow-up of patients. Patients should be instructed to inject the full amount of Cosentyx according to the instructions provided in the package leaflet. Comprehensive instructions for administration are given in the package leaflet.

4.3 Contraindications

Severe hypersensitivity reactions to the active substance or to any of the excipients listed in section 6.1.

Clinically important, active infection (e.g. active tuberculosis; see section 4.4).

4.4 Special warnings and precautions for use

Infections

Cosentyx has the potential to increase the risk of infections. In clinical studies, infections have been observed in patients receiving Cosentyx (see section 4.8). Most of these were mild or moderate upper respiratory tract infections such as nasopharyngitis and did not require treatment discontinuation.

Related to the mechanism of action of Cosentyx, non-serious mucocutaneous candida infections were more frequently reported for secukinumab than placebo in the psoriasis clinical studies (3.55 per 100 patient years for secukinumab 300 mg versus 1.00 per 100 patient years for placebo) (see section 4.8).

Caution should be exercised when considering the use of Cosentyx in patients with a chronic infection or a history of recurrent infection.

Patients should be instructed to seek medical advice if signs or symptoms suggestive of an infection occur. If a patient develops a serious infection, the patient should be closely monitored and Cosentyx should not be administered until the infection resolves.

No increased susceptibility to tuberculosis was reported from clinical studies. However, Cosentyx should not be given to patients with active tuberculosis. Anti-tuberculosis therapy should be considered prior to initiation of Cosentyx in patients with latent tuberculosis.

Crohn’s disease

Caution should be exercised when prescribing Cosentyx to patients with Crohn’s disease as exacerbations of Crohn’s disease, in some cases serious, were observed in clinical studies in both Cosentyx and placebo groups. Patients who are treated with Cosentyx and have Crohn’s disease should be followed closely.

Hypersensitivity reactions

If an anaphylactic or other serious allergic reactions occur, administration of Cosentyx should be discontinued immediately and appropriate therapy initiated.

Latex-sensitive individuals

The removable cap of the Cosentyx pre-filled pen contains a derivative of natural rubber latex. No natural rubber latex has to date been detected in the removable cap. Nevertheless, the use of Cosentyx pre-filled pens in latex-sensitive individuals has not been studied and there is therefore a potential risk for hypersensitivity reactions which cannot be completely ruled out.

Vaccinations

Live vaccines should not be given concurrently with Cosentyx.

Patients receiving Cosentyx may receive concurrent inactivated or non-live vaccinations. In a study, after *meningococcal* and inactivated *influenza* vaccinations, a similar proportion of healthy volunteers treated with 150 mg of secukinumab and those treated with placebo were able to mount an adequate immune response of at least a 4-fold increase in antibody titres to *meningococcal* and *influenza* vaccines. The data suggest that Cosentyx does not suppress the humoral immune response to the *meningococcal* or *influenza* vaccines.

Concomitant immunosuppressive therapy

In psoriasis studies, the safety and efficacy of Cosentyx in combination with immunosuppressants, including biologics, or phototherapy have not been evaluated (see also section 4.5).

4.5 Interaction with other medicinal products and other forms of interaction

Live vaccines should not be given concurrently with Cosentyx (see also section 4.4).

No interaction studies have been performed in humans. There is no direct evidence for the role of IL-17A in the expression of CYP450 enzymes. The formation of some CYP450 enzymes is suppressed by increased levels of cytokines during chronic inflammation. Thus, anti-inflammatory treatments, such as with the IL-17A inhibitor secukinumab, may result in normalisation of CYP450 levels with accompanying lower exposure of CYP450-metabolised co-medications. Therefore, a clinically relevant effect on CYP450 substrates with a narrow therapeutic index, where the dose is individually adjusted (e.g. warfarin) cannot be excluded. On initiation of secukinumab therapy in patients being treated with these types of medicinal products, therapeutic monitoring should be considered.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

Women of childbearing potential should use an effective method of contraception during treatment and for at least 20 weeks after treatment.

Pregnancy

There are no adequate data from the use of secukinumab in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development (see section 5.3). As a precautionary measure, it is preferable to avoid the use of Cosentyx in pregnancy.

Breast-feeding

It is not known whether secukinumab is excreted in human milk. Immunoglobulins are excreted in human milk and it is not known if secukinumab is absorbed systemically after ingestion. Because of the potential for adverse reactions in nursing infants from secukinumab, a decision on whether to discontinue breast-feeding during treatment and up to 20 weeks after treatment or to discontinue therapy with Cosentyx must be made taking into account the benefit of breast-feeding to the child and the benefit of Cosentyx therapy to the woman.

Fertility

The effect of secukinumab on human fertility has not been evaluated. Animal studies do not indicate direct or indirect harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Cosentyx has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

A total of 4,498 patients have been treated with Cosentyx in blinded and open-label clinical studies in various indications (plaque psoriasis and other autoimmune conditions). Of these, 1,900 patients were exposed to Cosentyx for at least one year, representing 3,588 patient years of exposure.

Four placebo-controlled phase III studies in plaque psoriasis were pooled to evaluate the safety of Cosentyx in comparison to placebo up to 12 weeks after treatment initiation. In total, 2,076 patients were evaluated (692 patients on 150 mg, 690 patients on 300 mg and 694 patients on placebo).

The most frequently reported adverse drug reactions (ADRs) were upper respiratory tract infections (most frequently nasopharyngitis, rhinitis). Most of the reactions were mild or moderate in severity.

Tabulated list of adverse reactions

ADRs from clinical studies (Table 1) are listed by MedDRA system organ class. Within each system organ class, the ADRs are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000).

Table 1 List of adverse reactions in clinical studies[1)]

System Organ Class		**Cosentyx**		**Placebo** (N=694) n (%)
		300 mg (N=690) n (%)	150 mg (N=692) n (%)	
Infections and infestations				
Very common	Upper respiratory tract infections	117 (17.0)	129 (18.6)	72 (10.4)
Common	Oral herpes	9 (1.3)	1 (0.1)	2 (0.3)
Uncommon	Oral candidiasis	4 (0.6)	1 (0.1)	1 (0.1)
Uncommon	Tinea pedis	5 (0.7)	5 (0.7)	0 (0)
Uncommon	Otitis externa	5 (0.7)	3 (0.4)	0 (0)
Blood and lymphatic system disorders				
Uncommon	Neutropenia	2 (0.3)	1 (0.1)	0 (0)
Eye disorders				
Uncommon	Conjunctivitis	5 (0.7)	2 (0.3)	1 (0.1)
Respiratory, thoracic and mediastinal disorders				
Common	Rhinorrhoea	8 (1.2)	2 (0.3)	1 (0.1)
Gastrointestinal disorders				
Common	Diarrhoea	28 (4.1)	18 (2.6)	10 (1.4)
Skin and subcutaneous tissue disorders				
Common	Urticaria	4 (0.6)	8 (1.2)	1 (0.1)

[1)] Placebo-controlled clinical studies (phase III) in plaque psoriasis patients exposed to 300 mg, 150 mg or placebo up to 12 weeks treatment duration
Note: A single case of anaphylactic reaction was observed in a non-psoriasis study as outlined below.

Description of selected adverse reactions

Infections
In the placebo-controlled period of clinical studies in plaque psoriasis (a total of 1,382 patients treated with Cosentyx and 694 patients treated with placebo for up to 12 weeks), infections were reported in 28.7% of patients treated with Cosentyx compared with 18.9% of patients treated with placebo. The majority of infections consisted of non-serious and mild to moderate upper respiratory tract infections, such as nasopharyngitis, which did not necessitate treatment discontinuation. There was an increase in mucosal or cutaneous candidiasis, consistent with the mechanism of action, but the cases were mild or moderate in severity, non-serious, responsive to standard treatment and did not necessitate treatment discontinuation. Serious infections occurred in 0.14% of patients treated with Cosentyx and in 0.3% of patients treated with placebo (see section 4.4).

Over the entire treatment period (a total of 3,430 patients treated with Cosentyx for up to 52 weeks for the majority of patients), infections were reported in 47.5% of patients treated with Cosentyx (0.9 per patient-year of follow-up). Serious infections were reported in 1.2% of patients treated with Cosentyx (0.015 per patient-year of follow-up).

Neutropenia
Neutropenia was more frequently observed with secukinumab than with placebo, but most cases were mild, transient and reversible. Neutropenia <1.0-0.5x10^9/l (CTCAE Grade 3) was reported in 18 out of 3,430 (0.5%) patients on secukinumab, with no dose dependence and no temporal relationship to infections in 15 out of 18 cases. There were no reported cases of more severe neutropenia. Non-serious infections with usual response to standard care and not requiring discontinuation of Cosentyx were reported in the remaining 3 cases.

Hypersensitivity reactions
In clinical studies, urticaria and one case of anaphylactic reaction to Cosentyx were observed (see also section 4.4).

Immunogenicity
Less than 1% of patients treated with Cosentyx developed antibodies to secukinumab up to 52 weeks of treatment. About half of the treatment-emergent anti-drug antibodies were neutralising, but this was not associated with loss of efficacy or pharmacokinetic abnormalities.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

No cases of overdose have been reported in clinical studies.

Doses up to 30 mg/kg (approximately 2000 to 3000 mg) have been administered intravenously in clinical studies without dose-limiting toxicity. In the event of overdose, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions and appropriate symptomatic treatment be instituted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Immunosuppressants, interleukin inhibitors, ATC code: L04AC10

Mechanism of action

Secukinumab is a fully human IgG1/κ monoclonal antibody that selectively binds to and neutralises the proinflammatory cytokine interleukin-17A (IL-17A). Secukinumab works by targeting IL-17A and inhibiting its interaction with the IL-17 receptor, which is expressed on various cell types including keratinocytes. As a result, secukinumab inhibits the release of proinflammatory cytokines, chemokines and mediators of tissue damage and reduces IL-17A-mediated contributions to autoimmune and inflammatory diseases. Clinically relevant levels of secukinumab reach the skin and reduce local inflammatory markers. As a direct consequence treatment with secukinumab reduces erythema, induration and desquamation present in plaque psoriasis lesions.

IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. IL-17A plays a key role in the pathogenesis of plaque psoriasis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients.

Pharmacodynamic effects

Serum levels of total IL-17A (free and secukinumab-bound IL-17A) are initially increased in patients receiving secukinumab. This is followed by a slow decrease due to reduced clearance of secukinumab-bound IL-17A, indicating that secukinumab selectively captures free IL-17A, which plays a key role in the pathogenesis of plaque psoriasis.

In a study with secukinumab, infiltrating epidermal neutrophils and various neutrophil-associated markers that are increased in lesional skin of plaque psoriasis patients were significantly reduced after one to two weeks of treatment.

Clinical efficacy and safety

The safety and efficacy of Cosentyx were assessed in four randomised, double-blind, placebo-controlled phase III studies in patients with moderate to severe plaque psoriasis who were candidates for phototherapy or systemic therapy [ERASURE, FIXTURE, FEATURE, JUNCTURE]. The efficacy and safety of Cosentyx 150 mg and 300 mg were evaluated versus either placebo or etanercept. In addition, one study assessed a chronic treatment regimen versus a "retreatment as needed" regimen [SCULPTURE].

Of the 2,403 patients who were included in the placebo-controlled studies, 79% were biologic-naive, 45% were non-biologic failures and 8% were biologic failures (6% were anti-TNF failures, and 2% were anti-p40 failures). Approximately 15 to 25% of patients in phase III studies had psoriatic arthritis (PsA) at baseline.

Psoriasis Study 1 (ERASURE) evaluated 738 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Psoriasis Study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Patients randomised to etanercept received 50 mg doses twice per week for 12 weeks followed by 50 mg every week. In both Study 1 and Study 2, patients randomised to receive placebo who were non-responders at Week 12 then crossed over to receive Cosentyx (either 150 mg or 300 mg) at Weeks 12, 13, 14, and 15, followed by the same dose every month starting at Week 16. All patients were followed for up to 52 weeks following first administration of study treatment.

Psoriasis Study 3 (FEATURE) evaluated 177 patients using a pre-filled syringe compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of Cosentyx self-administration via the pre-filled syringe. Psoriasis Study 4 (JUNCTURE) evaluated 182 patients using a pre-filled pen compared with placebo after 12 weeks of treatment to assess the safety, tolerability, and usability of Cosentyx self-administration via the pre-filled pen. In both Study 3 and Study 4, patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4. Patients were also randomised to receive placebo at Weeks 0, 1, 2, and 3, followed by the same dose every month starting at Week 4.

Psoriasis Study 5 (SCULPTURE) evaluated 966 patients. All patients received Cosentyx 150 mg or 300 mg doses at Weeks 0, 1, 2, 3, 4, 8 and 12 and then were randomised to receive either a maintenance regimen of the same dose every month starting at Week 12 or a "retreatment as needed" regimen of the same dose. Patients randomised to "retreatment as needed" did not achieve adequate maintenance of response and therefore a fixed monthly maintenance regimen is recommended.

The co-primary endpoints in the placebo and active-controlled studies were the proportion of patients who achieved a PASI 75 response and IGA mod 2011 "clear" or "almost clear" response versus placebo at Week 12 (see Tables 2 and 3). The 300 mg dose provided improved skin clearance particularly for "clear" or "almost clear" skin across the efficacy endpoints of PASI 90, PASI 100, and IGA mod 2011 0 or 1 response across all studies with peak effects seen at Week 16, therefore this dose is recommended.

Table 2 Summary of PASI 50/75/90/100 & IGA* mod 2011 "clear" or "almost clear" clinical response in Psoriasis Studies 1, 3 and 4 (ERASURE, FEATURE and JUNCTURE)

	Week 12			Week 16		Week 52	
	Placebo	**150 mg**	**300 mg**	**150 mg**	**300 mg**	**150 mg**	**300 mg**
Study 1							
Number of patients	246	244	245	244	245	244	245
PASI 50 response n (%)	22 (8.9%)	203 (83.5%)	222 (90.6%)	212 (87.2%)	224 (91.4%)	187 (77%)	207 (84.5%)
PASI 75 response n (%)	11 (4.5%)	174 (71.6%)**	200 (81.6%)**	188 (77.4%)	211 (86.1%)	146 (60.1%)	182 (74.3%)
PASI 90 response n (%)	3 (1.2%)	95 (39.1%)**	145 (59.2%)**	130 (53.5%)	171 (69.8%)	88 (36.2%)	147 (60.0%)
PASI 100 response n (%)	2 (0.8%)	31 (12.8%)	70 (28.6%)	51 (21.0%)	102 (41.6%)	49 (20.2%)	96 (39.2%)
IGA mod 2011 "clear" or "almost clear" response n (%)	6 (2.40%)	125 (51.2%)**	160 (65.3%)**	142 (58.2%)	180 (73.5%)	101 (41.4%)	148 (60.4%)
Study 3							
Number of patients	59	59	58	-	-	-	-
PASI 50 response n (%)	3 (5.1%)	51 (86.4%)	51 (87.9%)	-	-	-	-
PASI 75 response n (%)	0 (0.0%)	41 (69.5%)**	44 (75.9%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	27 (45.8%)	35 (60.3%)	-	-	-	-
PASI 100 response n (%)	0 (0.0%)	5 (8.5%)	25 (43.1%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	31 (52.5%)**	40 (69.0%)**	-	-	-	-
Study 4							
Number of patients	61	60	60	-	-	-	-
PASI 50 response n (%)	5 (8.2%)	48 (80.0%)	58 (96.7%)	-	-	-	-
PASI 75 response n (%)	2 (3.3%)	43 (71.7%)**	52 (86.7%)**	-	-	-	-
PASI 90 response n (%)	0 (0.0%)	24 (40.0%)	33 (55.0%)	-	-	-	-
PASI 100 response n(%)	0 (0.0%)	10 (16.7%)	16 (26.7%)	-	-	-	-
IGA mod 2011 "clear" or "almost clear" response n (%)	0 (0.0%)	32 (53.3%)**	44 (73.3%)**	-	-	-	-

* The IGA mod 2011 is a 5-category scale including "0 = clear", "1 = almost clear", "2 = mild", "3 = moderate" or "4 = severe", indicating the physician's overall assessment of the psoriasis severity focusing on induration, erythema and scaling. Treatment success of "clear" or "almost clear" consisted of no signs of psoriasis or normal to pink colouration of lesions, no thickening of the plaque and none to minimal focal scaling.

** p values versus placebo and adjusted for multiplicity: $p<0.0001$.

Table 3 Summary of clinical response on Psoriasis Study 2 (FIXTURE)

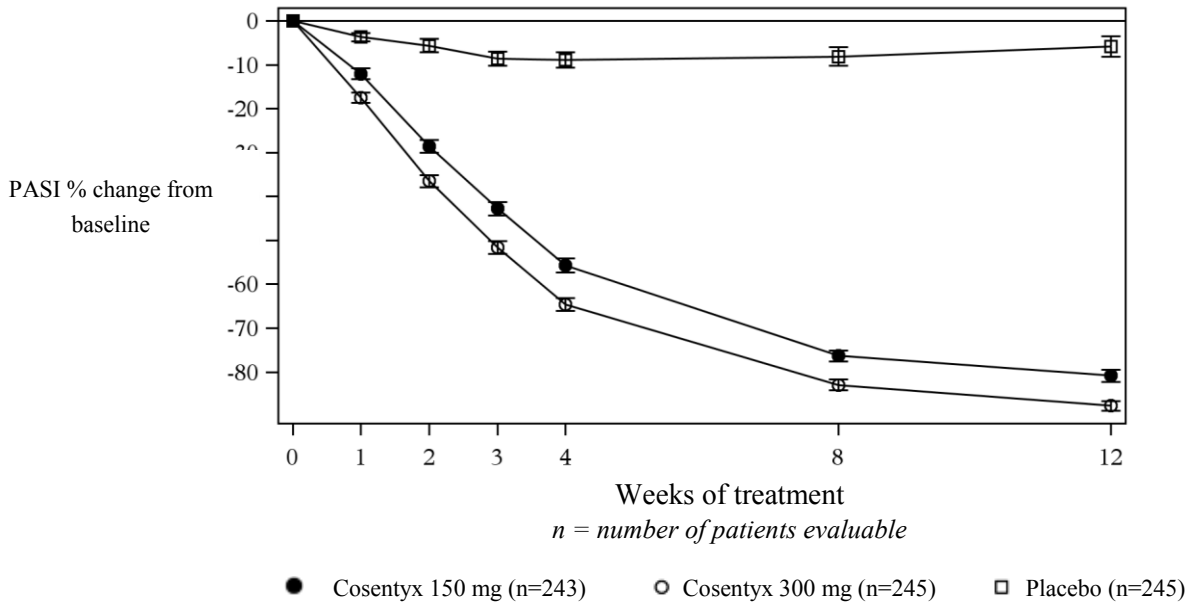
	Week 12				Week 16			Week 52		
	Placebo	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**	**150 mg**	**300 mg**	**Etanercept**
Number of patients	324	327	323	323	327	323	323	327	323	323
PASI 50 response n (%)	49 (15.1%)	266 (81.3%)	296 (91.6%)	226 (70.0%)	290 (88.7%)	302 (93.5%)	257 (79.6%)	249 (76.1%)	274 (84.8%)	234 (72.4%)
PASI 75 response n (%)	16 (4.9%)	219 (67.0%) **	249 (77.1%) **	142 (44.0%)	247 (75.5%)	280 (86.7%)	189 (58.5%)	215 (65.7%)	254 (78.6%)	179 (55.4%)
PASI 90 response n (%)	5 (1.5%)	137 (41.9%)	175 (54.2%)	67 (20.7%)	176 (53.8%)	234 (72.4%)	101 (31.3%)	147 (45.0%)	210 (65.0%)	108 (33.4%)
PASI 100 response n (%)	0 (0%)	47 (14.4%)	78 (24.1%)	14 (4.3%)	84 (25.7%)	119 (36.8%)	24 (7.4%)	65 (19.9%)	117 (36.2%)	32 (9.9%)
IGA mod 2011 "clear" or "almost clear" response n (%)	9 (2.8%)	167 (51.1%) **	202 (62.5%) **	88 (27.2%)	200 (61.2%)	244 (75.5%)	127 (39.3%)	168 (51.4%)	219 (67.8%)	120 (37.2%)

** p values versus etanercept: p=0.0250

Cosentyx was efficacious in systemic treatment-naive, biologic-naive, biologic/anti-TNF-exposed and biologic/anti-TNF-failure patients. Improvements in PASI 75 in patients with concurrent psoriatic arthritis at baseline were similar to those in the overall plaque psoriasis population.

Cosentyx was associated with a fast onset of efficacy with a 50% reduction in mean PASI by Week 3 for the 300 mg dose.

Figure 1 Time course of percentage change from baseline of mean PASI score in Study 1 (ERASURE)



Quality of life/patient-reported outcomes
Statistically significant improvements at Week 12 (Studies 1-4) from baseline compared to placebo were demonstrated in the DLQI (Dermatology Life Quality Index). Mean decreases (improvements) in DLQI from baseline ranged from -10.4 to -11.6 with secukinumab 300 mg, from -7.7 to -10.1 with secukinumab 150 mg, versus -1.1 to -1.9 for placebo at Week 12. These improvements were maintained for 52 weeks (Studies 1 and 2).

Forty percent of the participants in Studies 1 and 2 completed the Psoriasis Symptom Diary©. For the participants completing the diary in each of these studies, statistically significant improvements at Week 12 from baseline compared to placebo in patient-reported signs and symptoms of itching, pain and scaling were demonstrated.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from birth to less than 6 years (see section 4.2 for information on paediatric use).

The European Medicines Agency has deferred the obligation to submit the results of studies with Cosentyx in plaque psoriasis in paediatric patients aged from 6 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Following a single subcutaneous dose of 300 mg as a liquid formulation in healthy volunteers, secukinumab reached peak serum concentrations of 43.2±10.4 µg/ml between 2 and 14 days post dose.

Based on population pharmacokinetic analysis, following a single subcutaneous dose of either 150 mg or 300 mg in plaque psoriasis patients, secukinumab reached peak serum concentrations of 13.7±4.8 µg/ml or 27.3±9.5 µg/ml, respectively, between 5 and 6 days post dose.

After initial weekly dosing during the first month, time to reach the maximum concentration was between 31 and 34 days based on population pharmacokinetic analysis.

On the basis of simulated data, peak concentrations at steady-state ($C_{max,ss}$) following subcutaneous administration of 150 mg or 300 mg were 27.6 µg/ml and 55.2 µg/ml, respectively. Population pharmacokinetic analysis suggests that steady-state is reached after 20 weeks with monthly dosing regimens.

Compared with exposure after a single dose, the population pharmacokinetic analysis showed that patients exhibited a 2-fold increase in peak serum concentrations and area under the curve (AUC) following repeated monthly dosing during maintenance.

Population pharmacokinetic analysis showed that secukinumab was absorbed with an average absolute bioavailability of 73% in patients with plaque psoriasis. Across studies, absolute bioavailabilities in the range between 60 and 77% were calculated.

Distribution

The mean volume of distribution during the terminal phase (V_z) following single intravenous administration ranged from 7.10 to 8.60 litres in plaque psoriasis patients, suggesting that secukinumab undergoes limited distribution to peripheral compartments.

Biotransformation

The majority of IgG elimination occurs via intracellular catabolism, following fluid-phase or receptor mediated endocytosis.

Elimination

Mean systemic clearance (CL) following a single intravenous administration to patients with plaque psoriasis ranged from 0.13 to 0.36 l/day. In a population pharmacokinetic analysis, the mean systemic clearance (CL) was 0.19 l/day in plaque psoriasis patients. The CL was not impacted by gender. Clearance was dose- and time-independent.

The mean elimination half-life, as estimated from population pharmacokinetic analysis, was 27 days in plaque psoriasis patients, ranging from 18 to 46 days across psoriasis studies with intravenous administration.

Linearity/non-linearity

The single and multiple dose pharmacokinetics of secukinumab in plaque psoriasis patients were determined in several studies with intravenous doses ranging from 1x 0.3 mg/kg to 3x 10 mg/kg and with subcutaneous doses ranging from 1x 25 mg to multiple doses of 300 mg. Exposure was dose proportional across all dosing regimens.

Elderly patients

Of the 3,430 plaque psoriasis patients exposed to Cosentyx in clinical studies, a total of 230 were 65 years of age or older and 32 patients were 75 years of age or older.

Based on population pharmacokinetic analysis with a limited number of elderly patients (n=71 for age ≥65 years and n=7 for age ≥75 years), clearance in elderly patients and patients less than 65 years of age was similar.

Patients with renal or hepatic impairment

No pharmacokinetic data are available in patients with renal or hepatic impairment. The renal elimination of intact Cosentyx, an IgG monoclonal antibody, is expected to be low and of minor importance. IgGs are mainly eliminated via catabolism and hepatic impairment is not expected to influence clearance of Cosentyx.

5.3 Preclinical safety data

Non-clinical data revealed no special risks for humans based on tissue cross-reactivity testing, safety pharmacology, repeated dose and reproductive toxicity studies performed with secukinumab or a murine anti-murine IL-17A antibody.

Since secukinumab binds to cynomolgus monkey and human IL-17A, its safety was studied in the cynomolgus monkey. No undesirable effects of secukinumab were seen following subcutaneous administration to cynomolgus monkeys for up to 13 weeks and intravenous administration up to 26 weeks (including pharmacokinetic, pharmacodynamic, immunogenicity and immunotoxicity (e.g. T-cell dependent antibody response and NK cell activity) evaluations). The average serum concentrations observed in monkeys after 13 weekly subcutaneous doses of 150 mg/kg were considerably higher than the predicted average serum concentration expected in psoriatic patients at the highest clinical dose. Antibodies to secukinumab were detected in only one of the exposed animals. No non-specific tissue cross-reactivity was observed when secukinumab was applied to normal human tissue.

Animal studies have not been conducted to evaluate the carcinogenic potential of secukinumab.

In an embryofoetal development study in cynomolgus monkeys, secukinumab showed no maternal toxicity, embryotoxicity or teratogenicity when administered throughout organogenesis and late gestation.

No undesirable effects of a murine anti-murine IL-17A antibody were seen in fertility and early embryonic development and pre-and postnatal development studies in mice. The high dose used in these studies was in excess of the maximum effective dose in terms of IL-17A suppression and activity (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Trehalose dihydrate
L-histidine
L-histidine hydrochloride monohydrate
L-methionine
Polysorbate 80
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Store the pens in the original package in order to protect from light.

6.5 Nature and contents of container

Cosentyx is supplied in a single-use pre-filled syringe assembled into a triangular-shaped pen with transparent window and label (SensoReady pen). The pre-filled syringe inside the pen is a 1 ml glass syringe with a FluroTec-coated plunger stopper, staked 27G x ½″ needle and rigid needle shield of styrene butadiene rubber.

Cosentyx is available in packs containing 1 or 2 pre-filled pens.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Cosentyx 150 mg solution for injection is supplied in a single-use pre-filled pen for individual use. Do not shake or freeze the pen. The pen should be taken out of the refrigerator 20 minutes before injecting to allow it to reach room temperature.

Prior to use, a visual inspection of the pre-filled pen is recommended. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. Detailed instructions for use are provided in the package leaflet.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/004
EU/1/14/980/005

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Novartis Pharma S.A.S.
Centre de Biotechnologie
8, rue de l'Industrie
F-68330 Huningue
France

Name and address of the manufacturer responsible for batch release

Novartis Pharma GmbH
Roonstraße 25
D-90429 Nuremberg
Germany

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation. Subsequently, the marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – vial

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg powder for solution for injection
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One vial contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.

3. LIST OF EXCIPIENTS

Also contains: Sucrose, L-histidine, L-histidine hydrochloride monohydrate, polysorbate 80.

4. PHARMACEUTICAL FORM AND CONTENTS

Powder for solution for injection

1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg powder for solution for injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – pre-filled syringe

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled syringe contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled syringe
2 pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled syringe in the outer carton in order to protect from light.
Keep the pre-filled syringes in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/002	Pack containing 1 pre-filled syringe
EU/1/14/980/003	Pack containing 2 pre-filled syringes

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER OF PRE-FILLED SYRINGE

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled syringe
secukinumab

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

SYRINGE LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg injection
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON – pre-filled pen

1. NAME OF THE MEDICINAL PRODUCT

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

One pre-filled pen contains 150 mg secukinumab in 1 ml of solution.

3. LIST OF EXCIPIENTS

Also contains: Trehalose dihydrate, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80, water for injections.

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

1 pre-filled SensoReady pen
2 pre-filled SensoReady pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Subcutaneous use
Read the package leaflet before use.
Single use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator. Do not freeze.
Keep the pre-filled SensoReady pen in the outer carton in order to protect from light.
Keep the pre-filled SensoReady pens in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/14/980/004	Pack containing 1 pre-filled SensoReady pen
EU/1/14/980/005	Pack containing 2 pre-filled SensoReady pens

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Cosentyx 150 mg

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

PEN LABEL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Cosentyx 150 mg solution for injection in pre-filled pen
secukinumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

SensoReady pen

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

Cosentyx 150 mg powder for solution for injection

Secukinumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain proteins in the body.

Cosentyx belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis.

Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults with moderate to severe plaque psoriasis.

Using Cosentyx will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Tell your doctor or pharmacist before using Cosentyx:
- if you currently have an infection or if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have Crohn's disease.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children and adolescents (under 18 years of age) because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy and breast-feeding
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose. Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx has no or negligible influence on the ability to drive and use machines.

3. How to use Cosentyx

Cosentyx is given via injection under your skin (known as a subcutaneous injection) by a healthcare professional.

Make sure you discuss with your doctor when you will have your injections and your follow-up appointments.

For detailed instructions on how to reconstitute and inject Cosentyx, see "Instructions for use of Cosentyx powder for solution for injection" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at Weeks 1, 2 and 3. From Week 4, you will receive monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have missed a Cosentyx injection, talk to your doctor.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects. Your doctor will decide if and when you may restart the treatment:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Some side effects are very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Some side effects are common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- itchy rash (urticaria)
- runny nose (rhinorrhoea)

Some side effects are uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- athlete's foot (tinea pedis)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the outer box or vial after "EXP".

Before reconstitution: Store the vial in the refrigerator between 2°C and 8°C.

After reconstitution: The solution can be used immediately or can be stored at 2°C to 8°C for up to 24 hours. Do not freeze. The solution should be administered within one hour after removal from 2°C to 8°C storage.

This medicine is for single use only. Ask your pharmacist how to dispose of medicines no longer required.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each vial of powder for solution for injection contains 150 mg secukinumab. After reconstitution, 1 ml of solution contains 150 mg secukinumab.
- The other ingredients are sucrose, L-histidine, L-histidine hydrochloride monohydrate and polysorbate 80.

What Cosentyx looks like and contents of the pack
Cosentyx powder for solution for injection is a white solid powder in a glass vial. Cosentyx is supplied in a pack containing one vial.

Marketing Authorisation Holder
Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

Manufacturer
Novartis Pharma GmbH
Roonstraße 25
D-90429 Nuremberg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

България
Novartis Pharma Services Inc.
Тел: +359 2 489 98 28

Česká republika
Novartis s.r.o.
Tel: +420 225 775 111

Danmark
Novartis Healthcare A/S
Tlf: +45 39 16 84 00

Deutschland
Novartis Pharma GmbH
Tel: +49 911 273 0

Eesti
Novartis Pharma Services Inc.
Tel: +372 66 30 810

Ελλάδα
Novartis (Hellas) A.E.B.E.
Τηλ: +30 210 281 17 12

España
Novartis Farmacéutica, S.A.
Tel: +34 93 306 42 00

France
Novartis Pharma S.A.S.
Tél: +33 1 55 47 66 00

Lietuva
Novartis Pharma Services Inc.
Tel: +370 5 269 16 50

Luxembourg/Luxemburg
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

Magyarország
Novartis Hungária Kft. Pharma
Tel.: +36 1 457 65 00

Malta
Novartis Pharma Services Inc.
Tel: +356 2122 2872

Nederland
Novartis Pharma B.V.
Tel: +31 26 37 82 111

Norge
Novartis Norge AS
Tlf: +47 23 05 20 00

Österreich
Novartis Pharma GmbH
Tel: +43 1 86 6570

Polska
Novartis Poland Sp. z o.o.
Tel.: +48 22 375 4888

Portugal
Novartis Farma - Produtos Farmacêuticos, S.A.
Tel: +351 21 000 8600

Hrvatska
Novartis Hrvatska d.o.o.
Tel. +385 1 6274 220

Ireland
Novartis Ireland Limited
Tel: +353 1 260 12 55

Ísland
Vistor hf.
Sími: +354 535 7000

Italia
Novartis Farma S.p.A.
Tel: +39 02 96 54 1

Κύπρος
Novartis Pharma Services Inc.
Τηλ: +357 22 690 690

Latvija
Novartis Pharma Services Inc.
Tel: +371 67 887 070

România
Novartis Pharma Services Romania SRL
Tel: +40 21 31299 01

Slovenija
Novartis Pharma Services Inc.
Tel: +386 1 300 75 50

Slovenská republika
Novartis Slovakia s.r.o.
Tel: +421 2 5542 5439

Suomi/Finland
Novartis Finland Oy
Puh/Tel: +358 (0)10 6133 200

Sverige
Novartis Sverige AB
Tel: +46 8 732 32 00

United Kingdom
Novartis Pharmaceuticals UK Ltd.
Tel: +44 1276 698370

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx powder for solution for injection

The following information is intended for medical or healthcare professionals only.

Store the vial of powder in the refrigerator between 2°C to 8°C.

The single-use vial contains 150 mg secukinumab for reconstitution with sterile water for injections. Do not use the vial after the expiry date shown on the outer box or vial. If it has expired, return the entire pack to the pharmacy.

The preparation of the solution for subcutaneous injection must be done without interruption and ensuring that aseptic technique is used. The preparation time from piercing the stopper until end of reconstitution takes 20 minutes on average and should not exceed 90 minutes.

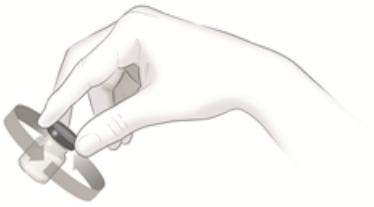
To prepare Cosentyx 150 mg powder for solution for injection, please adhere to the following instructions:

Instructions for reconstitution of Cosentyx 150 mg powder for solution for injection:

1. Bring the vial of powder to room temperature and ensure that the sterile water for injections is at room temperature.
2. Withdraw slightly more than 1.0 ml sterile water for injections into a 1 ml graduated disposable syringe and adjust to 1.0 ml.
3. Remove the plastic cap from the vial.
4. Insert the syringe needle into the vial containing the powder through the centre of the rubber stopper and reconstitute the powder by slowly injecting 1.0 ml of sterile water for injections into the vial. The stream of sterile water for injections should be directed onto the powder.

5. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.

6. Keep the vial standing at room temperature for a minimum of 10 minutes to allow for dissolution. Note that foaming of the solution may occur.
7. Tilt the vial to an angle of approx. 45° and gently rotate between the fingertips for approx. 1 minute. Do not shake or invert the vial.

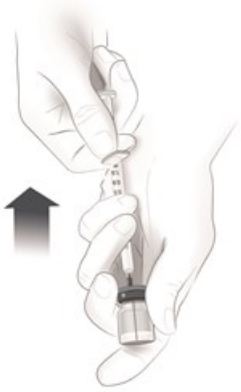


8. Allow the vial to stand undisturbed at room temperature for approximately 5 minutes. The resulting solution should be clear. Its colour may vary from colourless to slightly yellow. Do not use if the lyophilised powder has not fully dissolved or if the liquid contains easily visible particles, is cloudy or is distinctly brown.
9. Prepare the required number of vials (2 vials for the 300 mg dose).

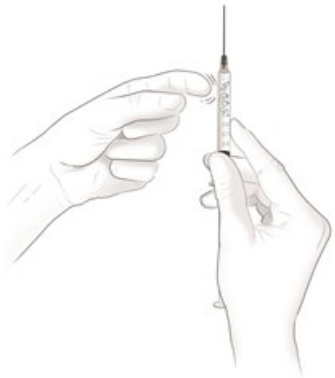
After preparation, the solution for subcutaneous injection can be used immediately or can be stored at 2°C to 8°C for up to 24 hours. Do not freeze. After storage at 2°C to 8°C, the solution should be allowed to come to room temperature for approximately 20 minutes before administration. The solution should be administered within one hour after removal from the 2°C to 8°C storage.

Instructions for administration of Cosentyx solution

1. Tilt the vial to an angle of approximately 45° and position the needle tip at the very bottom of the solution in the vial when drawing the solution into the syringe. DO NOT invert the vial.

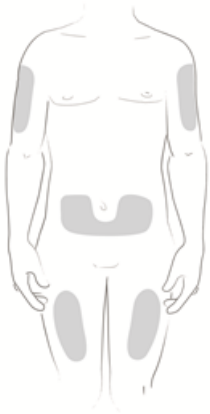


2. Carefully withdraw slightly more than 1.0 ml of the solution for subcutaneous injection from the vial into a 1 ml graduated disposable syringe using a suitable needle (e.g. 21G x 2″). This needle will only be used for withdrawing Cosentyx into the disposable syringe. Prepare the required number of syringes (2 syringes for the 300 mg dose).
3. With the needle pointing upward, gently tap the syringe to move any air bubbles to the top.



4. Replace the attached needle with a 27G x ½″ needle.

5. Expel the air bubbles and advance the plunger to the 1.0 ml mark.
6. Clean the injection site with an alcohol swab.
7. Inject the Cosentyx solution subcutaneously into the front of thighs, lower abdomen (but not the area 5 centimetres around the navel) or outer upper arms. Choose a different site each time an injection is administered. Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.



8. Any remaining solution in the vial must not be used and should be discarded in accordance with local requirements. Vials are for single use only. Dispose of the used syringe in a sharps container (closable, puncture-resistant container). For the safety and health of you and others, needles and used syringes must never be re-used.

Package leaflet: Information for the patient

Cosentyx 150 mg solution for injection in pre-filled syringe

Secukinumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain proteins in the body.

Cosentyx belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis.

Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults with moderate to severe plaque psoriasis.

Using Cosentyx will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Tell your doctor or pharmacist before using Cosentyx:
- if you currently have an infection or if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have ever had an allergic reaction to latex.
- if you have Crohn's disease.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children and adolescents (under 18 years of age) because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy and breast-feeding
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose. Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx has no or negligible influence on the ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of Cosentyx pre-filled syringe" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at Weeks 1, 2 and 3. From Week 4, you will receive monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects. Your doctor will decide if and when you may restart the treatment:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Some side effects are very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Some side effects are common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- itchy rash (urticaria)
- runny nose (rhinorrhoea)

Some side effects are uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- athlete's foot (tinea pedis)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the syringe after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the syringe sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.

This medicine is for single use only. Ask your pharmacist how to dispose of medicines no longer required.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled syringe contains 150 mg secukinumab.
- The other ingredients are trehalose dihydrate, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow. Cosentyx is available in packs containing 1 or 2 pre-filled syringe(s). Not all pack sizes may be marketed.

Marketing Authorisation Holder
Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

Manufacturer
Novartis Pharma GmbH
Roonstraße 25
D-90429 Nuremberg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

България
Novartis Pharma Services Inc.
Тел: +359 2 489 98 28

Česká republika
Novartis s.r.o.
Tel: +420 225 775 111

Danmark
Novartis Healthcare A/S
Tlf: +45 39 16 84 00

Deutschland
Novartis Pharma GmbH
Tel: +49 911 273 0

Eesti
Novartis Pharma Services Inc.
Tel: +372 66 30 810

Ελλάδα
Novartis (Hellas) A.E.B.E.
Τηλ: +30 210 281 17 12

España
Novartis Farmacéutica, S.A.
Tel: +34 93 306 42 00

France
Novartis Pharma S.A.S.
Tél: +33 1 55 47 66 00

Hrvatska
Novartis Hrvatska d.o.o.
Tel. +385 1 6274 220

Lietuva
Novartis Pharma Services Inc.
Tel: +370 5 269 16 50

Luxembourg/Luxemburg
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

Magyarország
Novartis Hungária Kft. Pharma
Tel.: +36 1 457 65 00

Malta
Novartis Pharma Services Inc.
Tel: +356 2122 2872

Nederland
Novartis Pharma B.V.
Tel: +31 26 37 82 111

Norge
Novartis Norge AS
Tlf: +47 23 05 20 00

Österreich
Novartis Pharma GmbH
Tel: +43 1 86 6570

Polska
Novartis Poland Sp. z o.o.
Tel.: +48 22 375 4888

Portugal
Novartis Farma - Produtos Farmacêuticos, S.A.
Tel: +351 21 000 8600

România
Novartis Pharma Services Romania SRL
Tel: +40 21 31299 01

Ireland
Novartis Ireland Limited
Tel: +353 1 260 12 55

Ísland
Vistor hf.
Sími: +354 535 7000

Italia
Novartis Farma S.p.A.
Tel: +39 02 96 54 1

Κύπρος
Novartis Pharma Services Inc.
Τηλ: +357 22 690 690

Latvija
Novartis Pharma Services Inc.
Tel: +371 67 887 070

Slovenija
Novartis Pharma Services Inc.
Tel: +386 1 300 75 50

Slovenská republika
Novartis Slovakia s.r.o.
Tel: +421 2 5542 5439

Suomi/Finland
Novartis Finland Oy
Puh/Tel: +358 (0)10 6133 200

Sverige
Novartis Sverige AB
Tel: +46 8 732 32 00

United Kingdom
Novartis Pharmaceuticals UK Ltd.
Tel: +44 1276 698370

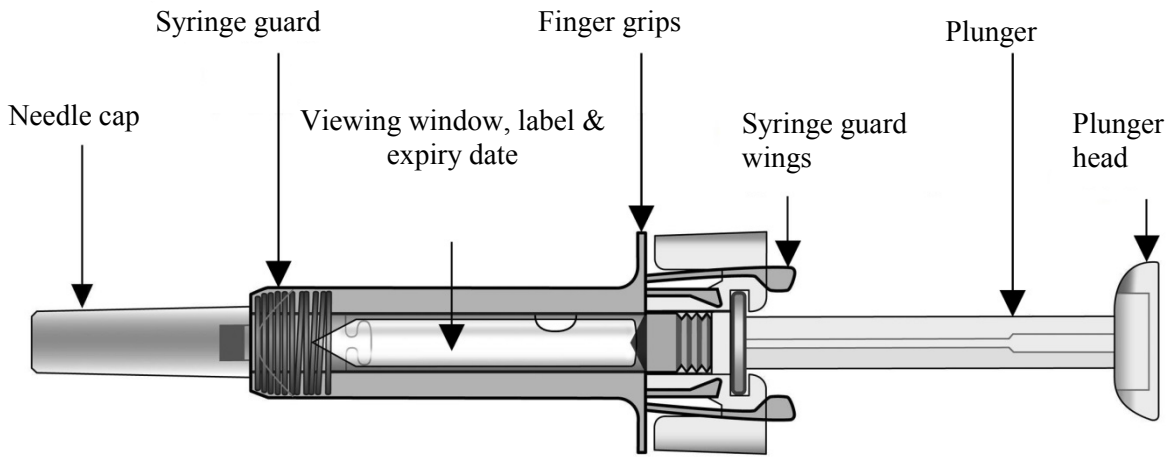
This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of Cosentyx pre-filled syringe

Read ALL the way through these instructions before injecting. It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. The box contains Cosentyx pre-filled syringe(s) individually sealed in a plastic blister.

Your Cosentyx pre-filled syringe



After the medicine has been injected the syringe guard will be activated to cover the needle. This is intended to aid in the protection of healthcare professionals, patients who self-inject doctor-prescribed medicines, and individuals who assist self-injecting patients from accidental needlestick injuries.

What you additionally need for your injection:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Important safety information

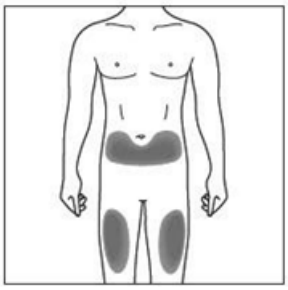
Caution: Keep the syringe out of the sight and reach of children.

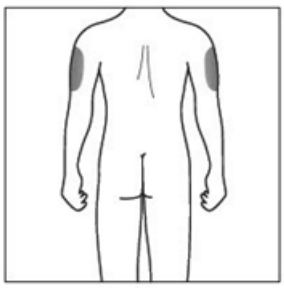
1. The needle cap of the syringe may contain dry rubber (latex), which should not be handled by persons sensitive to this substance.
2. Do not open the sealed outer box until you are ready to use this medicine.
3. Do not use this medicine if either the seal on the outer box or the seal of the blister is broken, as it may not be safe for you to use.
4. Never leave the syringe lying around where others might tamper with it.
5. Do not shake the syringe.
6. Be careful not to touch the syringe guard wings before use. By touching them, the syringe guard may be activated too early.
7. Do not remove the needle cap until just before you give the injection.
8. The syringe cannot be re-used. Dispose of the used syringe immediately after use in a sharps container.

Storage of the Cosentyx pre-filled syringe

1. Store this medicine sealed in its outer box to protect it from light. Store in the refrigerator between 2°C and 8°C. DO NOT FREEZE.
2. Remember to take the syringe out of the refrigerator and allow it to reach room temperature before preparing it for injection (15-30 minutes).
3. Do not use the syringe after the expiry date which is stated on the outer box or syringe label after "EXP". If it has expired, return the entire pack to the pharmacy.

The injection site





The injection site is the place on the body where you are going to use the syringe.

- The recommended site is the front of your thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

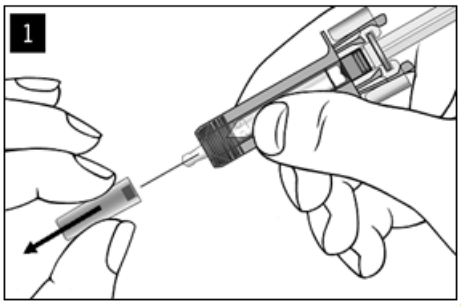
If a caregiver is giving you the injection, the outer upper arms may also be used.

Preparing the Cosentyx pre-filled syringe ready for use

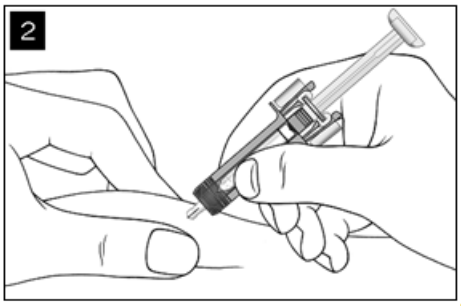
Note: For a 300 mg dose, prepare 2 pre-filled syringes and inject the contents of both.

1. Take the box containing the syringe out of the refrigerator and leave it **unopened** for about 15-30 minutes so that it reaches room temperature.
2. When you are ready to use the syringe, wash your hands thoroughly with soap and water.
3. Clean the injection site with an alcohol swab.
4. Remove the syringe from the outer box and take it out of the blister.
5. Inspect the syringe. The liquid should be clear. Its colour may vary from colourless to slightly yellow. You may see a small air bubble, which is normal. DO NOT USE if the liquid contains easily visible particles, is cloudy or is distinctly brown. DO NOT USE if the syringe is broken. In all these cases, return the entire product pack to the pharmacy.

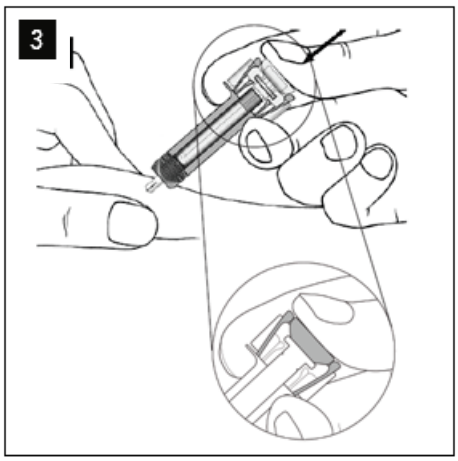
How to use the Cosentyx pre-filled syringe



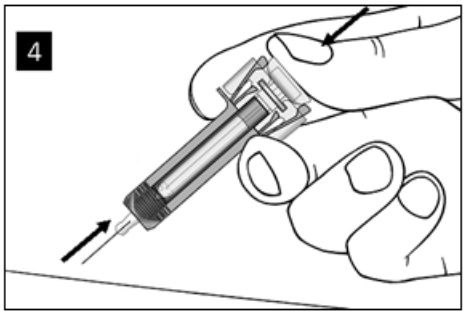
Carefully remove the needle cap from the syringe. Discard the needle cap. You may see a drop of liquid at the end of the needle. This is normal.



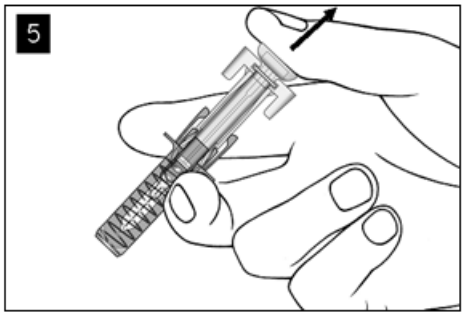
Gently pinch the skin at the injection site and insert the needle as shown. Push the needle all the way in to ensure that the medicine can be fully administered.



Hold the syringe as shown. **Slowly** depress the plunger **as far as it will go** so that the plunger head is completely between the syringe guard wings.
Keep the plunger pressed fully down while you hold the syringe in place for 5 seconds.



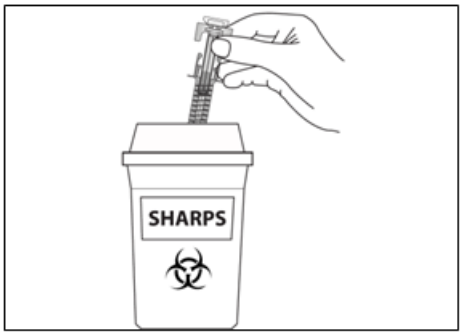
Keep the plunger fully depressed while you carefully lift the needle straight out from the injection site.



Slowly release the plunger and allow the syringe guard to automatically cover the exposed needle.

There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

Disposal instructions



Dispose of the used syringe in a sharps container (closable, puncture resistant container). For the safety and health of you and others, needles and used syringes **must never** be re-used.

Package leaflet: Information for the patient

Cosentyx 150 mg solution for injection in pre-filled pen

Secukinumab

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Cosentyx is and what it is used for

Cosentyx contains the active substance secukinumab. Secukinumab is a monoclonal antibody. Monoclonal antibodies are proteins that recognise and bind specifically to certain proteins in the body.

Cosentyx belongs to a group of medicines called interleukin (IL) inhibitors. This medicine works by neutralising the activity of a protein called IL-17A, which is present at increased levels in diseases such as psoriasis.

Cosentyx is used to treat a skin condition called “plaque psoriasis”, which causes inflammation affecting the skin. Cosentyx reduces the inflammation and other symptoms of the disease. Cosentyx is used in adults with moderate to severe plaque psoriasis.

Using Cosentyx will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

2. What you need to know before you use Cosentyx

Do not use Cosentyx:
- **if you are allergic** to secukinumab or any of the other ingredients of this medicine (listed in section 6).
  If you think you may be allergic, ask your doctor for advice before using Cosentyx.
- **if you have an active infection** which your doctor thinks is important.

Warnings and precautions
Tell your doctor or pharmacist before using Cosentyx:
- if you currently have an infection or if you have long-term or repeated infections.
- if you have tuberculosis.
- if you have ever had an allergic reaction to latex.
- if you have Crohn's disease.
- if you have recently had a vaccination or if you are due to have a vaccination during treatment with Cosentyx.
- if you are receiving any other treatment for psoriasis, such as another immunosuppressant or phototherapy with ultraviolet (UV) light.

Look out for infections and allergic reactions
Cosentyx can potentially cause serious side effects, including infections and allergic reactions. You must look out for signs of these conditions while you are taking Cosentyx.

Stop using Cosentyx and tell your doctor or seek medical help immediately if you notice any signs indicating a possible serious infection or an allergic reaction. Such signs are listed under "Serious side effects" in section 4.

Children and adolescents
Cosentyx is not recommended for children and adolescents (under 18 years of age) because it has not been studied in this age group.

Other medicines and Cosentyx
Tell your doctor or pharmacist:
- if you are taking, have recently taken or might take any other medicines.
- if you have recently had or are due to have a vaccination. You should not be given certain types of vaccines (live vaccines) while using Cosentyx.

Pregnancy and breast-feeding
- It is preferable to avoid the use of Cosentyx in pregnancy. The effects of this medicine in pregnant women are not known. If you are a woman of childbearing potential, you are advised to avoid becoming pregnant and must use adequate contraception while using Cosentyx and for at least 20 weeks after the last Cosentyx dose. Talk to your doctor if you are pregnant, think you may be pregnant or are planning to have a baby.
- Talk to your doctor if you are breast-feeding or are planning to breast-feed. You and your doctor should decide if you will breast-feed or use Cosentyx. You should not do both. After using Cosentyx you should not breast-feed for at least 20 weeks after the last dose.

Driving and using machines
Cosentyx has no or negligible influence on the ability to drive and use machines.

3. How to use Cosentyx

Always use this medicine exactly as your doctor has told you. Check with your doctor, nurse or pharmacist if you are not sure.

Cosentyx is given via injection under your skin (known as a subcutaneous injection). You and your doctor should decide if you should inject Cosentyx yourself.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist. A caregiver may also give you your Cosentyx injection after proper training.

For detailed instructions on how to inject Cosentyx, see "Instructions for use of the Cosentyx SensoReady pen" at the end of this leaflet.

How much Cosentyx is given and for how long
Your doctor will decide how much Cosentyx you need and for how long.

- The recommended dose is 300 mg by subcutaneous injection.
- Each 300 mg dose **is given as two injections of 150 mg**.

After the first dose you will receive further weekly injections at Weeks 1, 2 and 3. From Week 4, you will receive monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Cosentyx is for long-term treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you use more Cosentyx than you should
If you have received more Cosentyx than you should or the dose has been administered sooner than according to your doctor's prescription, inform your doctor.

If you forget to use Cosentyx
If you have forgotten to inject a dose of Cosentyx, inject the next dose as soon as you remember. Then talk to your doctor to discuss when you should inject the next dose.

If you stop using Cosentyx
It is not dangerous to stop using Cosentyx. However, if you stop, your psoriasis symptoms may come back.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Stop using Cosentyx and tell your doctor or seek medical help immediately if you get any of the following side effects. Your doctor will decide if and when you may restart the treatment:

Possible serious infection - the signs may include:
- fever, flu-like symptoms, night sweats
- feeling tired or short of breath, cough which will not go away
- warm, red and painful skin, or a painful skin rash with blisters
- burning sensation when passing urine.

Serious allergic reaction - the signs may include:
- difficulty breathing or swallowing
- low blood pressure, which can cause dizziness or light-headedness
- swelling of the face, lips, tongue or throat
- severe itching of the skin, with a red rash or raised bumps.

Other side effects
Most of the following side effects are mild to moderate. If any of these side effects becomes severe, tell your doctor, pharmacist or nurse.

Some side effects are very common (may affect more than 1 in 10 people):
- upper respiratory tract infections with symptoms such as sore throat and stuffy nose (nasopharyngitis, rhinitis)

Some side effects are common (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- itchy rash (urticaria)
- runny nose (rhinorrhoea)

Some side effects are uncommon (may affect up to 1 in 100 people):
- oral thrush (oral candidiasis)
- signs of low levels of white blood cells, such as fever, sore throat or mouth ulcers due to infections (neutropenia)
- athlete's foot (tinea pedis)
- infection of the external ear (otitis externa)
- discharge from the eye with itching, redness and swelling (conjunctivitis).

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Cosentyx

Keep this medicine out of the sight and reach of children.

Do not use this medicine:
- after the expiry date which is stated on the outer box or the label on the pen after "EXP".
- if the liquid contains easily visible particles, is cloudy or is distinctly brown.

Store the pen sealed in its box to protect from light. Store in the refrigerator between 2°C and 8°C. Do not freeze. Do not shake.

This medicine is for single use only. Ask your pharmacist how to dispose of medicines no longer required.

6. Contents of the pack and other information

What Cosentyx contains
- The active substance is secukinumab. Each pre-filled pen contains 150 mg secukinumab.
- The other ingredients are trehalose dihydrate, L-histidine, L-histidine hydrochloride monohydrate, L-methionine, polysorbate 80 and water for injections.

What Cosentyx looks like and contents of the pack
Cosentyx solution for injection is a clear liquid. Its colour may vary from colourless to slightly yellow. Cosentyx is available in packs containing 1 or 2 pre-filled pen(s). Not all pack sizes may be marketed.

Marketing Authorisation Holder
Novartis Europharm Limited
Frimley Business Park
Camberley GU16 7SR
United Kingdom

Manufacturer
Novartis Pharma GmbH
Roonstraße 25
D-90429 Nuremberg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

България
Novartis Pharma Services Inc.
Тел: +359 2 489 98 28

Česká republika
Novartis s.r.o.
Tel: +420 225 775 111

Danmark
Novartis Healthcare A/S
Tlf: +45 39 16 84 00

Deutschland
Novartis Pharma GmbH
Tel: +49 911 273 0

Eesti
Novartis Pharma Services Inc.
Tel: +372 66 30 810

Ελλάδα
Novartis (Hellas) A.E.B.E.
Τηλ: +30 210 281 17 12

España
Novartis Farmacéutica, S.A.
Tel: +34 93 306 42 00

France
Novartis Pharma S.A.S.
Tél: +33 1 55 47 66 00

Hrvatska
Novartis Hrvatska d.o.o.
Tel. +385 1 6274 220

Lietuva
Novartis Pharma Services Inc.
Tel: +370 5 269 16 50

Luxembourg/Luxemburg
Novartis Pharma N.V.
Tél/Tel: +32 2 246 16 11

Magyarország
Novartis Hungária Kft. Pharma
Tel.: +36 1 457 65 00

Malta
Novartis Pharma Services Inc.
Tel: +356 2122 2872

Nederland
Novartis Pharma B.V.
Tel: +31 26 37 82 111

Norge
Novartis Norge AS
Tlf: +47 23 05 20 00

Österreich
Novartis Pharma GmbH
Tel: +43 1 86 6570

Polska
Novartis Poland Sp. z o.o.
Tel.: +48 22 375 4888

Portugal
Novartis Farma - Produtos Farmacêuticos, S.A.
Tel: +351 21 000 8600

România
Novartis Pharma Services Romania SRL
Tel: +40 21 31299 01

Ireland
Novartis Ireland Limited
Tel: +353 1 260 12 55

Ísland
Vistor hf.
Sími: +354 535 7000

Italia
Novartis Farma S.p.A.
Tel: +39 02 96 54 1

Κύπρος
Novartis Pharma Services Inc.
Τηλ: +357 22 690 690

Latvija
Novartis Pharma Services Inc.
Tel: +371 67 887 070

Slovenija
Novartis Pharma Services Inc.
Tel: +386 1 300 75 50

Slovenská republika
Novartis Slovakia s.r.o.
Tel: +421 2 5542 5439

Suomi/Finland
Novartis Finland Oy
Puh/Tel: +358 (0)10 6133 200

Sverige
Novartis Sverige AB
Tel: +46 8 732 32 00

United Kingdom
Novartis Pharmaceuticals UK Ltd.
Tel: +44 1276 698370

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu

Instructions for use of the Cosentyx SensoReady pen

Cosentyx SensoReady pen 150 mg

Solution for injection in a pre-filled pen

Secukinumab

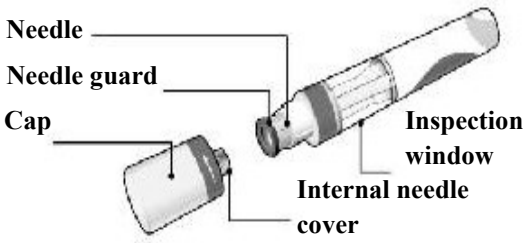
Patient Instructions for Use

Read ALL the way through these instructions before injecting.

These instructions are to help you to inject correctly using the Cosentyx SensoReady pen.

It is important not to try to inject yourself until you have been trained by your doctor, nurse or pharmacist.

Your Cosentyx SensoReady pen:



Cosentyx SensoReady pen shown with the cap removed. **Do not** remove the cap until you are ready to inject.

Store your boxed pen in a **refrigerator** between 2°C and 8°C and **out of the reach of children**.

- **Do not freeze** the pen.
- **Do not shake** the pen.
- Do not use the pen if it has been **dropped** with the cap removed.

For a more comfortable injection, take the pen out of the refrigerator **15-30 minutes before injecting** to allow it to reach room temperature.

What you need for your injection:

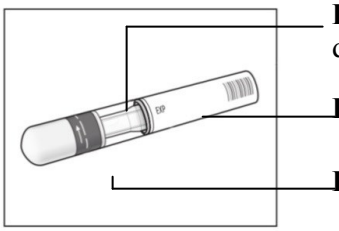
Included in the carton:

A new and unused Cosentyx SensoReady pen (2 pens are needed for a 300 mg dose).

Not included in the carton:

- Alcohol swab.
- Cotton ball or gauze.
- Sharps disposal container.

Before your injection:



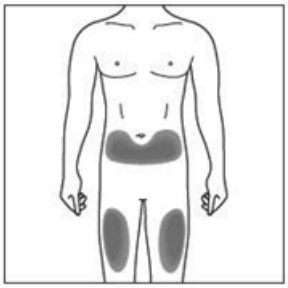
1. Important safety checks before you inject:
The liquid should be clear. Its colour may vary from colourless to slightly yellow.

Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. You may see a small air bubble, which is normal.

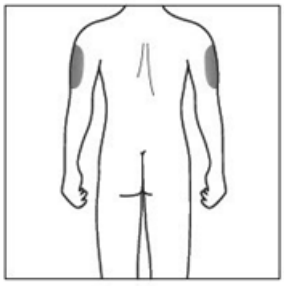
Do not use the pen if the **expiry date** has passed.

Do not use if the **safety seal** has been broken.

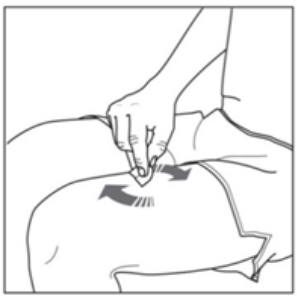
Contact your pharmacist if the pen fails any of these checks.



2a. Choose your injection site:
- The recommended site is the front of the thighs. You may also use the lower abdomen, but **not** the area 5 centimetres around the navel (belly button).
- Choose a different site each time you give yourself an injection.
- Do not inject into areas where the skin is tender, bruised, red, scaly or hard. Avoid areas with scars or stretch marks.

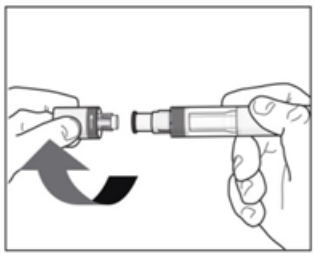


2b. Caregivers and healthcare professionals only:
- If a **caregiver** or **healthcare professional** is giving you your injection, they may also inject into your outer upper arm.



3. Cleaning your injection site:
- Wash your hands with soap and hot water.
- Using a circular motion, clean the injection site with the alcohol swab. Leave it to dry before injecting.
- Do not touch the cleaned area again before injecting.

Your injection:

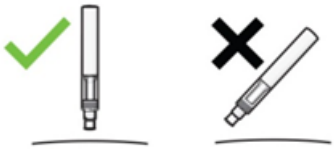


4. Removing the cap:

- Only remove the cap when you are ready to use the pen.
- Twist off the cap in the direction of the arrows.
- Once removed, throw away the cap. **Do not try to re-attach the cap.**
- Use the pen within 5 minutes of removing the cap.

5. Holding your pen:

- Hold the pen at 90 degrees to the cleaned injection site.



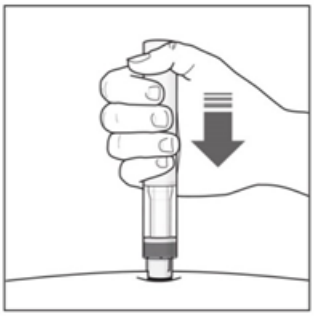
Correct **Incorrect**

YOU MUST READ THIS BEFORE INJECTING.

During the injection you will hear **2 loud clicks**.

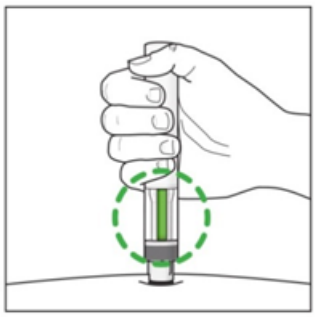
The **1st click** indicates that the injection has started. Several seconds later a **2nd click** will indicate that the injection is **almost** finished.

You must keep holding the pen firmly against your skin until you see a **green indicator** fill the window and stop moving.



6. Starting your injection:

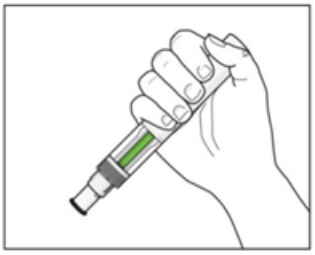
- Press the pen firmly against the skin to start the injection.
- The **1st click** indicates the injection has started.
- **Keep holding** the pen firmly against your skin.
- The **green indicator** shows the progress of the injection.



7. Completing your injection:

- Listen for the **2nd click**. This indicates the injection is **almost** complete.
- Check the **green indicator** fills the window and has stopped moving.
- The pen can now be removed.

After your injection:



8. Check the green indicator fills the window:

- This means the medicine has been delivered. Contact your doctor if the green indicator is not visible.
- There may be a small amount of blood at the injection site. You can press a cotton ball or gauze over the injection site and hold it for 10 seconds. Do not rub the injection site. You may cover the injection site with a small adhesive bandage, if needed.

9. Disposing of your Cosentyx SensoReady pen:

- Dispose of the used pen in a sharps disposal container (i.e. a puncture-resistant closable container, or similar).
- Never try to reuse your pen.