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

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

Psoriatic arthritis
Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

Ankylosing spondylitis
Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional 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 conditions for which Cosentyx is indicated.

Posology

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

Psoriatic arthritis
For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing.

Ankylosing spondylitis
The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3, and 4, followed by monthly maintenance dosing.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Special populations

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

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving Cosentyx. 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).

In a study in subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when Cosentyx was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis).

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 6,804 patients have been treated with Cosentyx in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and other autoimmune conditions). Of these, 3,671 patients were exposed to Cosentyx for at least one year, representing 6,450 patient years of exposure.

Adverse reactions in plaque psoriasis

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.

**Adverse reactions in psoriatic arthritis**

Cosentyx was studied in two placebo-controlled psoriatic arthritis studies with 1,003 patients (703 patients on Cosentyx and 300 patients on placebo) for a total exposure of 1,061 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 456 days in PsA Study 1 and 245 days in PsA Study 2). The safety profile observed in patients with psoriatic arthritis treated with Cosentyx is consistent with the safety profile in psoriasis.

**Adverse reactions in ankylosing spondylitis**

Cosentyx was studied in two placebo-controlled ankylosing spondylitis studies with 590 patients (394 patients on Cosentyx and 196 patients on placebo) for a total of 755 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 469 days in AS Study 1 and 460 days in AS Study 2). The safety profile observed in patients with ankylosing spondylitis treated with Cosentyx is consistent with the safety profile in psoriasis.

**Tabulated list of adverse reactions**

ADRs from psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies as well as from post-marketing experience (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); and not known (cannot be estimated from the available data).

**Table 1 List of adverse reactions in clinical studies and post-marketing experience**

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Very common</td>
<td>Upper respiratory tract infections</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Oral herpes</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Oral candidiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tinea pedis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Otitis externa</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Mucosal and cutaneous candidiasis (including oesophageal candidiasis)</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Uncommon</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Rare</td>
<td>Anaphylactic reactions</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>Uncommon</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal</td>
<td>Common</td>
<td>Rhinorrhoea</td>
</tr>
<tr>
<td>disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Common</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Skin and subcutaneous disorders</td>
<td>Uncommon</td>
<td>Urticaria</td>
</tr>
</tbody>
</table>

1) Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA and AS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA and AS) treatment duration.
**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).

Infection rates observed in psoriatic arthritis and ankylosing spondylitis clinical studies were similar to those observed in the psoriasis studies.

**Neutropenia**

In psoriasis phase 3 clinical studies, 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.

The frequency of neutropenia in psoriatic arthritis and ankylosing spondylitis is similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE Grade 4) were reported.

**Hypersensitivity reactions**

In clinical studies, urticaria and rare cases of anaphylactic reaction to Cosentyx were observed (see also section 4.4).

**Immunogenicity**

In psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies, 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, psoriatic arthritis and ankylosing spondylitis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis.

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.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

Clinical efficacy and safety

Plaque psoriasis

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, 3 and 4, followed by the same dose every month. Psoriasis Study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. 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, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

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)

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients</th>
<th>Placebo PASI 50 response n (%)</th>
<th>Placebo PASI 75 response n (%)</th>
<th>Placebo PASI 90 response n (%)</th>
<th>Placebo PASI 100 response n (%)</th>
<th>IGA mod 2011 “clear” or “almost clear” response n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td></td>
<td>Week 12</td>
<td>Week 16</td>
<td>Week 52</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Placebo 150 mg</td>
<td>300 mg</td>
<td>150 mg 300 mg</td>
<td>150 mg 300 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Number of patients</td>
<td>246</td>
<td>244</td>
<td>245</td>
<td>244</td>
<td>245</td>
</tr>
<tr>
<td></td>
<td>150 mg</td>
<td>(8.9%)</td>
<td>(83.5%)</td>
<td>(90.6%)</td>
<td>(82.7%)</td>
<td>(91.4%)</td>
</tr>
<tr>
<td></td>
<td>300 mg</td>
<td>(8.9%)</td>
<td>(83.5%)</td>
<td>(90.6%)</td>
<td>(82.7%)</td>
<td>(91.4%)</td>
</tr>
<tr>
<td></td>
<td>150 mg</td>
<td>11</td>
<td>174</td>
<td>200</td>
<td>188</td>
<td>211</td>
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<td></td>
<td>300 mg</td>
<td>(4.5%)</td>
<td>(71.6%)**</td>
<td>(81.6%)**</td>
<td>(77.4%)</td>
<td>(86.1%)</td>
</tr>
<tr>
<td></td>
<td>150 mg</td>
<td>3 (1.2%)</td>
<td>95</td>
<td>145</td>
<td>130</td>
<td>171</td>
</tr>
<tr>
<td></td>
<td>300 mg</td>
<td>(3.9%)**</td>
<td>(59.2%)**</td>
<td>(53.5%)**</td>
<td>(69.8%)</td>
<td>(36.2%)</td>
</tr>
<tr>
<td></td>
<td>150 mg</td>
<td>2 (0.8%)</td>
<td>31</td>
<td>70</td>
<td>51</td>
<td>102</td>
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<tr>
<td></td>
<td>300 mg</td>
<td>(12.8%)</td>
<td>(28.6%)</td>
<td>(21.0%)</td>
<td>(41.6%)</td>
<td>(20.2%)</td>
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<tr>
<td></td>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>6 (2.4%)</td>
<td>(51.2%)**</td>
<td>(65.3%)**</td>
<td>(58.2%)</td>
<td>(73.5%)</td>
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<tr>
<td>Study 3</td>
<td>Number of patients</td>
<td>59</td>
<td>59</td>
<td>58</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 50 response n (%)</td>
<td>3 (5.1%)</td>
<td>51</td>
<td>51</td>
<td>-</td>
<td>-</td>
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<tr>
<td></td>
<td>Placebo PASI 75 response n (%)</td>
<td>0 (0.0%)</td>
<td>(86.4%)</td>
<td>(87.9%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 90 response n (%)</td>
<td>0 (0.0%)</td>
<td>(69.5%)**</td>
<td>(75.9%)**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 100 response n (%)</td>
<td>0 (0.0%)</td>
<td>(45.8%)</td>
<td>(60.3%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>0 (0.0%)</td>
<td>(65.3%)**</td>
<td>(69.0%)**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Study 4</td>
<td>Number of patients</td>
<td>61</td>
<td>60</td>
<td>60</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 50 response n (%)</td>
<td>5 (8.2%)</td>
<td>48</td>
<td>58</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 75 response n (%)</td>
<td>2 (3.3%)</td>
<td>43</td>
<td>52</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 90 response n (%)</td>
<td>0 (0.0%)</td>
<td>(71.7%)**</td>
<td>(86.7%)**</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Placebo PASI 100 response n (%)</td>
<td>0 (0.0%)</td>
<td>(40.0%)</td>
<td>(55.0%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>0 (0.0%)</td>
<td>(35.3%)**</td>
<td>(73.3%)**</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* 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)

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

** p values versus etanercept: p=0.0250

In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at Week 16 (primary endpoint), speed of onset of PASI 75 response at Week 4, and long-term PASI 90 response at Week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to Week 52.

Table 4  Summary of clinical response on CLEAR Study

<table>
<thead>
<tr>
<th></th>
<th>Secukinumab 300 mg</th>
<th>Ustekinumab* 300 mg</th>
<th>Secukinumab 300 mg</th>
<th>Ustekinumab* 300 mg</th>
<th>Secukinumab 300 mg</th>
<th>Ustekinumab* 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients</strong></td>
<td>334</td>
<td>335</td>
<td>334</td>
<td>335</td>
<td>334</td>
<td>335</td>
</tr>
<tr>
<td><strong>PASI 75 response n (%)</strong></td>
<td>166 (49.7%)**</td>
<td>69 (20.6%)</td>
<td>311 (93.1%)</td>
<td>276 (82.4%)</td>
<td>306 (91.6%)</td>
<td>262 (78.2%)</td>
</tr>
<tr>
<td><strong>PASI 90 response n (%)</strong></td>
<td>70 (21.0%)</td>
<td>18 (5.4%)</td>
<td>264 (79.0%)**</td>
<td>192 (57.3%)</td>
<td>250 (74.9%)***</td>
<td>203 (60.6%)</td>
</tr>
<tr>
<td><strong>PASI 100 response n (%)</strong></td>
<td>14 (4.2%)</td>
<td>3 (0.9%)</td>
<td>148 (44.3%)</td>
<td>95 (28.4%)</td>
<td>150 (44.9%)</td>
<td>123 (36.7%)</td>
</tr>
<tr>
<td><strong>IGA mod 2011 “clear” or “almost clear” response n (%)</strong></td>
<td>128 (38.3%)</td>
<td>41 (12.2%)</td>
<td>278 (83.2%)</td>
<td>226 (67.5%)</td>
<td>261 (78.1%)</td>
<td>213 (63.6%)</td>
</tr>
</tbody>
</table>

* Patients treated with secukinumab received 300 mg doses at Weeks 0, 1, 2, 3 and 4, followed by the same dose every 4 weeks until Week 52. Patients treated with ustekinumab received 45 mg or 90 mg at Weeks 0 and 4, then every 12 weeks until Week 52 (dosed by weight as per approved posology).

** p values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at Week 16 and secondary endpoint of PASI 75 at Week 4

*** p values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at Week 52
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)

![Graph showing time course of percentage change from baseline of mean PASI score](image)

**Specific locations/forms of plaque psoriasis**
In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE Study, secukinumab was superior to placebo at Week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE Study, secukinumab was superior to placebo at Week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response (“clear” or “almost clear”) for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at Week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to Week 24.

**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.

Statistically significant improvements at Week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at Week 16 and Week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at Week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Psoriatic arthritis
The safety and efficacy of Cosentyx were assessed in 1,003 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA for a median of 3.9 to 5.3 years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 62% and 47% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For both studies, the primary endpoint was American College of Rheumatology (ACR) 20 response at Week 24.

In Psoriatic Arthritis Study 1 (PsA Study 1) and Psoriatic Arthritis Study 2 (PsA Study 2) 29% and 35% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA Study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to Cosentyx received 10 mg/kg intravenously at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at Week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and other placebo patients at Week 24 were crossed over to receive Cosentyx (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA Study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to Cosentyx received 75 mg, 150 mg or 300 mg subcutaneously at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at Week 16 (early rescue) were crossed over to receive Cosentyx (either 150 mg or 300 mg subcutaneously) at Week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at Week 16 were crossed over to receive Cosentyx (either 150 mg or 300 mg subcutaneously) at Week 24 followed by the same dose every month.
Signs and symptoms

Treatment with Cosentyx resulted in significant improvement in measures of disease activity compared to placebo at Week 24 (see Table 5).

Table 5  Clinical response in PsA Study 2 at Week 24

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>75 mg</th>
<th>150 mg</th>
<th>300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients randomised</td>
<td>98</td>
<td>99</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>ACR20 response n (%)</td>
<td>15 (15.3%)</td>
<td>29 (29.3%)</td>
<td>51 (51.0%)***</td>
<td>54 (54.0%)***</td>
</tr>
<tr>
<td>ACR50 response n (%)</td>
<td>7 (7.1%)</td>
<td>18 (18.2%)</td>
<td>35 (35.0%)</td>
<td>35 (35.0%)**</td>
</tr>
<tr>
<td>ACR70 response n (%)</td>
<td>1 (1.0%)</td>
<td>6 (6.1%)</td>
<td>21 (21.0%)**</td>
<td>20 (20.0%)**</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>-0.96</td>
<td>-1.12</td>
<td>-1.58**</td>
<td>-1.61**</td>
</tr>
<tr>
<td>Number of patients with ≥3% BSA psoriasis skin involvement at baseline</td>
<td>43 (43.9%)</td>
<td>50 (50.5%)</td>
<td>58 (58.0%)</td>
<td>41 (41.0%)</td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>7 (16.3%)</td>
<td>14 (28.0%)</td>
<td>28 (48.3%)**</td>
<td>26 (63.4%)***</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>4 (9.3%)</td>
<td>6 (12.0%)</td>
<td>19 (32.8%)**</td>
<td>20 (48.8%)***</td>
</tr>
<tr>
<td>Dactylitis Resolution n (%) †</td>
<td>4 (14.8%)</td>
<td>10 (30.3%)</td>
<td>16 (50.0%)**</td>
<td>26 (56.5%)**</td>
</tr>
<tr>
<td>Enthesitis Resolution n (%) ‡</td>
<td>14 (21.5%)</td>
<td>22 (32.4%)</td>
<td>27 (42.2%)*</td>
<td>27 (48.2%)**</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area
†In patients with dactylitis at baseline (n=27, 33, 32, 46, respectively)
‡In patients with enthesitis at baseline (n=65, 68, 64, 56, respectively)

The onset of action of Cosentyx occurred as early as Week 2. Statistically significant difference in ACR 20 versus placebo was reached at Week 3. At Week 16, Cosentyx-treated patients demonstrated significant improvements in signs and symptoms among which significantly higher responses in ACR 20 (33.3%, 60.0% and 57.0% for 75 mg, 150 mg and 300 mg, respectively) compared to placebo (18.4%).

The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.
Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. At Week 24, Cosentyx-treated patients with concomitant MTX use had a higher ACR 20 response (44.7%, 47.7% and 54.4% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (27.7%, 31.8% and 38.6% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 8.0%). Cosentyx-treated patients without concomitant MTX use had a higher ACR 20 response (15.4%, 53.6% and 53.6% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (9.6%, 37.5% and 32.1% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 6.3%).

Both anti-TNFα-naive and anti-TNFα-IR Cosentyx-treated patients had a significantly higher ACR 20 response compared to placebo at Week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 37%, 64% and 58% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 15%, 30% and 46% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo (p<0.05) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

The number of PsA patients with axial involvement was too small to allow meaningful assessment.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. The proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the Cosentyx-treated patients (37.4%, 59.0% and 61.0% for 75 mg, 150 mg and 300 mg, respectively) compared to placebo (26.5%) at Week 24.

In PsA Study 1 and PsA Study 2, efficacy was maintained up to Week 52. In PsA Study 2, among 200 patients initially randomised to Cosentyx 150 mg and 300 mg, 178 (89%) patients were still on treatment at Week 52. Of the 100 patients randomised to Cosentyx 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to Cosentyx 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.
Radiographic response
Inhibition of progression of structural damage in PsA has not yet been demonstrated using the subcutaneous loading regimen approved for clinical use.

In PsA Study 1, inhibition of progression of structural damage was assessed radiographically and expressed as the change in modified total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing score (JSN) at Weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 6.

### Table 6 Change in modified Total Sharp Score in psoriatic arthritis

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=179</th>
<th>Cosentyx 75 mg¹ N=181</th>
<th>Cosentyx 150 mg¹ N=185</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
<td>28.4 (63.5)</td>
<td>20.4 (39.4)</td>
<td>22.3 (48.0)</td>
</tr>
<tr>
<td><strong>Mean change at Week 24</strong></td>
<td>0.57</td>
<td>0.02*</td>
<td>0.13*</td>
</tr>
</tbody>
</table>

¹10 mg/kg at Weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg

*p<0.05 based on nominal, but non adjusted, p-value

Inhibition of structural damage was maintained with Cosentyx treatment up to Week 52.

The percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to Week 24 was 92.3% in secukinumab 10 mg/kg intravenous load – 75 mg subcutaneous maintenance, 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from Week 24 to Week 52 for secukinumab 10 mg/kg intravenous load – followed by either 75 mg or 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at Week 16 or Week 24 was 85.8%, 85.7% and 86.8%, respectively.

**Physical function and health-related quality of life**
In PsA Study 2, patients treated with Cosentyx 150 mg (p=0.0555) and 300 mg (p=0.0040) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 24. Improvements in HAQ-DI scores were seen regardless of previous anti-TNFα exposure. Similar responses were seen in PsA Study 1.

Cosentyx-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively). Similar responses were seen in PsA Study 1 and efficacy was maintained up to Week 52.

**Ankylosing spondylitis**
The safety and efficacy of Cosentyx were assessed in 590 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in these studies had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of Spondyloarthritis International Society (ASAS 20) criteria at Week 16.

In Ankylosing Spondylitis Study 1 (AS Study 1) and Ankylosing Spondylitis Study 2 (AS Study 2) 27.0% and 38.8% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).
AS Study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to Cosentyx received 10 mg/kg intravenously at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at Week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and all other placebo patients at Week 24 were crossed over to receive Cosentyx (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS Study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to Cosentyx received 75 mg or 150 mg subcutaneously at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At Week 16, patients who were randomised to placebo at baseline were re-randomised to receive Cosentyx (either 75 mg or 150 mg subcutaneously) every month.

**Signs and symptoms**

In AS Study 2, treatment with Cosentyx 150 mg resulted in greater improvement in measures of disease activity compared with placebo at Week 16 (see Table 7).

**Table 7  Clinical response in AS Study 2 at Week 16**

<table>
<thead>
<tr>
<th>Outcome (p-value versus placebo)</th>
<th>Placebo (n = 74)</th>
<th>75 mg (n = 73)</th>
<th>150 mg (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS 20 response, %</td>
<td>28.4</td>
<td>41.1</td>
<td>61.1***</td>
</tr>
<tr>
<td>ASAS 40 response, %</td>
<td>10.8</td>
<td>26.0</td>
<td>36.1***</td>
</tr>
<tr>
<td>hsCRP, (post-BSL/BSL ratio)</td>
<td>1.13</td>
<td>0.61</td>
<td>0.55***</td>
</tr>
<tr>
<td>ASAS 5/6, %</td>
<td>8.1</td>
<td>34.2</td>
<td>43.1***</td>
</tr>
<tr>
<td>ASAS partial remission, %</td>
<td>4.1</td>
<td>15.1</td>
<td>13.9</td>
</tr>
<tr>
<td>BASDAI 50, %</td>
<td>10.8</td>
<td>24.7*</td>
<td>30.6**</td>
</tr>
<tr>
<td>ASDAS-CRP major improvement</td>
<td>4.1</td>
<td>15.1*</td>
<td>25.0***</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01, *** p<0.001; versus placebo

All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP

Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of Cosentyx 150 mg occurred as early as Week 1 for ASAS 20 and Week 2 for ASAS 40 (superior to placebo) in AS Study 2.

ASAS 20 responses were improved at Week 16 in both anti-TNFα-naïve patients (68.2% versus 31.1%; p<0.05) and anti-TNFα-IR patients (50.0% versus 24.1%; p<0.05) for Cosentyx 150 mg compared with placebo, respectively.

In both AS studies, Cosentyx-treated patients (150 mg in AS Study 2 and both regimens in AS Study 1) demonstrated significantly improved signs and symptoms at Week 16, with comparable magnitude of response and efficacy maintained up to Week 52 in both anti-TNFα-naïve and anti-TNFα-IR patients. In AS Study 2, among 72 patients initially randomised to Cosentyx 150 mg, 61 (84.7%) patients were still on treatment at Week 52. Of the 72 patients randomised to Cosentyx 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.
Spinal mobility
Patients treated with Cosentyx 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at Week 16 for both AS Study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS Study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to Week 52.

Physical function and health-related quality of life
In AS Study 1 and Study 2, patients treated with Cosentyx 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with Cosentyx 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACTIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to Week 52.

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 and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 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 and in chronic idiopathic arthritis for paediatric patients aged from 2 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Plaque psoriasis

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 (Cmax,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.

Psoriatic arthritis
The pharmacokinetic properties of secukinumab observed in psoriatic arthritis patients were similar to those displayed in plaque psoriasis patients. The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Ankylosing spondylitis
The pharmacokinetic properties of secukinumab observed in ankylosing spondylitis patients were similar to those displayed in plaque psoriasis patients.

Special populations

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

Of the 974 psoriatic arthritis patients exposed to Cosentyx in clinical studies, a total of 85 patients were 65 years of age or older and 4 patients were 75 years of age or older.

Of the 571 ankylosing spondylitis patients exposed to Cosentyx in clinical studies, a total of 24 patients were 65 years of age or older and 3 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.
Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

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 embryofetal 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 2°C to 8°C. 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

15.01.2015

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**

**Plaque psoriasis**

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

**Psoriatic arthritis**

Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

**Ankylosing spondylitis**

Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional 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 conditions for which Cosentyx is indicated.

**Posology**

*Plaque psoriasis*

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

*Psoriatic arthritis*

For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

*Ankylosing spondylitis*

The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

**Special populations**

*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

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving Cosentyx. 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).

In a study in subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when Cosentyx was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis).

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 6,804 patients have been treated with Cosentyx in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and other autoimmune conditions). Of these, 3,671 patients were exposed to Cosentyx for at least one year, representing 6,450 patient years of exposure.

Adverse reactions in plaque psoriasis

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.

Adverse reactions in psoriatic arthritis

Cosentyx was studied in two placebo-controlled psoriatic arthritis studies with 1,003 patients (703 patients on Cosentyx and 300 patients on placebo) for a total exposure of 1,061 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 456 days in PsA Study 1 and 245 days in PsA Study 2). The safety profile observed in patients with psoriatic arthritis treated with Cosentyx is consistent with the safety profile in psoriasis.

Adverse reactions in ankylosing spondylitis

Cosentyx was studied in two placebo-controlled ankylosing spondylitis studies with 590 patients (394 patients on Cosentyx and 196 patients on placebo) for a total of 755 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 469 days in AS Study 1 and 460 days in AS Study 2). The safety profile observed in patients with ankylosing spondylitis treated with Cosentyx is consistent with the safety profile in psoriasis.
Tabulated list of adverse reactions

ADRs from psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies as well as from post-marketing experience (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); and not known (cannot be estimated from the available data).

Table 1 List of adverse reactions in clinical studies1) and post-marketing experience

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Very common</td>
<td>Upper respiratory tract infections</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Oral herpes</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Oral candidiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tinea pedis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Otitis externa</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Mucosal and cutaneous candidiasis (including oesophageal candidiasis)</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Uncommon</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Rare</td>
<td>Anaphylactic reactions</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>Uncommon</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Common</td>
<td>Rhinorrhoea</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Common</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Skin and subcutaneous disorders</td>
<td>Uncommon</td>
<td>Urticaria</td>
</tr>
</tbody>
</table>

1) Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA and AS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA and AS) treatment duration

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).

Infection rates observed in psoriatic arthritis and ankylosing spondylitis clinical studies were similar to those observed in the psoriasis studies.
**Neutropenia**
In psoriasis phase 3 clinical studies, 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.

The frequency of neutropenia in psoriatic arthritis and ankylosing spondylitis is similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE Grade 4) were reported.

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

**Immunogenicity**
In psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies, 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, psoriatic arthritis and ankylosing spondylitis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis.

**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.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

**Clinical efficacy and safety**

**Plaque psoriasis**

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, 3 and 4, followed by the same dose every month. Psoriasis Study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. 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, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

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)

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Study 3

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<td>0 (0.0%)</td>
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Study 4

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* 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.
In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at Week 16 (primary endpoint), speed of onset of PASI 75 response at Week 4, and long-term PASI 90 response at Week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to Week 52.

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

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<tr>
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<td>PASI 50 response n (%)</td>
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<td>(55.4%)</td>
<td>(65.7%)</td>
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<td>PASI 90 response n (%)</td>
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<td>175 (54.2%)</td>
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<td>108 (33.4%)</td>
<td>147 (45.0%)</td>
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<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
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<td>219 (67.8%)</td>
<td>120 (37.2%)</td>
<td>168 (51.4%)</td>
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</table>

** p values versus etanercept: p=0.0250

** p values versus etanercept: p=0.0001 for primary endpoint of PASI 90 at Week 16 and secondary endpoint of PASI 75 at Week 4

### Table 4  Summary of clinical response on CLEAR Study

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<th>Secukinumab 300 mg</th>
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<td>PASI 75 response n (%)</td>
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<td>95 (28.4%)</td>
<td>150 (44.9%)</td>
<td>123 (36.7%)</td>
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<tr>
<td>PASI 90 response n (%)</td>
<td>70 (21.0%)</td>
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<td>264 (79.0%)**</td>
<td>192 (57.3%)</td>
<td>250 (74.9%)***</td>
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<td>128 (38.3%)</td>
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<td>PASI 100 response n (%)</td>
<td>14 (4.2%)</td>
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<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
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<td>261 (78.1%)</td>
<td>213 (63.6%)</td>
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* Patients treated with secukinumab received 300 mg doses at Weeks 0, 1, 2, 3 and 4, followed by the same dose every 4 weeks until Week 52. Patients treated with ustekinumab received 45 mg or 90 mg at Weeks 0 and 4, then every 12 weeks until Week 52 (dosed by weight as per approved posology)

** p values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at Week 16 and secondary endpoint of PASI 75 at Week 4

*** p values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at Week 52
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)

![Graph showing percentage change from baseline of mean PASI score](image)

**Specific locations/forms of plaque psoriasis**

In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE Study, secukinumab was superior to placebo at Week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE Study, secukinumab was superior to placebo at Week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response (“clear” or “almost clear”) for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at Week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to Week 24.

**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.

Statistically significant improvements at Week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at Week 16 and Week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary© in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at Week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Psoriatic arthritis
The safety and efficacy of Cosentyx were assessed in 1,003 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA for a median of 3.9 to 5.3 years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 62% and 47% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For both studies, the primary endpoint was American College of Rheumatology (ACR) 20 response at Week 24.

In Psoriatic Arthritis Study 1 (PsA Study 1) and Psoriatic Arthritis Study 2 (PsA Study 2) 29% and 35% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA Study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to Cosentyx received 10 mg/kg intravenously at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at Week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and other placebo patients at Week 24 were crossed over to receive Cosentyx (either 75 mg or 150 mg subcutaneously) followed by the same dose every month.

PsA Study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to Cosentyx received 75 mg, 150 mg or 300 mg subcutaneously at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at Week 16 (early rescue) were crossed over to receive Cosentyx (either 150 mg or 300 mg subcutaneously) at Week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at Week 16 were crossed over to receive Cosentyx (either 150 mg or 300 mg subcutaneously) at Week 24 followed by the same dose every month.
Signs and symptoms
Treatment with Cosentyx resulted in significant improvement in measures of disease activity compared to placebo at Week 24 (see Table 5).

Table 5  Clinical response in PsA Study 2 at Week 24

<table>
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<th>300 mg</th>
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<td>99</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>ACR20 response n (%)</td>
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<td>29 (29.3%*)</td>
<td>51 (51.0%***</td>
<td>54 (54.0%***</td>
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<td>ACR50 response n (%)</td>
<td>7 (7.1%)</td>
<td>18 (18.2%)</td>
<td>35 (35.0%)</td>
<td>35 (35.0%**</td>
</tr>
<tr>
<td>ACR70 response n (%)</td>
<td>1 (1.0%)</td>
<td>6 (6.1%)</td>
<td>21 (21.0%**)</td>
<td>20 (20.0%**</td>
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<td>DAS28-CRP</td>
<td>-0.96</td>
<td>-1.12</td>
<td>-1.58**</td>
<td>-1.61**</td>
</tr>
<tr>
<td>Number of patients with ≥3% BSA psoriasis skin involvement at baseline</td>
<td>43 (43.9%)</td>
<td>50 (50.5%)</td>
<td>58 (58.0%)</td>
<td>41 (41.0%)</td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>7 (16.3%)</td>
<td>14 (28.0%)</td>
<td>28 (48.3%**)</td>
<td>26 (63.4%***</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>4 (9.3%)</td>
<td>6 (12.0%)</td>
<td>19 (32.8%**)</td>
<td>20 (48.8%***</td>
</tr>
<tr>
<td>Dactylitis Resolution n (%) †</td>
<td>4 (14.8%)</td>
<td>10 (30.3%)</td>
<td>16 (50.0%**)</td>
<td>26 (56.5%**</td>
</tr>
<tr>
<td>Enthesitis Resolution n (%) ‡</td>
<td>14 (21.5%)</td>
<td>22 (32.4%)</td>
<td>27 (42.2%*)</td>
<td>27 (48.2%**</td>
</tr>
</tbody>
</table>

* p<0.05; ** p<0.01; *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area
†In patients with dactylitis at baseline (n=27, 33, 32, 46, respectively)
‡In patients with enthesitis at baseline (n=65, 68, 64, 56, respectively)

The onset of action of Cosentyx occurred as early as Week 2. Statistically significant difference in ACR 20 versus placebo was reached at Week 3. At Week 16, Cosentyx-treated patients demonstrated significant improvements in signs and symptoms among which significantly higher responses in ACR 20 (33.3%, 60.0% and 57.0% for 75 mg, 150 mg and 300 mg, respectively) compared to placebo (18.4%).
The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.

**Figure 2**  
ACR20 response in PsA Study 2 over time up to Week 24

![Graph showing ACR20 response over time up to Week 24.](image)

Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. At Week 24, Cosentyx-treated patients with concomitant MTX use had a higher ACR 20 response (44.7%, 47.7% and 54.4% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (27.7%, 31.8% and 38.6% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 8.0%). Cosentyx-treated patients without concomitant MTX use had a higher ACR 20 response (15.4%, 37.5% and 32.1% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (9.6%, 37.5% and 32.1% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 6.3%).

Both anti-TNFα-naive and anti-TNFα-IR Cosentyx-treated patients had a significantly higher ACR 20 response compared to placebo at Week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 37%, 64% and 58% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 15%, 30% and 46% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo (p<0.05) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

The number of PsA patients with axial involvement was too small to allow meaningful assessment.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. The proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the Cosentyx-treated patients (37.4%, 59.0% and 61.0% for 75 mg, 150 mg and 300 mg, respectively) compared to placebo (26.5%) at Week 24.

In PsA Study 1 and PsA Study 2, efficacy was maintained up to Week 52. In PsA Study 2, among 200 patients initially randomised to Cosentyx 150 mg and 300 mg, 178 (89%) patients were still on treatment at Week 52. Of the 100 patients randomised to Cosentyx 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to Cosentyx 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.
Radiographic response
Inhibition of progression of structural damage in PsA has not yet been demonstrated using the subcutaneous loading regimen approved for clinical use.

In PsA Study 1, inhibition of progression of structural damage was assessed radiographically and expressed as the change in modified total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing score (JSN) at Weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 6.

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Cosentyx 75 mg</th>
<th>Cosentyx 150 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=179</td>
<td>N=181</td>
<td>N=185</td>
</tr>
<tr>
<td>Total score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (SD)</td>
<td>28.4 (63.5)</td>
<td>20.4 (39.4)</td>
</tr>
<tr>
<td>Mean change at Week 24</td>
<td>0.57</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

*p<0.05 based on nominal, but non adjusted, p-value

10 mg/kg at Weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg

Inhibition of structural damage was maintained with Cosentyx treatment up to Week 52.

The percentage of patients with no disease progression (defined as a change from baseline in mTSS of ≤0.5) from randomisation to Week 24 was 92.3% in secukinumab 10 mg/kg intravenous load – 75 mg subcutaneous maintenance, 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from Week 24 to Week 52 for secukinumab 10 mg/kg intravenous load – followed by either 75 mg or 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at Week 16 or Week 24 was 85.8%, 85.7% and 86.8%, respectively.

Physical function and health-related quality of life
In PsA Study 2, patients treated with Cosentyx 150 mg (p=0.0555) and 300 mg (p=0.0040) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 24. Improvements in HAQ-DI scores were seen regardless of previous anti-TNFα exposure. Similar responses were seen in PsA Study 1.

Cosentyx-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (p<0.001). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively). Similar responses were seen in PsA Study 1 and efficacy was maintained up to Week 52.

Ankylosing spondylitis
The safety and efficacy of Cosentyx were assessed in 590 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥4 despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in these studies had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of Spondyloarthritis International Society (ASAS 20) criteria at Week 16.

In Ankylosing Spondylitis Study 1 (AS Study 1) and Ankylosing Spondylitis Study 2 (AS Study 2) 27.0% and 38.8% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).
AS Study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to Cosentyx received 10 mg/kg intravenously at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at Week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and all other placebo patients at Week 24 were crossed over to receive Cosentyx (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS Study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to Cosentyx received 75 mg or 150 mg subcutaneously at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At Week 16, patients who were randomised to placebo at baseline were re-randomised to receive Cosentyx (either 75 mg or 150 mg subcutaneously) every month.

Signs and symptoms
In AS Study 2, treatment with Cosentyx 150 mg resulted in greater improvement in measures of disease activity compared with placebo at Week 16 (see Table 7).

Table 7  Clinical response in AS Study 2 at Week 16

<table>
<thead>
<tr>
<th>Outcome (p-value versus placebo)</th>
<th>Placebo (n = 74)</th>
<th>75 mg (n = 73)</th>
<th>150 mg (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS 20 response, %</td>
<td>28.4</td>
<td>41.1</td>
<td>61.1***</td>
</tr>
<tr>
<td>ASAS 40 response, %</td>
<td>10.8</td>
<td>26.0</td>
<td>36.1***</td>
</tr>
<tr>
<td>hsCRP, (post-BSL/BSL ratio)</td>
<td>1.13</td>
<td>0.61</td>
<td>0.55***</td>
</tr>
<tr>
<td>ASAS 5/6, %</td>
<td>8.1</td>
<td>34.2</td>
<td>43.1***</td>
</tr>
<tr>
<td>ASAS partial remission, %</td>
<td>4.1</td>
<td>15.1</td>
<td>13.9</td>
</tr>
<tr>
<td>BASDAI 50, %</td>
<td>10.8</td>
<td>24.7*</td>
<td>30.6**</td>
</tr>
<tr>
<td>ASDAS-CRP major improvement</td>
<td>4.1</td>
<td>15.1*</td>
<td>25.0***</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP
Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of Cosentyx 150 mg occurred as early as Week 1 for ASAS 20 and Week 2 for ASAS 40 (superior to placebo) in AS Study 2.

ASAS 20 responses were improved at Week 16 in both anti-TNFα- naïve patients (68.2% versus 31.1%; p<0.05) and anti-TNFα-IR patients (50.0% versus 24.1%; p<0.05) for Cosentyx 150 mg compared with placebo, respectively.

In both AS studies, Cosentyx-treated patients (150 mg in AS Study 2 and both regimens in AS Study 1) demonstrated significantly improved signs and symptoms at Week 16, with comparable magnitude of response and efficacy maintained up to Week 52 in both anti-TNFα- naïve and anti-TNFα-IR patients. In AS Study 2, among 72 patients initially randomised to Cosentyx 150 mg, 61 (84.7%) patients were still on treatment at Week 52. Of the 72 patients randomised to Cosentyx 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.
Spinal mobility

Patients treated with Cosentyx 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at Week 16 for both AS Study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS Study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to Week 52.

Physical function and health-related quality of life

In AS Study 1 and Study 2, patients treated with Cosentyx 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with Cosentyx 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to Week 52.

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 and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 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 and in chronic idiopathic arthritis for paediatric patients aged from 2 years to less than 18 years (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Plaque psoriasis

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 (Cmax,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 ($V_d$) 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.

Psoriatic arthritis
The pharmacokinetic properties of secukinumab observed in psoriatic arthritis patients were similar to those displayed in plaque psoriasis patients. The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

Ankylosing spondylitis
The pharmacokinetic properties of secukinumab observed in ankylosing spondylitis patients were similar to those displayed in plaque psoriasis patients.

Special populations

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

Of the 974 psoriatic arthritis patients exposed to Cosentyx in clinical studies, a total of 85 patients were 65 years of age or older and 4 patients were 75 years of age or older.

Of the 571 ankylosing spondylitis patients exposed to Cosentyx in clinical studies, a total of 24 patients were 65 years of age or older and 3 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.

Effect of weight on pharmacokinetics
Secukinumab clearance and volume of distribution increase as body weight increases.

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. If necessary, Cosentyx may be stored unrefrigerated for a single period of up to 4 days at room temperature, not above 30°C. 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 unit packs containing 1 or 2 pre-filled syringes and in multipacks containing 6 (3 packs of 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
EU/1/14/980/006
9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15.01.2015

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**

   **Plaque psoriasis**

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

   **Psoriatic arthritis**

   Cosentyx, alone or in combination with methotrexate (MTX), is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate (see section 5.1).

   **Ankylosing spondylitis**

   Cosentyx is indicated for the treatment of active ankylosing spondylitis in adults who have responded inadequately to conventional 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 conditions for which Cosentyx is indicated.

Posology

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

Psoriatic arthritis
For patients with concomitant moderate to severe plaque psoriasis or who are anti-TNFα inadequate responders (IR), the recommended dose is 300 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing. Each 300 mg dose is given as two subcutaneous injections of 150 mg.

For other patients, the recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

Ankylosing spondylitis
The recommended dose is 150 mg by subcutaneous injection with initial dosing at Weeks 0, 1, 2, 3 and 4, followed by monthly maintenance dosing.

For all of the above indications, available data suggest that a clinical response is usually achieved within 16 weeks of treatment. Consideration should be given to discontinuing treatment in patients who have shown no response by 16 weeks of treatment. Some patients with an initial partial response may subsequently improve with continued treatment beyond 16 weeks.

Special populations

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

In clinical studies, rare cases of anaphylactic reactions have been observed in patients receiving Cosentyx. 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).

In a study in subjects with plaque psoriasis, no interaction was observed between secukinumab and midazolam (CYP3A4 substrate).

No interaction was seen when Cosentyx was administered concomitantly with methotrexate (MTX) and/or corticosteroids in arthritis studies (including in patients with psoriatic arthritis and ankylosing spondylitis).

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 6,804 patients have been treated with Cosentyx in blinded and open-label clinical studies in various indications (plaque psoriasis, psoriatic arthritis, ankylosing spondylitis and other autoimmune conditions). Of these, 3,671 patients were exposed to Cosentyx for at least one year, representing 6,450 patient years of exposure.

Adverse reactions in plaque psoriasis

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.

Adverse reactions in psoriatic arthritis

Cosentyx was studied in two placebo-controlled psoriatic arthritis studies with 1,003 patients (703 patients on Cosentyx and 300 patients on placebo) for a total exposure of 1,061 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 456 days in PsA Study 1 and 245 days in PsA Study 2). The safety profile observed in patients with psoriatic arthritis treated with Cosentyx is consistent with the safety profile in psoriasis.

Adverse reactions in ankylosing spondylitis

Cosentyx was studied in two placebo-controlled ankylosing spondylitis studies with 590 patients (394 patients on Cosentyx and 196 patients on placebo) for a total of 755 patient-years of study exposure (median duration of exposure for secukinumab-treated patients: 469 days in AS Study 1 and 460 days in AS Study 2). The safety profile observed in patients with ankylosing spondylitis treated with Cosentyx is consistent with the safety profile in psoriasis.
Tabulated list of adverse reactions

ADRs from psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies as well as from post-marketing experience (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); and not known (cannot be estimated from the available data).

Table 1  List of adverse reactions in clinical studies\(^1\) and post-marketing experience

<table>
<thead>
<tr>
<th>System Organ Class</th>
<th>Frequency</th>
<th>Adverse reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infections and infestations</td>
<td>Very common</td>
<td>Upper respiratory tract infections</td>
</tr>
<tr>
<td></td>
<td>Common</td>
<td>Oral herpes</td>
</tr>
<tr>
<td></td>
<td>Uncommon</td>
<td>Oral candidiasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tinea pedis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Otitis externa</td>
</tr>
<tr>
<td></td>
<td>Not known</td>
<td>Mucosal and cutaneous candidiasis (including oesophageal candidiasis)</td>
</tr>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Uncommon</td>
<td>Neutropenia</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td>Rare</td>
<td>Anaphylactic reactions</td>
</tr>
<tr>
<td>Eye disorders</td>
<td>Uncommon</td>
<td>Conjunctivitis</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>Common</td>
<td>Rhinorrhoea</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>Common</td>
<td>Diarrhoea</td>
</tr>
<tr>
<td>Skin and subcutaneous disorders</td>
<td>Uncommon</td>
<td>Urticaria</td>
</tr>
</tbody>
</table>

\(^1\) Placebo-controlled clinical studies (phase III) in plaque psoriasis, PsA and AS patients exposed to 300 mg, 150 mg, 75 mg or placebo up to 12 weeks (psoriasis) or 16 weeks (PsA and AS) treatment duration

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).

Infection rates observed in psoriatic arthritis and ankylosing spondylitis clinical studies were similar to those observed in the psoriasis studies.
Neutropenia
In psoriasis phase 3 clinical studies, 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.

The frequency of neutropenia in psoriatic arthritis and ankylosing spondylitis is similar to psoriasis.

Rare cases of neutropenia <0.5x10^9/l (CTCAE Grade 4) were reported.

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

Immunogenicity
In psoriasis, psoriatic arthritis and ankylosing spondylitis clinical studies, 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, psoriatic arthritis, and ankylosing spondylitis and is up-regulated in lesional skin in contrast to non-lesional skin of plaque psoriasis patients and in synovial tissue of psoriatic arthritis patients. The frequency of IL-17-producing cells was also significantly higher in the subchondral bone marrow of facet joints from patients with ankylosing spondylitis.

**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.

Secukinumab has been shown to lower (within 1 to 2 weeks of treatment) levels of C-reactive protein, which is a marker of inflammation.

**Clinical efficacy and safety**

**Plaque psoriasis**

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, 3 and 4, followed by the same dose every month. Psoriasis Study 2 (FIXTURE) evaluated 1,306 patients. Patients randomised to Cosentyx received 150 mg or 300 mg doses at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. 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, 3 and 4, followed by the same dose every month. Patients were also randomised to receive placebo at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month.

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)

<table>
<thead>
<tr>
<th>Study 1</th>
<th>Placebo 150 mg</th>
<th>300 mg</th>
<th>150 mg</th>
<th>300 mg</th>
<th>150 mg</th>
<th>300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
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<td>244</td>
<td>245</td>
<td>244</td>
<td>245</td>
<td>245</td>
</tr>
<tr>
<td>PASI 50 response n (%)</td>
<td>(8.9%)</td>
<td>(85.3%) (90.6%) (87.2%) (91.4%) (77%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>11</td>
<td>174 (71.6%)** (81.6%)**</td>
<td>200</td>
<td>188</td>
<td>211</td>
<td>146</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>3 (1.2%)</td>
<td>95 (39.1%)**</td>
<td>145</td>
<td>130</td>
<td>171</td>
<td>88</td>
</tr>
<tr>
<td>PASI 100 response n (%)</td>
<td>2 (0.8%)</td>
<td>27 (12.8%)</td>
<td>70 (28.6%)</td>
<td>51 (21.0%)</td>
<td>102 (41.6%)</td>
<td>49</td>
</tr>
<tr>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>6 (2.40%)</td>
<td>125 (51.2%)**</td>
<td>160 (65.3%)**</td>
<td>142 (58.2%)</td>
<td>180 (73.5%)</td>
<td>101</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study 3</th>
<th>Placebo 150 mg</th>
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<td>58</td>
<td>-</td>
<td>-</td>
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<tr>
<td>PASI 50 response n (%)</td>
<td>3 (5.1%)</td>
<td>51</td>
<td>51</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>0 (0.0%)</td>
<td>41 (86.4%)</td>
<td>44 (87.9%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>0 (0.0%)</td>
<td>27 (69.5%)**</td>
<td>35 (75.9%)**</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 100 response n (%)</td>
<td>0 (0.0%)</td>
<td>5 (45.8%)</td>
<td>25 (60.3%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>0 (0.0%)</td>
<td>31 (52.5%)**</td>
<td>40 (69.0%)**</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study 4</th>
<th>Placebo 150 mg</th>
<th>300 mg</th>
<th>150 mg</th>
<th>300 mg</th>
<th>150 mg</th>
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</thead>
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<td>60</td>
<td>60</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 50 response n (%)</td>
<td>5 (8.2%)</td>
<td>48</td>
<td>58</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>2 (3.3%)</td>
<td>43 (80.5%)</td>
<td>52 (96.7%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>0 (0.0%)</td>
<td>24 (71.7%)**</td>
<td>33 (86.7%)**</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PASI 100 response n (%)</td>
<td>0 (0.0%)</td>
<td>10 (40.0%)</td>
<td>16 (55.0%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>0 (0.0%)</td>
<td>32 (53.3%)**</td>
<td>44 (73.3%)**</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* 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.
In an additional psoriasis study (CLEAR) 676 patients were evaluated. Secukinumab 300 mg met the primary and secondary endpoints by showing superiority to ustekinumab based on PASI 90 response at Week 16 (primary endpoint), speed of onset of PASI 75 response at Week 4, and long-term PASI 90 response at Week 52. Greater efficacy of secukinumab compared to ustekinumab for the endpoints PASI 75/90/100 and IGA mod 2011 0 or 1 response (“clear” or “almost clear”) was observed early and continued through to Week 52.

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

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>150 mg</th>
<th>300 mg</th>
<th>Etanercept</th>
<th>Placebo</th>
<th>150 mg</th>
<th>300 mg</th>
<th>Etanercept</th>
<th>Placebo</th>
<th>150 mg</th>
<th>300 mg</th>
<th>Etanercept</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>324</td>
<td>327</td>
<td>323</td>
<td>323</td>
<td>327</td>
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<td>323</td>
<td>323</td>
<td>327</td>
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<td>323</td>
<td>323</td>
<td>327</td>
<td>323</td>
<td>323</td>
<td>323</td>
</tr>
<tr>
<td>PASI 50 response n (%)</td>
<td>15 (1.5%)</td>
<td>17 (5.4%)</td>
<td>20 (6.2%)</td>
<td><strong>25 (7.8%)</strong></td>
<td>15 (1.5%)</td>
<td>17 (5.4%)</td>
<td>20 (6.2%)</td>
<td><strong>25 (7.8%)</strong></td>
<td>15 (1.5%)</td>
<td>17 (5.4%)</td>
<td>20 (6.2%)</td>
<td><strong>25 (7.8%)</strong></td>
<td>15 (1.5%)</td>
<td>17 (5.4%)</td>
<td>20 (6.2%)</td>
<td><strong>25 (7.8%)</strong></td>
</tr>
</tbody>
</table>

**Table 4  Summary of clinical response on CLEAR Study**

<table>
<thead>
<tr>
<th></th>
<th>Secukinumab 300 mg</th>
<th>Ustekinumab 300 mg</th>
<th>Secukinumab 300 mg</th>
<th>Ustekinumab 300 mg</th>
<th>Secukinumab 300 mg</th>
<th>Ustekinumab 300 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>334</td>
<td>335</td>
<td>334</td>
<td>335</td>
<td>334</td>
<td>335</td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>166 (49.7%)**</td>
<td>69 (20.6%)</td>
<td>311 (93.1%)</td>
<td>276 (82.4%)</td>
<td>306 (91.6%)</td>
<td>262 (78.2%)</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>70 (21.0%)</td>
<td>18 (5.4%)</td>
<td>264 (79.0%)**</td>
<td>192 (57.3%)</td>
<td>250 (74.9%)***</td>
<td>203 (60.6%)</td>
</tr>
<tr>
<td>PASI 100 response n (%)</td>
<td>14 (4.2%)</td>
<td>3 (0.9%)</td>
<td>148 (44.3%)</td>
<td>95 (28.4%)</td>
<td>150 (44.9%)</td>
<td>123 (36.7%)</td>
</tr>
<tr>
<td>IGA mod 2011 “clear” or “almost clear” response n (%)</td>
<td>128 (38.3%)</td>
<td>41 (12.2%)</td>
<td>278 (83.2%)</td>
<td>226 (67.5%)</td>
<td>261 (78.1%)</td>
<td>213 (63.6%)</td>
</tr>
</tbody>
</table>

* Patients treated with secukinumab received 300 mg doses at Weeks 0, 1, 2, 3 and 4, followed by the same dose every 4 weeks until Week 52. Patients treated with ustekinumab received 45 mg or 90 mg at Weeks 0 and 4, then every 12 weeks until Week 52 (dosed by weight as per approved posology)

** p values versus ustekinumab: p<0.0001 for primary endpoint of PASI 90 at Week 16 and secondary endpoint of PASI 75 at Week 4

*** p values versus ustekinumab: p=0.0001 for secondary endpoint of PASI 90 at Week 52

52
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)

![Graph showing PASI score improvement over time]

**Specific locations/forms of plaque psoriasis**

In two additional placebo-controlled studies, improvement was seen in both nail psoriasis (TRANSFIGURE, 198 patients) and palmoplantar plaque psoriasis (GESTURE, 205 patients). In the TRANSFIGURE Study, secukinumab was superior to placebo at Week 16 (46.1% for 300 mg, 38.4% for 150 mg and 11.7% for placebo) as assessed by significant improvement from baseline in the Nail Psoriasis Severity Index (NAPSI %) for patients with moderate to severe plaque psoriasis with nail involvement. In the GESTURE Study, secukinumab was superior to placebo at Week 16 (33.3% for 300 mg, 22.1% for 150 mg, and 1.5% for placebo) as assessed by significant improvement of ppIGA 0 or 1 response (“clear” or “almost clear”) for patients with moderate to severe palmoplantar plaque psoriasis.

A placebo-controlled study evaluated 102 patients with moderate to severe scalp psoriasis, defined as having a Psoriasis Scalp Severity Index (PSSI) score of ≥12, an IGA mod 2011 scalp only score of 3 or greater and at least 30% of the scalp surface area affected. Secukinumab 300 mg was superior to placebo at Week 12 as assessed by significant improvement from baseline in both the PSSI 90 response (52.9% versus 2.0%) and IGA mod 2011 0 or 1 scalp only response (56.9% versus 5.9%). Improvement in both endpoints was sustained for secukinumab patients who continued treatment through to Week 24.
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.

Statistically significant improvements at Week 4 from baseline in patients treated with secukinumab compared to patients treated with ustekinumab (CLEAR) were demonstrated in the DLQI and these improvements were maintained for up to 52 weeks.

Statistically significant improvements in patient-reported signs and symptoms of itching, pain and scaling at Week 16 and Week 52 (CLEAR) were demonstrated in the Psoriasis Symptom Diary® in patients treated with secukinumab compared to patients treated with ustekinumab.

Statistically significant improvements (decreases) at Week 12 from baseline in the scalp psoriasis study were demonstrated in patient reported signs and symptoms of scalp itching, pain and scaling compared to placebo.

Psoriatic arthritis
The safety and efficacy of Cosentyx were assessed in 1,003 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active psoriatic arthritis (≥3 swollen and ≥3 tender joints) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients with each subtype of PsA were enrolled in these studies, including polyarticular arthritis with no evidence of rheumatoid nodules, spondylitis with peripheral arthritis, asymmetric peripheral arthritis, distal interphalangeal involvement and arthritis mutilans. Patients in these studies had a diagnosis of PsA for a median of 3.9 to 5.3 years. The majority of patients also had active psoriasis skin lesions or a documented history of psoriasis. Over 62% and 47% of the PsA patients had enthesitis and dactylitis at baseline, respectively. For both studies, the primary endpoint was American College of Rheumatology (ACR) 20 response at Week 24.

In Psoriatic Arthritis Study 1 (PsA Study 1) and Psoriatic Arthritis Study 2 (PsA Study 2) 29% and 35% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

PsA Study 1 (FUTURE 1) evaluated 606 patients, of whom 60.7% had concomitant MTX. Patients randomised to Cosentyx received 10 mg/kg intravenously at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at Week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and other placebo patients at Week 24 were crossed over to receive Cosentyx (either 75 mg or 150 mg subcutaneously) following the same dose every month.

PsA Study 2 (FUTURE 2) evaluated 397 patients, of whom 46.6% had concomitant MTX. Patients randomised to Cosentyx received 75 mg, 150 mg or 300 mg subcutaneously at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. Patients randomised to receive placebo who were non-responders at Week 16 (early rescue) were crossed over to receive Cosentyx (either 150 mg or 300 mg subcutaneously) at Week 16 followed by the same dose every month. Patients randomised to receive placebo who were responders at Week 16 were crossed over to receive Cosentyx (either 150 mg or 300 mg subcutaneously) at Week 24 followed by the same dose every month.
Signs and symptoms
Treatment with Cosentyx resulted in significant improvement in measures of disease activity compared to placebo at Week 24 (see Table 5).

Table 5  Clinical response in PsA Study 2 at Week 24

<table>
<thead>
<tr>
<th></th>
<th>Week 24</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td>Number of patients randomised</td>
<td>98</td>
</tr>
<tr>
<td>ACR20 response n (%)</td>
<td>15 (15.3%)</td>
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<tr>
<td>ACR50 response n (%)</td>
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</tr>
<tr>
<td>ACR70 response n (%)</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>-0.96</td>
</tr>
<tr>
<td>Number of patients with ≥3% BSA psoriasis skin involvement at baseline</td>
<td>43 (43.9%)</td>
</tr>
<tr>
<td>PASI 75 response n (%)</td>
<td>7 (16.3%)</td>
</tr>
<tr>
<td>PASI 90 response n (%)</td>
<td>4 (9.3%)</td>
</tr>
<tr>
<td>Dactylitis Resolution n (%) †</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>Enthesitis Resolution n (%) ‡</td>
<td>14 (21.5%)</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values are adjusted for multiplicity of testing based on pre-defined hierarchy, except for ACR70, Dactylitis and Enthesitis, which were exploratory endpoints.
Non-responder imputation used for missing binary endpoint.
ACR: American College of Rheumatology; PASI: Psoriasis Area and Severity Index; DAS: Disease Activity Score; BSA: Body Surface Area
†In patients with dactylitis at baseline (n=27, 33, 32, 46, respectively)
‡In patients with enthesitis at baseline (n=65, 68, 64, 56, respectively)

The onset of action of Cosentyx occurred as early as Week 2. Statistically significant difference in ACR 20 versus placebo was reached at Week 3. At Week 16, Cosentyx-treated patients demonstrated significant improvements in signs and symptoms among which significantly higher responses in ACR 20 (33.3%, 60.0% and 57.0% for 75 mg, 150 mg and 300 mg, respectively) compared to placebo (18.4%).
The percentage of patients achieving ACR 20 response by visit is shown in Figure 2.

**Figure 2** ACR20 response in PsA Study 2 over time up to Week 24

![ACR20 response graph]

Similar responses for primary and key secondary endpoints were seen in PsA patients regardless of whether they were on concomitant MTX treatment or not. At Week 24, Cosentyx-treated patients with concomitant MTX use had a higher ACR 20 response (44.7%, 47.7% and 54.4% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 20.0%) and ACR 50 response (27.7%, 31.8% and 38.6% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 8.0%). Cosentyx-treated patients without concomitant MTX use had a higher ACR 20 response (15.4%, 30.6% and 46.0% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 10.4%) and ACR 50 response (9.6%, 37.5% and 32.1% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 6.3%).

Both anti-TNFα-naive and anti-TNFα-IR Cosentyx-treated patients had a significantly higher ACR 20 response compared to placebo at Week 24, with a slightly higher response in the anti-TNFα-naive group (anti-TNFα-naive: 37%, 64% and 58% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 15.9%; anti-TNFα-IR: 15%, 30% and 46% for 75 mg, 150 mg and 300 mg, respectively, compared to placebo 14.3%). In the anti-TNFα-IR patients subgroup, only the 300 mg dose showed significantly higher response rate for ACR 20 compared to placebo (p<0.05) and demonstrated clinical meaningful benefit over 150 mg on multiple secondary endpoints. Improvements in the PASI 75 response were seen in both subgroups and the 300 mg dose showed statistically significant benefit in the anti-TNFα-IR patients.

The number of PsA patients with axial involvement was too small to allow meaningful assessment.

Improvements were shown in all components of the ACR scores, including patient assessment of pain. The proportion of patients achieving a modified PsA Response Criteria (PsARC) response was greater in the Cosentyx-treated patients (37.4%, 59.0% and 61.0% for 75 mg, 150 mg and 300 mg, respectively) compared to placebo (26.5%) at Week 24.

In PsA Study 1 and PsA Study 2, efficacy was maintained up to Week 52. In PsA Study 2, among 200 patients initially randomised to Cosentyx 150 mg and 300 mg, 178 (89%) patients were still on treatment at Week 52. Of the 100 patients randomised to Cosentyx 150 mg, 64, 39 and 20 had an ACR 20/50/70 response, respectively. Of the 100 patients randomised to Cosentyx 300 mg, 64, 44 and 24 had an ACR 20/50/70 response, respectively.
Radiographic response

Inhibition of progression of structural damage in PsA has not yet been demonstrated using the subcutaneous loading regimen approved for clinical use.

In PsA Study 1, inhibition of progression of structural damage was assessed radiographically and expressed as the change in modified total Sharp Score (mTSS) and its components, the Erosion Score (ES) and the Joint Space Narrowing score (JSN) at Weeks 24 and 52, compared to baseline. Week 24 data are presented in Table 6.

Table 6  Change in modified Total Sharp Score in psoriatic arthritis

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=179</th>
<th>Cosentyx 75 mg(^1) N=181</th>
<th>Cosentyx 150 mg(^1) N=185</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline (SD)</td>
<td>28.4 (63.5)</td>
<td>20.4 (39.4)</td>
<td>22.3 (48.0)</td>
</tr>
<tr>
<td><strong>Mean change at Week 24</strong></td>
<td>0.57</td>
<td>0.02*</td>
<td>0.13*</td>
</tr>
</tbody>
</table>

\( ^* p<0.05 \) based on nominal, but non adjusted, \( p \)-value

\(^1\)10 mg/kg at Weeks 0, 2 and 4 followed by subcutaneous doses of 75 mg or 150 mg

Inhibition of structural damage was maintained with Cosentyx treatment up to Week 52.

The percentage of patients with no disease progression (defined as a change from baseline in mTSS of \( \leq 0.5 \)) from randomisation to Week 24 was 92.3% in secukinumab 10 mg/kg intravenous load – 75 mg subcutaneous maintenance, 82.3% in secukinumab 10 mg/kg intravenous load – 150 mg subcutaneous maintenance and 75.7% in placebo. The percentage of patients with no disease progression from Week 24 to Week 52 for secukinumab 10 mg/kg intravenous load – followed by either 75 mg or 150 mg subcutaneous maintenance and for placebo patients who switched to 75 mg or 150 mg subcutaneous every 4 weeks at Week 16 or Week 24 was 85.8%, 85.7% and 86.8%, respectively.

Physical function and health-related quality of life

In PsA Study 2, patients treated with Cosentyx 150 mg (\( p=0.0555 \)) and 300 mg (\( p=0.0040 \)) showed improvement in physical function compared to patients treated with placebo as assessed by Health Assessment Questionnaire-Disability Index (HAQ-DI) at Week 24. Improvements in HAQ-DI scores were seen regardless of previous anti-TNF\( \alpha \) exposure. Similar responses were seen in PsA Study 1.

Cosentyx-treated patients reported significant improvements in health-related quality of life as measured by the Short Form-36 Health Survey Physical Component Summary (SF-36 PCS) score (\( p<0.001 \)). There were also statistically significant improvements demonstrated in exploratory endpoints assessed by the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F) scores for 150 mg and 300 mg compared to placebo (7.97, 5.97 versus 1.63, respectively). Similar responses were seen in PsA Study 1 and efficacy was maintained up to Week 52.

Ankylosing spondylitis

The safety and efficacy of Cosentyx were assessed in 590 patients in two randomised, double-blind, placebo-controlled phase III studies in patients with active ankylosing spondylitis (AS) with a Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) \( \geq 4 \) despite non-steroidal anti-inflammatory drug (NSAID), corticosteroid or disease-modifying anti-rheumatic drug (DMARD) therapy. Patients in these studies had a diagnosis of AS for a median of 2.7 to 5.8 years. For both studies, the primary endpoint was at least a 20% improvement in Assessment of Spondyloarthritis International Society (ASAS 20) criteria at Week 16.
In Ankylosing Spondylitis Study 1 (AS Study 1) and Ankylosing Spondylitis Study 2 (AS Study 2) 27.0% and 38.8% of patients, respectively, were previously treated with an anti-TNFα agent and discontinued the anti-TNFα agent for either lack of efficacy or intolerance (anti-TNFα-IR patients).

AS Study 1 (MEASURE 1) evaluated 371 patients, of whom 14.8% and 33.4% used concomitant MTX or sulfasalazine, respectively. Patients randomised to Cosentyx received 10 mg/kg intravenously at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg subcutaneously every month starting at Week 8. Patients randomised to placebo who were non-responders at Week 16 (early rescue) and all other placebo patients at Week 24 were crossed over to receive Cosentyx (either 75 mg or 150 mg subcutaneously), followed by the same dose every month.

AS Study 2 (MEASURE 2) evaluated 219 patients, of whom 11.9% and 14.2% used concomitant MTX or sulfasalazine, respectively. Patients randomised to Cosentyx received 75 mg or 150 mg subcutaneously at Weeks 0, 1, 2, 3 and 4, followed by the same dose every month. At Week 16, patients who were randomised to placebo at baseline were re-randomised to receive Cosentyx (either 75 mg or 150 mg subcutaneously) every month.

**Signs and symptoms**

In AS Study 2, treatment with Cosentyx 150 mg resulted in greater improvement in measures of disease activity compared with placebo at Week 16 (see Table 7).

**Table 7 Clinical response in AS Study 2 at Week 16**

<table>
<thead>
<tr>
<th>Outcome (p-value versus placebo)</th>
<th>Placebo (n = 74)</th>
<th>75 mg (n = 73)</th>
<th>150 mg (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASAS 20 response, %</td>
<td>28.4</td>
<td>41.1</td>
<td>61.1***</td>
</tr>
<tr>
<td>ASAS 40 response, %</td>
<td>10.8</td>
<td>26.0</td>
<td>36.1***</td>
</tr>
<tr>
<td>hsCRP, (post-BSL/BSL ratio)</td>
<td>1.13</td>
<td>0.61</td>
<td>0.55***</td>
</tr>
<tr>
<td>ASAS 5/6, %</td>
<td>8.1</td>
<td>34.2</td>
<td>43.1***</td>
</tr>
<tr>
<td>ASAS partial remission, %</td>
<td>4.1</td>
<td>15.1</td>
<td>13.9</td>
</tr>
<tr>
<td>BASDAI 50, %</td>
<td>10.8</td>
<td>24.7*</td>
<td>30.6**</td>
</tr>
<tr>
<td>ASDAS-CRP major improvement</td>
<td>4.1</td>
<td>15.1*</td>
<td>25.0***</td>
</tr>
</tbody>
</table>

* p<0.05, ** p<0.01, *** p<0.001; versus placebo
All p-values adjusted for multiplicity of testing based on pre-defined hierarchy, except BASDAI 50 and ASDAS-CRP
Non-responder imputation used for missing binary endpoint

ASAS: Assessment of SpondyloArthritis International Society Criteria; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; hsCRP: high-sensitivity C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score; BSL: baseline

The onset of action of Cosentyx 150 mg occurred as early as Week 1 for ASAS 20 and Week 2 for ASAS 40 (superior to placebo) in AS Study 2.

ASAS 20 responses were improved at Week 16 in both anti-TNFα-naïve patients (68.2% versus 31.1%; p<0.05) and anti-TNFα-IR patients (50.0% versus 24.1%; p<0.05) for Cosentyx 150 mg compared with placebo, respectively.
In both AS studies, Cosentyx-treated patients (150 mg in AS Study 2 and both regimens in AS Study 1) demonstrated significantly improved signs and symptoms at Week 16, with comparable magnitude of response and efficacy maintained up to Week 52 in both anti-TNFα-naive and anti-TNFα-IR patients. In AS Study 2, among 72 patients initially randomised to Cosentyx 150 mg, 61 (84.7%) patients were still on treatment at Week 52. Of the 72 patients randomised to Cosentyx 150 mg, 45 and 35 had an ASAS 20/40 response, respectively.

**Spinal mobility**

Patients treated with Cosentyx 150 mg showed improvements in spinal mobility as measured by change from baseline in BASMI at Week 16 for both AS Study 1 (-0.40 versus -0.12 for placebo; p=0.0114) and AS Study 2 (-0.51 versus -0.22 for placebo; p=0.0533). These improvements were sustained up to Week 52.

**Physical function and health-related quality of life**

In AS Study 1 and Study 2, patients treated with Cosentyx 150 mg showed improvements in health-related quality of life as measured by AS Quality of Life Questionnaire (ASQoL) (p=0.001) and SF-36 Physical Component Summary (SF-36PCS) (p<0.001). Patients treated with Cosentyx 150 mg also showed statistically significant improvements on exploratory endpoints in physical function as assessed by the Bath Ankylosing Spondylitis Functional Index (BASFI) compared to placebo (-2.15 versus -0.68), and in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) scale compared to placebo (8.10 versus 3.30). These improvements were sustained up to Week 52.

**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 and in chronic idiopathic arthritis for paediatric patients aged from birth to less than 2 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 and in chronic idiopathic arthritis for paediatric patients aged from 2 years to less than 18 years (see section 4.2 for information on paediatric use).

### 5.2 Pharmacokinetic properties

#### Plaque psoriasis

**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.

**Psoriatic arthritis**
The pharmacokinetic properties of secukinumab observed in psoriatic arthritis patients were similar to those displayed in plaque psoriasis patients. The bioavailability of secukinumab in PsA patients was 85% on the basis of the population pharmacokinetic model.

**Ankylosing spondylitis**
The pharmacokinetic properties of secukinumab observed in ankylosing spondylitis patients were similar to those displayed in plaque psoriasis patients.

**Special populations**

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

Of the 974 psoriatic arthritis patients exposed to Cosentyx in clinical studies, a total of 85 patients were 65 years of age or older and 4 patients were 75 years of age or older.

Of the 571 ankylosing spondylitis patients exposed to Cosentyx in clinical studies, a total of 24 patients were 65 years of age or older and 3 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.

**Effect of weight on pharmacokinetics**
Secukinumab clearance and volume of distribution increase as body weight increases.

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. If necessary, Cosentyx may be stored unrefrigerated for a single period of up to 4 days at room temperature, not above 30°C. 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 unit packs containing 1 or 2 pre-filled pens and in multipacks containing 6 (3 packs of 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
EU/1/14/980/007
9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

15.01.2015

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 requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates 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.
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

17. **UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

18. **UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC:  
SN:  
NN:
### MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

#### VIAL LABEL

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosentyx 150 mg powder for solution for injection</td>
</tr>
<tr>
<td>secukinumab</td>
</tr>
<tr>
<td>SC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2. METHOD OF ADMINISTRATION</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>3. EXPIRY DATE</th>
</tr>
</thead>
<tbody>
<tr>
<td>EXP</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>4. BATCH NUMBER</th>
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</thead>
<tbody>
<tr>
<td>Lot</td>
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<table>
<thead>
<tr>
<th>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>6. OTHER</th>
</tr>
</thead>
</table>
### PARTICULARS TO APPEAR ON THE OUTER PACKAGING

**CARTON OF UNIT PACK – 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

17. **UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

18. **UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC:
SN:
NN:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – 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
Multipack: 6 (3 packs of 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 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/1/14/980/006 Multipack containing 6 (3 x 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

17. **UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

18. **UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC:
SN:
NN:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING
INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – 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

2 pre-filled syringes. Component of a multipack. Not to be sold separately.

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 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/1/14/980/006  
Multipack containing 6 (3 x 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
<table>
<thead>
<tr>
<th>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLISTER OF PRE-FILLED SYRINGE</td>
</tr>
</tbody>
</table>

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**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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<tbody>
<tr>
<td><strong>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</strong></td>
<td></td>
</tr>
<tr>
<td>Cosentyx 150 mg injection</td>
<td>secukinumab</td>
</tr>
<tr>
<td>SC</td>
<td></td>
</tr>
<tr>
<td><strong>2. METHOD OF ADMINISTRATION</strong></td>
<td></td>
</tr>
<tr>
<td><strong>3. EXPIRY DATE</strong></td>
<td>EXP</td>
</tr>
<tr>
<td><strong>4. BATCH NUMBER</strong></td>
<td>Lot</td>
</tr>
<tr>
<td><strong>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</strong></td>
<td></td>
</tr>
<tr>
<td><strong>6. OTHER</strong></td>
<td></td>
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</tbody>
</table>
### PARTICULARS TO APPEAR ON THE OUTER PACKAGING

**CARTON OF UNIT PACK – 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

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (INCLUDING BLUE BOX) – 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

Multipack: 6 (3 packs of 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 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/1/14/980/007  
Multipack containing 6 (3 x 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

17. **UNIQUE IDENTIFIER – 2D BARCODE**

2D barcode carrying the unique identifier included.

18. **UNIQUE IDENTIFIER - HUMAN READABLE DATA**

PC:  
SN:  
NN:
PARTICULARS TO APPEAR ON THE OUTER PACKAGING
INTERMEDIATE CARTON OF MULTIPACK (WITHOUT BLUE BOX) – 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

2 pre-filled SensoReady pens. Component of a multipack. Not to be sold separately.

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 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/1/14/980/007  
Multipack containing 6 (3 x 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

<table>
<thead>
<tr>
<th>1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cosentyx 150 mg solution for injection in pre-filled pen seckininumab SC</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>2. METHOD OF ADMINISTRATION</th>
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<table>
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<tr>
<th>3. EXPIRY DATE</th>
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<tr>
<td>EXP</td>
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<tr>
<th>4. BATCH NUMBER</th>
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<td>Lot</td>
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<table>
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<tr>
<th>5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT</th>
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</table>

<table>
<thead>
<tr>
<th>6. OTHER</th>
</tr>
</thead>
<tbody>
<tr>
<td>SensoReady pen</td>
</tr>
</tbody>
</table>
B. PACKAGE LEAFLET
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
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

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, psoriatic arthritis and ankylosing spondylitis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Ankylosing spondylitis

**Plaque 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 in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.
Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.

Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

Ankylosing spondylitis
Cosentyx is used to treat a condition called “ankylosing spondylitis”. The condition is an inflammatory disease primarily affecting the spine which causes inflammation of the spinal joints. If you have ankylosing spondylitis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis.

Using Cosentyx in ankylosing spondylitis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

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
• 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, breast-feeding and fertility
• 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.

Plaque psoriasis
• 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, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Psoriatic arthritis
For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
• 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, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.
For other psoriatic arthritis patients:
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at Weeks 1, 2, 3 and 4 followed by monthly injections.

**Ankylosing spondylitis**
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at Weeks 1, 2, 3 and 4 followed by monthly injections.

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, psoriatic arthritis or ankylosing spondylitis 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:

**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.

Your doctor will decide if and when you may restart the treatment.
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.

**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)

**Common** (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhea)

**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)
- itchy rash (urticaria)

**Rare** (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)

**Not known** (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

**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. 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. 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:

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Sverige
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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 injection is at room temperature.
2. Withdraw slightly more than 1.0 ml sterile water for injection 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.
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 this leaflet
1. What Cosentyx is and what it is used for
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

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, psoriatic arthritis and ankylosing spondylitis.

Cosentyx is used for the treatment of the following inflammatory diseases:
- Plaque psoriasis
- Psoriatic arthritis
- Ankylosing spondylitis

Plaque 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 in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

Psoriatic arthritis
Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.
Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

**Ankylosing spondylitis**
Cosentyx is used to treat a condition called “ankylosing spondylitis”. The condition is an inflammatory disease primarily affecting the spine which causes inflammation of the spinal joints. If you have ankylosing spondylitis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis.

Using Cosentyx in ankylosing spondylitis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

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
- 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, breast-feeding and fertility
• 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.

Plaque psoriasis
• 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, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Psoriatic arthritis
For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
• 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, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.
For other psoriatic arthritis patients:
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at Weeks 1, 2, 3 and 4 followed by monthly injections.

**Ankylosing spondylitis**
- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at Weeks 1, 2, 3 and 4 followed by monthly injections.

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, psoriatic arthritis or ankylosing spondylitis 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:

**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.

Your doctor will decide if and when you may restart the treatment.
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.

**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)

**Common** (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhea)

**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)
- itchy rash (urticaria)

**Rare** (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)

**Not known** (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

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.
If necessary, Cosentyx can be left out of the refrigerator for up to 4 days at room temperature, not above 30°C.

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. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. Cosentyx is available in unit packs containing 1 or 2 pre-filled syringe(s) and in multipacks containing 6 (3 packs of 2) pre-filled syringes. Not all pack sizes may be marketed.

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**Manufacturer**
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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.
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

\(\text{\textbullet\hspace{1cm}}}\) 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
2. What you need to know before you use Cosentyx
3. How to use Cosentyx
4. Possible side effects
5. How to store Cosentyx
6. Contents of the pack and other information

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, psoriatic arthritis and ankylosing spondylitis.

Cosentyx is used for the treatment of the following inflammatory diseases:

- **Plaque psoriasis**
- **Psoriatic arthritis**
- **Ankylosing spondylitis**

**Plaque 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 in plaque psoriasis will benefit you by leading to improvements of skin clearance and reducing your symptoms such as scaling, itching and pain.

**Psoriatic arthritis**

Cosentyx is used to treat a condition called “psoriatic arthritis”. The condition is an inflammatory disease of the joints, often accompanied by psoriasis. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of active psoriatic arthritis, improve physical function and slow down the damage to the cartilage and bone of the joints involved in the disease.
Cosentyx is used in adults with active psoriatic arthritis and can be used alone or with another medicine called methotrexate.

Using Cosentyx in psoriatic arthritis will benefit you by reducing the signs and symptoms of the disease, slowing down the damage to the cartilage and bone of the joints and improving your ability to do normal daily activities.

**Ankylosing spondylitis**

Cosentyx is used to treat a condition called “ankylosing spondylitis”. The condition is an inflammatory disease primarily affecting the spine which causes inflammation of the spinal joints. If you have ankylosing spondylitis you will first be given other medicines. If you do not respond well enough to these medicines, you will be given Cosentyx to reduce the signs and symptoms of the disease, reduce inflammation and improve your physical function.

Cosentyx is used in adults with active ankylosing spondylitis.

Using Cosentyx in ankylosing spondylitis will benefit you by reducing the signs and symptoms of your disease and improving your physical function.

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
- 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, breast-feeding and fertility
- 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.

Plaque psoriasis
- 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, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.

Psoriatic arthritis
For psoriatic arthritis patients who also have moderate to severe plaque psoriasis or patients who did not respond well to medicines called tumour necrosis factor (TNF) blockers:
- 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, 3 and 4 followed by monthly injections. At each timepoint you will receive a 300 mg dose given as two injections of 150 mg.
For other psoriatic arthritis patients:

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at Weeks 1, 2, 3 and 4 followed by monthly injections.

Ankylosing spondylitis

- The recommended dose is 150 mg by subcutaneous injection.

After the first dose you will receive further weekly injections at Weeks 1, 2, 3 and 4 followed by monthly injections.

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, psoriatic arthritis or ankylosing spondylitis 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:

**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.

Your doctor will decide if and when you may restart the treatment.
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.

**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)

**Common** (may affect up to 1 in 10 people):
- cold sores (oral herpes)
- diarrhoea
- runny nose (rhinorrhea)

**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)
- itchy rash (urticaria)

**Rare** (may affect up to 1 in 1,000 people):
- severe allergic reaction with shock (anaphylactic reaction)

**Not known** (frequency cannot be estimated from the available data):
- fungal infections of the skin and mucous membranes (including oesophageal candidiasis)

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.
If necessary, Cosentyx can be left out of the refrigerator for up to 4 days at room temperature, not above 30°C.

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. Do not use if the liquid contains easily visible particles, is cloudy or is distinctly brown. Cosentyx is available in unit packs containing 1 or 2 pre-filled pen(s) and in multipacks containing 6 (3 packs of 2) pre-filled pens. Not all pack sizes may be marketed.

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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:

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](image)

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.