

Cosentyx[®] (secukinumab) Clinical Summary for Formulary Review

Please consult complete Prescribing Information

Indications and Usage¹

Plaque Psoriasis: Cosentyx is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.

Psoriatic Arthritis: Cosentyx is indicated for the treatment of adult patients with active psoriatic arthritis.

Ankylosing Spondylitis: Cosentyx is indicated for the treatment of adult patients with active ankylosing spondylitis.

Dosage and Administration¹

Plaque Psoriasis: The recommended dosage is 300 mg by subcutaneous injection at Weeks 0, 1, 2, 3, and 4 followed by 300 mg every 4 weeks. Each 300 mg dosage is given as 2 subcutaneous injections of 150 mg.

For some patients, a dosage of 150 mg may be acceptable.

Psoriatic Arthritis: For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing and administration recommendations for plaque psoriasis.

For other psoriatic arthritis patients, administer Cosentyx with or without a loading dosage by subcutaneous injection. Cosentyx may be administered with or without methotrexate. The recommended dosage:

- With loading dosage is 150 mg at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Without a loading dosage is 150 mg every 4 weeks
- If a patient continues to have active psoriatic arthritis, consider a dosage of 300 mg.

Ankylosing Spondylitis: Administer Cosentyx with or without a loading dosage by subcutaneous injection. The recommended dosage:

- With loading dosage is 150 mg at weeks 0, 1, 2, 3, and 4 and every 4 weeks thereafter
- Without a loading dosage is 150 mg every 4 weeks.

Efficacy¹⁻⁷

*Plaque Psoriasis*¹⁻⁴

The efficacy and safety of Cosentyx has been evaluated in 4 multicenter, randomized, double-blind, placebo controlled studies in a total of 2403 subjects 18 years of age and older with plaque psoriasis who had a minimum body surface area involvement of 10%, and Psoriasis Area and Severity Index (PASI) score greater than or equal to 12, and who were candidates for phototherapy or systemic therapy. Baseline PASI score ranged from 11 to 72 with a median of 20 and the baseline IGA modified 2011 score ranged from “moderate” (62%) to “severe” (38%). Of the 2077 plaque psoriasis subjects who were included in the placebo-controlled trials, 79% were biologic-naïve and 45% were non-biologic failures. Of the subjects who received a prior treatment with biologics, over one-third were biologic failures. Approximately 15 to 25% of trial subjects had a history of psoriatic arthritis.

Trial 1 (ERASURE):^{1,2} A total of 738 subjects (245 randomized to Cosentyx 300 mg, 245 to Cosentyx 150 mg, and 248 to placebo) received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by dosing every 4 weeks. Subjects randomized to receive placebo who were non-responders at Week 12 were then crossed over to receive Cosentyx (either 300 mg or 150 mg) at Weeks 12, 13, 14, 15, and 16 followed by the same dose every 4 weeks. All subjects were followed for up to 52 weeks following first administration of study treatment.

Results: Percentage of subjects achieving a PASI 75 response at Week 12 was statistically significant with Cosentyx 300 mg and 150 mg compared to placebo (p value < 0.0001 for each Cosentyx dose). Results of IGA modified 2011 at Week 12 was statistically significant compared to placebo (p<0.0001).

Trial 2 (FIXTURE):^{1,2} A total of 1306 subjects (327 randomized to Cosentyx 300 mg, 327 to Cosentyx 150 mg, 326 to placebo, and 323 to a biologic active control) received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by dosing every 4 weeks. Subjects randomized to receive placebo who were non-responders at Week 12 then crossed over to receive Cosentyx (either 300 mg or 150 mg) at Weeks 12, 13, 14, 15, and 16 followed by the same dose every 4 weeks. All subjects were followed for up to 52 weeks following first administration of study treatment. **Results:** Percentage of subjects achieving a PASI 75 response at Week 12 was statistically significant with Cosentyx 300 mg and 150 mg compared to placebo (p value < 0.0001 for each Cosentyx dose). Results of IGA modified 2011 at Week 12 was statistically significant compared to placebo (p<0.0001).

Trial 3 (FEATURE):^{1,3} A total of 177 subjects (59 randomized to Cosentyx 300 mg, 59 randomized to Cosentyx 150 mg, and 59 to placebo) were assessed for safety, tolerability, and usability of Cosentyx self-administration via prefilled syringe for 12 weeks. Subjects received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks for up to 12 weeks total. **Results:** Percentage of subjects who achieved a PASI 75 response at Week 12 was statistically significant with Cosentyx 300 mg and 150 mg compared to placebo (p value <0.0001 for each Cosentyx dose). Results of IGA mod 2011 at Week 12 was statistically significant compared to placebo (p<0.0001 for each Cosentyx dose).

Trial 4 (JUNCTURE):^{1,4} A total of 182 subjects (60 randomized to Cosentyx 300, 61 to Cosentyx 150 mg, and 61 to placebo) were assessed for safety, tolerability, and usability of Cosentyx self-administration via Sensoready pen for 12 weeks. Subjects received subcutaneous treatment at Weeks 0, 1, 2, 3, and 4 followed by the same dose every 4 weeks for up to 12 weeks total. **Results:** Percentage of subjects achieving a PASI 75 response at Week 12 was statistically significant with Cosentyx 300 mg and 150 mg compared to placebo (p value <0.0001 for each Cosentyx dose). Results of IGA mod 2011 at Week 12 was statistically significant compared to placebo.

Subjects in Trials 1 and 2 who were PASI 75 responders and/or achieved clear or almost clear on the IGA at Week 12 maintained their respective responses over 52 weeks with continued treatment. Among the subjects who chose to participate (39%) in assessments of patient reported outcomes, improvements in signs and symptoms related to itching, pain, and scaling, at Week 12 compared to placebo (Trials 1 and 2) were observed using the Psoriasis Symptom Diary[®].

Psoriatic Arthritis (PsA)^{1,5,6}

The safety and efficacy of Cosentyx were assessed in 1003 patients, in 2 randomized, double-blind, placebo-controlled studies (PsA1 and PsA2) in adult patients, aged 18 years and older with active PsA (>3 swollen and >3 tender joints) despite NSAID, corticosteroid, or

DMARD therapy. Patients had a diagnosis of PsA of at least 5 years across both studies. Overall, 32% of patients discontinued previous treatment with anti-TNF α agents due to lack of efficacy or intolerance, and ~55% of patients had concomitant methotrexate use.

Trial PsA1 (FUTURE 2):^{1,5}

A total of 397 patients received a loading dose of SC Cosentyx 300 mg, 150 mg, or 75 mg, or placebo at Weeks 0, 1, 2, 3, 4, followed by the same dose every 4 weeks. Patients receiving placebo were re-randomized to Cosentyx (either 300 mg or 150 mg every 4 weeks) at Week 16 or 24 based on responder status. The primary endpoint was the percentage of patients who achieved an ACR20 response at Week 24. **Results:** At Week 24, the ACR20 response rate was 54% for Cosentyx 300 mg (n=100), 51% for Cosentyx 150 mg (n=100), and 15% for placebo (n=98) (p<0.0001 for secukinumab 300 mg and 150 mg, compared to placebo). Responses were similar in patients regardless of concomitant methotrexate treatment and were seen regardless of prior anti-TNF α exposure.

Trial PsA2 (FUTURE 1):^{1,6}

A total of 606 patients received a loading dose of IV secukinumab 10 mg/kg or placebo at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg SC Cosentyx treatment (or placebo) every 4 weeks. Patients receiving placebo were re-randomized to Cosentyx (either 75 mg or 150 mg every 4 weeks) at Week 16 or 24 based on responder status.

Ankylosing Spondylitis (AS):^{1,7}

The safety and efficacy of Cosentyx were assessed in 590 patients in two randomized, double-blind, placebo-treated controlled studies (AS1 and AS2) in adult patients, aged 18 years and older with active AS (BASDAI \geq 4) despite NSAID, corticosteroid or DMARD therapy. At baseline, ~14% and 26% used concomitant methotrexate or sulfasalazine, respectively, and 33% of patients discontinued previous treatment with anti-TNF α agents due to lack of efficacy or intolerance.

Trial AS1 (MEASURE 2):^{1,7}

A total of 219 patients received a loading dose of SC Cosentyx 150 mg, 75 mg, or placebo at Weeks 0, 1, 2, 3, and 4, followed by the same dose every 4 weeks. At Week 16, patients receiving placebo were re-randomized to either Cosentyx 150 mg or 75 mg every 4 weeks. The primary endpoint was the percentage of patients who achieved an ASAS20 response at Week 16. **Results:** At Week 16, patients treated with Cosentyx 150 mg demonstrated greater improvement in ASAS20 response compared to placebo; the ASAS20 response rate was 61%, and 28% for Cosentyx 150 mg (n=72), and placebo (n=74) groups, respectively (p<0.001 for Cosentyx 150 mg vs. placebo; p=0.10 for secukinumab 75 mg vs placebo). Responses were similar in patients regardless of concomitant therapies.

Trial AS2 (MEASURE 1):^{1,7}

A total of 371 patients received a loading dose of IV secukinumab 10 mg/kg or placebo at Weeks 0, 2, and 4, followed by either 75 mg or 150 mg Cosentyx treatment every 4 weeks or placebo. Patients receiving placebo were re-randomized to Cosentyx (either 75 mg or 150 mg every 4 weeks) at Week 16 or Week 24 based on responder status.

Adverse Event Profile¹

The most common adverse reactions (incidence \geq 1% and >placebo) for Cosentyx were nasopharyngitis, diarrhea, and upper respiratory tract infection.

Warnings and Precautions¹

Infections: Cosentyx may increase the risk of infections. The incidence of some types of infections appeared to be dose-dependent in clinical studies. Exercise caution when considering use of Cosentyx in patients with a chronic infection or history of recurrent infection.

Tuberculosis: Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with Cosentyx.

Inflammatory Bowel Disease: Caution should be used in patients with inflammatory bowel disease. Patients should be monitored for signs and symptoms of inflammatory bowel disease. In patients with Crohn's disease, there were trends toward greater disease activity and increased adverse events. Exacerbation and new onset cases occurred in clinical trials.

Hypersensitivity Reactions: Anaphylaxis and cases of urticaria occurred in Cosentyx-treated patients in the clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of Cosentyx should be discontinued immediately and appropriate therapy initiated.

Latex-sensitive Individuals: The removable cap of the Cosentyx Sensoready pen and the Cosentyx prefilled syringe contains natural rubber latex which may cause an allergic reaction in latex-sensitive individuals. The safe use of Cosentyx Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.

Vaccinations: Prior to initiating therapy with Cosentyx, consider completion of all age appropriate immunizations according to current immunization guidelines. Patients treated with Cosentyx should not receive live vaccines. Non-live vaccines received during a course of Cosentyx may not elicit an immune response sufficient to prevent disease.

References:

1. Cosentyx (secukinumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation Jan.2016
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3. Blauvelt A, Prinz JC, Gottlieb AB et al. Secukinumab administration by pre-filled syringe: efficacy, safety, and usability results from a randomized controlled trial in psoriasis (FEATURE). *Br J Dermatol.* 2015;172(2):484-493.
4. Paul C, Lacour JP, Tedremets L, et al. Efficacy, safety and usability of secukinumab administration by autoinjector/pen in psoriasis: a randomized, controlled trial (JUNCTURE). *J Eur Acad Dermatol Venereol.* 2015;29(6):1082-1090.
5. McInnes IB, Mease PJ, Kirkham B, et al. Secukinumab, a human anti-interleukin-17A monoclonal antibody, in patients with psoriatic arthritis (FUTURE 2): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet.* 2015;386(9999):1137-1146.
6. Mease PJ, McInnes IB, Kirkham B, et al. Secukinumab inhibition of interleukin-17A in patients with psoriatic arthritis. *N Engl J Med.* 2015;373(14):1329-1339.
7. Baeten D, Sieper J, Braun J, et al. Secukinumab, an interleukin-17A inhibitor, in ankylosing spondylitis. *N Engl J Med.* 2015;373(26):2534-48.