Cosentyx® [koe-sen-tix] (secukinumab) [sek-ue-kin-ue-mab] Clinical Summary for Formulary Review
Please utilize in conjunction with accompanying Prescribing Information (PI) (link)

***Indications & Usage*[1]**

Plaque Psoriasis (PsO): Cosentyx (COS) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy.
Psoriatic Arthritis (PsA): COS is indicated for the treatment of adult patients with active psoriatic arthritis.
Ankylosing Spondylitis (AS): COS is indicated for the treatment of adult patients with active ankylosing spondylitis.
Non-radiographic axial spondyloarthritis (nr-axSpA): COS is indicated for the treatment of adult patients with active non-radiographic axial spondyloarthrtiis (nr-axSpA) with objective signs of inflammation.

Mechanism of Action[1] Human IgG1 monoclonal antibody that selectively binds to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor. IL-17A is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Secukinumab inhibits the release of pro-inflammatory cytokines and chemokines.

Dosage & Administration[1]
PsO: The recommended dosage is 300 mg by subcutaneous (SC) injection at Weeks 0, 1, 2, 3, & 4 followed by 300 mg every 4 weeks. Each 300 mg dosage is given as 2 SC injections of 150 mg. For some patients, a dosage of 150 mg may be acceptable.
PsA: For psoriatic arthritis patients with coexistent moderate to severe plaque psoriasis, use the dosing & administration recommendations for plaque psoriasis. For other PsA patients, administer COS with or without a loading dosage (LD) by SC injection. The recommended dosage with LD is 150 mg at weeks 0, 1, 2, 3, & 4 and every 4 weeks thereafter; without a LD is 150 mg every 4 weeks; if a patient continues to have active PsA, consider a dosage of 300 mg every 4 weeks. COS may be administered with or without methotrexate (MTX).
AS: Administer COS with or without a LD by SC injection. The recommended dosage with LD is 150 mg at weeks 0, 1, 2, 3, & 4 and every 4 weeks thereafter; without a LD is 150 mg every 4 weeks; If a patient continues to have active AS, consider a dosage of 300 mg every 4 weeks
Nr-axSpA: Administer COS with or without a LD by SC injection. The recommended dosage with LD is 150 mg at weeks 0, 1, 2, 3, & 4 and every 4 weeks thereafter; without a LD is 150 mg every 4 weeks

Efficacy[1-9]

- ***Plaque Psoriasis (PsO)***[1-4]
  4 multicenter, randomized, double-blind, placebo (PBO) controlled studies in a total of 2403 patients ≥18 years with plaque psoriasis who had a minimum body surface area involvement of 10%, & Psoriasis Area and Severity Index (PASI) score ≥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 patients who were included in the placebo-controlled trials, 79% were biologic-naïve and 45% were non-biologic failures. Of the patients who received a prior treatment with biologics, over one-third were biologic failures. Approximately 15 to 25% of trial patients had a history of psoriatic arthritis.
  Trial 1 (ERASURE):[1,2] 738 patients (245 randomized to COS 300 mg, 245 to COS 150 mg, and 248 to PBO) received SC treatment at Weeks 0, 1, 2, 3, & 4 followed by every 4 weeks. Patients randomized to receive PBO who were non-responders at Week 12 were then crossed over to receive COS (either 300 mg or 150 mg) at Weeks 12, 13, 14, 15, & 16 followed by the same dose every 4 weeks. All patients were followed for up to 52 weeks following first administration of study treatment. ***Results***: PASI 75 response rates at Week 12 were statistically significant with COS 300 mg & 150 mg vs. PBO (p value < 0.0001 for each COS dose). IGA modified 2011 result at Week 12 was statistically significant vs. PBO (p<0.0001).
  Trial 2 (FIXTURE):[1,2] 1306 patients (327 randomized to COS 300 mg, 327 to COS 150 mg, 326 to PBO, & 323 to a biologic active control) received SC treatment at Weeks 0, 1, 2, 3, & 4 followed by dosing every 4 weeks. Patients randomized to receive PBO who were non-responders at Week 12 then crossed over to receive COS (either 300 mg or 150 mg) at Weeks 12, 13, 14, 15, & 16 followed by the same dose every 4 weeks. All patients were followed for up to 52 weeks following first administration of study treatment. ***Results***: PASI 75 response rates at Week 12 were statistically significant with COS 300 mg & 150 mg vs. PBO (p value < 0.0001 for each COS dose). IGA modified 2011 result at Week 12 was statistically significant vs. PBO (p<0.0001).
  Trial 3 (FEATURE):[1,3] 177 patients (59 randomized to COS 300 mg, 59 randomized to COS 150 mg, & 59 to PBO) were assessed for safety, tolerability, & usability of COS self-administration via prefilled syringe for 12 weeks. Patients received SC treatment at Weeks 0, 1, 2, 3, & 4 followed by the same dose every 4 weeks for up to 12 weeks total. ***Results***: PASI 75 response rates at Week 12 were statistically significant with COS 300 mg & 150 mg vs. PBO (p value <0.0001 for each COS dose). IGA mod 2011 results at Week 12 was statistically significant vs. PBO p<0.0001 for each COS dose).
  Trial 4 (JUNCTURE):[1,4] 182 patients (60 randomized to COS 300, 61 to COS 150 mg, & 61 to PBO) were assessed for safety, tolerability, & usability of COS self-administration via Sensoready pen for 12 weeks. Patients received SC treatment at Weeks 0, 1, 2, 3, & 4 followed by the same dose every 4 weeks for up to 12 weeks total. ***Results***: PASI 75 response rates at Week 12 were statistically significant with COS 300 mg & 150 mg vs. PBO (p value <0.0001 for each COS dose). IGA mod 2011 result at Week 12 was statistically significant vs. PBO.

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

- Psoriatic Arthritis (PsA)1,5,6
  3 randomized, double-blind, PBO-controlled studies (PsA1, PsA2, & PSA3) in 1999 adult patients, aged 18 years & older with active PsA (≥3 swollen joints & ≥3 tender joints) despite NSAID, corticosteroid, or DMARD therapy. Patients had a diagnosis of PsA of at least 5 years across all studies. Overall, 31% of patients discontinued previous treatment with anti-TNFα agents due to lack of efficacy or intolerance, & 53% of patients had concomitant methotrexate use.
  Trial PsA1 (FUTURE 2):1,5 397 patients received a LD of SC COS 300 mg, 150 mg, or 75 mg, or PBO at Weeks 0, 1, 2, 3, 4, followed by the same dose every 4 weeks. Patients receiving PBO were re-randomized to COS (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, ACR20 response rates were 54% for COS 300 mg (n=100), 51% for COS 150 mg (n=100), & 15% for PBO (n=98) (p<0.0001 for COS 300 mg & 150 mg, vs. PBO), with similar responses seen regardless of concomitant methotrexate treatment or prior anti-TNFα exposure.
  Trial PsA2 (FUTURE 1):1,6 606 patients received a LD of IV COS 10 mg/kg (for both treatment arms) or PBO at Weeks 0, 2, & 4, followed by either 75 mg or 150 mg SC COS (or PBO) Q4W. Patients receiving PBO were re-randomized to COS (either 150 mg or 75 mg every 4 weeks)

at Week 16 or 24 based on responder status. Efficacy results from this study are not presented in the PI.
Trial PsA3 (FUTURE 5):[1,8] 996 patients received SC COS 300mg, 150mg, 150mg (no LD) or PBO at Weeks 0, 1, 2, 3, 4, followed by the same dose Q4W. Patients receiving PBO were re-randomized to COS (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 16 with the key secondary endpoint as change from baseline in modified Total Sharp Score (mTSS) at Week 24. Components of mTSS are Erosion Score (ES) & Joint Space Narrowing Score (JSN). ***Results***: The percent of patients with no disease progression (defined as mTSS change from baseline of ≤ 0.0) from randomization to Week 24 was 75.7%, 70.9%, & 76.5% for COS 150 mg no LD, 150 mg, 300 mg, respectively vs. 68.2% for PBO.

- ***Ankylosing Spondylitis (AS)***[1,7,9]
3 randomized, double-blind, PBO-treated controlled studies (AS1, AS2, & AS3) in 816 adult patients, ≥18 years with active AS (BASDAI ≥4) despite NSAID, corticosteroid or DMARD therapy. At baseline, ~13% & 25% used concomitant methotrexate or sulfasalazine, respectively, and 29% of patients discontinued previous treatment with anti-TNFα agents due to lack of efficacy or intolerance.
Trial AS1 (MEASURE 2):[1,7] 219 patients reload
ceived a LD of SC COS 150 mg, 75 mg, or PBO at Weeks 0, 1, 2, 3, & 4, followed by the same dose every 4 weeks. At Week 16, patients receiving PBO were re-randomized to either COS 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 COS 150 mg demonstrated greater improvement in ASAS20 response vs. PBO; the ASAS20 response rate was 61%, & 28% for COS 150 mg (n=72), & PBO (n=74) groups, respectively ($p<0.001$ for COS 150 mg vs. PBO), with similar responses seen regardless of concomitant therapies.
Trial AS2 (MEASURE 1):[1,7] 371 patients received a LD of IV COS 10 mg/kg (for both treatment arms) or PBO at Weeks 0, 2, & 4, followed by either 75 mg or 150 mg COS treatment every 4 weeks or PBO. Patients receiving PBO were re-randomized to COS (either 75 mg or 150 mg every 4 weeks) at Week 16 or Week 24 based on responder status. Efficacy results from this study are not presented in the PI.
Trial AS3 (MEASURE 3):[1,9] 226 patients received a LD of IV COS 10 mg/kg (for both treatment arms) or PBO at Weeks 0, 2, & 4 followed by either 150 mg or 300 mg SC COS treatment every 4 weeks or placebo. Patients receiving PBO were re-randomized to COS (either 150 mg or 300 mg every 4 weeks) at week 16. The primary endpoint was the percentage of patients who achieved an ASAS20 response at Week 16. ***Results:*** At Week 16, patients treated with COS (150 mg & 300 mg) demonstrated comparable efficacy responses, regardless of dose, that were superior to PBO at Week 16; the ASAS20 response rate was 58.1% for COS 150 mg & 60.5% for COS 300 mg.

- ***Non-radiographic Axial Spondyloarthritis (nr-axSpA)***[1]
Trial nr-axSpA1 (PREVENT):[1] One randomized, DB, PBO-controlled study in 555 adult patients ≥18 years with active nr-axSpA. Patients met ASAS criteria for ax-SpA & had active disease (BASDAI≥4), a Visual Analogue Scale (VAS) for total back pain ≥40 despite NSAID therapy & no evidence of radiographic changes in the sacroiliac joints that would meet the modified New York criteria for AS. Patients also had to have objective signs of inflammation with a C-reactive protein (CRP) level above the upper limit of normal and/or evidence of sacroiliitis on Magnetic Resonance imaging (MRI). Overall, 10% of patients discontinued previous treatment with anti-TNFα agents due to lack of efficacy or intolerance, and ~10% and ~15% of patients used concomitant MTX or sulfasalazine, respectively.
Patients received either SC COS 150 mg (with LD or no LD) or PBO for 52 weeks. Starting at Week 16, dose adjustment or addition of concomitant NSAIDs & DMARDs was permitted. Starting at Week 20, patients could switch to open-label COS 150 Q4W or other biologic at the discretion of the investigator & patient. The primary endpoint was ASAS40 at Week 52. ***Results:*** Treatment with COS 150 mg (LD & no LD) demonstrated significant improvements in the measure of disease activity vs. PBO at Week 16 & at Week 52; the ASAS40 response rate was 38% for COS 150 mg no LD, 34% for COS 150 mg with LD, & 19% for PBO. Treatment with COS 150 mg (LD & no LD) showed improvement vs. PBO in HR-QoL as measured by ASQoL (LS mean change at Week 16: -3.5 & -3.6 vs -1.8, respectively).

Adverse Event (AE) Profile[1]
The most common AEs (incidence ≥1% & >PBO) for COS were nasopharyngitis, diarrhea, & upper respiratory tract infection.

Warnings & Precautions[1]
Infections: COS 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 COS in patients with a chronic infection or history of recurrent infection. If a serious infection develops, discontinue COS until the infection resolves.
Tuberculosis*:* Evaluate patients for tuberculosis (TB) infection prior to initiating treatment with COS.
Inflammatory Bowel Disease: Caution should be used in patients with 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. Patients should be monitored for signs and symptoms of inflammatory bowel disease.
Hypersensitivity Reactions*:* Anaphylaxis and cases of urticaria occurred in COS-treated patients in the clinical trials. If an anaphylactic or other serious allergic reaction occurs, administration of COS should be discontinued immediately and appropriate therapy initiated.
Latex-sensitive Individuals*:* The removable cap of the COS Sensoready pen and the COS prefilled syringe contains natural rubber latex which may cause an allergic reaction in latex-sensitive individuals. The safe use of COS Sensoready pen or prefilled syringe in latex-sensitive individuals has not been studied.
Vaccinations: Prior to initiating therapy with COS, consider completion of all age appropriate immunizations according to current immunization guidelines. Patients treated with COS should not receive live vaccines. Non-live vaccines received during a course of COS may not elicit an immune response sufficient to prevent disease.

References:

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