PDL NEW DRUG REVIEW

Proprietary Name: Cosentyx®
Common Name: secukinumab
PDL Category: Anti-Inflammatories, Non-NSAID

Comparable Products	Preferred Drug List Status
Humira	Preferred with Conditions
Stelara	Non-Preferred with Conditions

Summary

Indications and Usage: Treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy. This is a pregnancy category B medication. The safety and efficacy of use in children have not been established in pediatric patients.

Dosage Forms: *Injection*: 150mg/ml solution in a single-use Sensoready pen OR in a single-use prefilled syringe; the removable caps on these products contain natural rubber latex, and the safe use of these Cosentyx® products in latex-sensitive patients has not been studied. *For injection*: 150mg lyophilized powder in a single-use vial for reconstitution (for healthcare professional use only)

Recommended Dosage: 300mg SC at weeks 0, 1, 2, 3, and 4 followed by 300mg Q4W; for some patients, a 150mg dose may be acceptable. It is recommended to administer Cosentyx® in the upper, outer arm, thigh, or any quadrant of the abdomen, using a different location of injection than the previous injection. The Sensoready pen and pre-filled syringe may be self-administered by the patient after proper training on use. These dosage forms should be stored in the refrigerator but allowed to reach room temperature (15-30 minutes) before use without removing the needle cap. (The lyophilized powder for injection vial should also be stored in the refrigerator but is for healthcare provider use only.)

Pharmacokinetic trials were not performed with Cosentyx® in those with renal or hepatic impairment.

While those treated with Cosentyx® may receive non-live vaccinations, they may NOT receive live vaccinations. Cosentyx® should not be given to those with active TB infection, therefore it is recommended to evaluate for TB infection prior to starting treatment. Furthermore, it is recommended to use Cosentyx® with caution in those with active Crohn's disease as there have been reports, and in some cases serious, of exacerbations of Crohn's disease with Cosentyx® use during clinical trials.

Drug interactions have not been performed with Cosentyx®; however, in those receiving CYP450 substrates concomitantly when starting or discontinuing Cosentyx®, especially those with a narrow therapeutic index, it is suggested to monitor for therapeutic effect (e.g. for warfarin) or drug concentration (e.g. for cyclosporine) and consider dose modifications for the CYP450 substrate.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Cosentyx® 300mg/150mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same for both drugs of that the incidence for the active drug was less than placebo*. The most commonly reported adverse events included nasopharyngitis (2.8%/3.7%), diarrhea (2.7%/1.2%), upper respiratory

tract infection (1.8%/2.5%), rhinitis (0.7%/0.7%), oral herpes (1%/0%), pharyngitis (1.2%/1.0%), urticaria (0.5%/1.1%), and rhinorrhea (1.1%/0.2%). Infections were also reported in clinical trials with Cosentyx® vs placebo (9.8%), as well as serious infections (0%).

Contraindications: Serious hypersensitivity reaction to secukinumab or any component of the compound

Manufacturer: Novartis Pharmaceuticals

Analysis: Secukinumab, the active ingredient of Cosentyx®, is a recombinant human monoclonal IgG1/k antibody that is expressed in a recombinant Chinese Hamster Ovary (CHO) cell line. It binds specifically to the interleukin-17A (IL-17A) cytokine and inhibits its interaction with the IL-17 receptor, thus prohibiting the release of pro-inflammatory cytokines and chemokines. (IL-17 is a naturally occurring cytokine involved in normal inflammatory and immune responses).

There were 4 multicenter, randomized, double-blind, placebo-controlled that assessed the safety and efficacy of Cosentyx® in adults (N=2403) with plaque psoriasis who had a minimum body surface area involvement of 10%, a Psoriasis Area and Severity Index (PASI) score ≥12, and who were candidates for phototherapy or systemic therapy. The table below includes additional information regarding each study.

Study #	Study Characteristics
Study 1	• N=738 randomized to placebo or Cosentyx® 150mg or 300mg • Non-responders randomized to placebo crossed over to Cosentyx® at week 12 • All treated for up to 52 weeks
Study 2	• N=1306 randomized to Cosentyx® 150mg or 300mg, placebo, or biologic active control • Non-responders randomized to placebo crossed over to Cosentyx® at week 12 • All treated for up to 52 weeks
Study 3	• N=177 randomized to placebo or Cosentyx® 150mg or 300mg • Assessed safety, tolerability, and usability of Cosentyx® pre-filled syringe for 12 weeks
Study 4	• N=182 randomized to placebo or Cosentyx® 150mg or 300mg • Assessed safety, tolerability, and usability of Cosentyx® Sensoready pen for 12 weeks

The endpoints for all the trials were the proportion who achieved a reduction in PASI score of ≥75% (PASI 75) from baseline to week 12 and treatment success (clear or almost clear) on the Investigator's Global Assessment modified 2011 (IGA).

Study 2 included a biologic active-control (N=323) that was administered as etanercept 50mg BIW for 12W then QW. PASI 75 was achieved in 44% the active-control arm. The Cosentyx® group had a significantly higher number of patients who met criteria vs comparators ($p<0.001$ for each Cosentyx® dose vs comparators). The proportion with a response of 0 or 1 on the IGA at week 12 was also significantly higher ($p<0.001$ for each Cosentyx® dose vs comparators) with each Cosentyx® dose vs placebo or etanercept (27.2%).[2]

PASI 90 at week 12 was an additional endpoint assessed; this was achieved in 59% (N=145) of the Cosentyx® 300mg group and 39% (N=95) of the 150mg group vs 1% (N=3) of the placebo group in trial 1. In trial 2, the results were 54% (N=175) and 42% (N=137) vs 2% (N=5), respectively. Similar results were seen in trials 3 and 4.

Results of the 4 trials are presented in the table below.

	PASI 75 response	IGA of clear or almost clear
Trial 1		
Cosentyx® 300mg (N=245)	200 (82%)	160 (65%)
Cosentyx® 150mg (N=245)	174 (71%)	125 (51%)

	PASI 75 response	IGA of clear or almost clear
Placebo (N=248)	11 (4%)	6 (2%)
Trial 2		
Cosentyx® 300mg (N=327)	249 (76%)	202 (62%)
Cosentyx® 150mg (N=327)	219 (67%)	167 (51%)
Placebo (N=326)	16 (5%)	9 (3%)
Trial 3		
Cosentyx® 300mg (N=59)	44 (75%)	40 (68%)
Cosentyx® 150mg (N=59)	41 (69%)	31 (53%)
Placebo (N=59)	0 (0%)	0 (0%)
Trial 4		
Cosentyx® 300mg (N=60)	52 (87%)	44 (73%)
Cosentyx® 150mg (N=61)	43 (70%)	32 (52%)
Placebo (N=61)	2 (3%)	0 (0%)

Place in Therapy: Per a noted reference source[3], phototherapy is suggested as treatment for moderate-to-severe plaque psoriasis "…if feasible and practical", with topical agents used for adjuvant treatment. It is suggested that systemic agents be given to those with a contraindication to or who have failed phototherapy. Among others, secukinumab is listed as a systemic treatment. Secukinumab (Cosentyx®) is indicated for the treatment of moderate to severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy as an SC injection with minimal drug interactions.

Beyond a single actively control trial that favored Cosentyx® over etanercept, there is no evidence at this time to support that Cosentyx® is safer or more effective than other currently available, more cost effective medications, based on data reviewed from registration trials in the package insert as well as a review of current treatments used in psoriasis. It is therefore recommended that Cosentyx® remain non-preferred and require prior authorization and be available to the few who are unable to tolerate or who have failed on preferred medications.

PDL Placement: ☐ **Preferred**
☒ **Non-Preferred with Conditions**

References

[1] Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals; 2015.

[2] Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis- results of two phase 3 trials. *NEJM*. 2014; 371(4): 326.

[3] UpToDate desktop version. Treatment of psoriasis. Assessed March 2015.