Brand Name: Cosentyx

Generic Name: secukinumab

Manufacturer[1]: Novartis Pharmaceuticals Corporation

Drug Class[2,3]: Antipsoriatic Agent, Interleukin-17A Receptor Antagonist

Uses:

Labeled Uses[1,2,3]: Treatment in adults (18 years old and older) with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
Unlabeled Uses: No reported unlabeled uses.

Mechanism of Action [1,2,3,4,5,6]: Secukinumab is a human IgG1 monoclonal antibody that inhibits the release of pro-inflammatory cytokines and chemokines by selectively binding to the interleukin-17A cytokine and inhibits its interaction with the IL-17 receptor. Interleukin 17A is a natural cytokine that is involved in immune responses and inflammatory processes.

Pharmackoinetics[1,2,3]:

Absorption:

V_d	7.1 – 8.6 L
t ½	22 – 31 days
Bioavailability	55% - 77%
Time to peak	Around 6 days

Metabolism: The metabolic pathway for Cosentyx has not been clearly identified but it is expected that Cosentyx is broken down into small peptides and amino acids through the catabolic pathways similar to endogenous IgG. In patients who are prescribed CYP450 substrates, especially those with a narrow therapeutic index (warfarin, cyclosporine), consider monitoring for therapeutic effect or drug concentration and consider dosage modification of the CYP450 substrate.

Elimination: The mean systemic clearance of Cosentyx ranged from 0.14L/day to 0.22L/day following subcutaneous injection.

Efficacy:

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. 2015Feb;172(2):484-93.

Study Design: Randomized, double-blind, placebo-controlled, parallel-group phase III study.
Description of study: *Objective:* To assess efficacy safety and usability of secukinumab using a prefilled syringe in subjects with moderate to severe plaque psoriasis. *Methods:* The study treatment was given for a 12 week period. Subjects were randomized into a 1:1:1 ratio to receive placebo or secukinumab 150mg or 300mg in 1mL doses. The sample size consisted of 177 subjects total, 59 in each of the three groups. The active drugs and placebo were given once weekly by subcutaneous injection at weeks 1, 2, 3 and 4 and then once every 4 weeks. Subjects who received the 300mg injection were given two doses of 150mg while the 150mg group received 1 active injection of 150mg and one placebo injection for blinding purposes. Subjects gave themselves the injections but were observed during administration at the observation site. Inclusion criteria included subjects 18 years and older, history of plaque psoriasis for at least 6 months, moderate to severe disease (PASI, Psoriasis Area and Severity Index, score of 12 or greater and IGA, Investigator's Global Assessment, score of 3 or greater) and inadequately controlled past treatment. *Outcome measures:* The primary endpoints were subjects who reached at least a 75% reduction in PASI and an IGA score of 0 or 1 at week 12. *Results:* A total of 170 patients completed the study with no patients discontinuing due to lack of efficacy. Most of the 7 patients were lost to follow up. 69.5% of subjects receiving the 150mg dose achieved a PASI reduction of at least 75% and 52.5% achieving an IGA score of 0 or 1. 75.9% of subjects receiving the 300mg dose achieved a PASI reduction of at least 75% and 69.0% achieving an IGA score of 0 or 1. A PASI of 100% was reported in 43.1% of subjects receiving 300mg of secukinumab and 8.5% for 150mg compared to 0% for placebo.
Limitations: The study was conducted with a fairly small sample size of 177 subjects. Previous trials report a 16 week study period in comparison to the current study that was conducted for only 12 weeks. The authors suggest that the shorter duration was not long enough to observe the maximum efficacy of secukinumab.
Conclusion: The study did produce positive results for those who suffer from moderate to severe plaque psoriasis with 150mg and 300mg injections of secukinumab compared to placebo. Subjects receiving the 300mg showed superiority to the 150mg dose based off of the PASI and IGA responses. However, other studies should be reviewed due to several limitations as mentioned earlier.

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 Jun;29(6):1082-90.

Study Design: Randomized, double-blind, placebo-controlled, parallel-group phase III study.
Description of study: *Objective:* To determine the efficacy, safety and usability of secukinumab when administered using an autoinjector/pen. *Methods:* The study treatment was given for a 12 week period. Subjects were randomized into a 1:1:1 ratio to receive placebo or secukinumab 150mg or 300mg subcutaneously via autoinjection. The sample size consisted of 182 subjects, 60 received secukinumab 300mg and 61 subjects in both the 150mg group and placebo. The active drugs and placebo were given once weekly by subcutaneous injection at weeks 1, 2, 3 and 4 and then once every 4 weeks. Subjects who received the 300mg injection were given two doses of 150mg while the 150mg group received 1 active injection of 150mg and one placebo injection for blinding purposes. Inclusion criteria included subjects 18 years and older, diagnosed moderate to severe plaque psoriasis for at least 6 months, and poorly controlled

plaque psoriasis through the use of other treatments. Moderate to severe disease was categorized as PASI great than or equal to 12, IGA score of 3 or 4 and body surface involvement of at least 10%. *Outcome measures:* The primary endpoints were subjects who reached at least a 75% improvement in PASI and an IGA score of 0 or 1 and a 2 or greater improvement from baseline with the IGA score at the end of 12 weeks. *Resutls:* 71.7% of subjects receiving the 150mg dose achieved a PASI reduction of at least 75% and 53.3% were reported to have clear or almost clear skin based on IGA. 86.7% of subjects receiving the 300mg dose achieved a PASI reduction of at least 75% and 73.3% were reported to have clear or almost clear skin based on IGA. A PASI of at least 90% was reported in 40.0% of subjects receiving 150mg and 55.0% receiving 300mg.
Limitations: Like the previous study mentioned, the sample size reported was small even though they report an adequate power. The 12 week duration period was not long enough to be able to observe the maximum efficacy of secukinumab.
Conclusion: The study did produce positive results for those who suffer from moderate to severe plaque psoriasis with 150mg and 300mg injections of secukinumab compared to placebo. Subjects receiving the 300mg showed superiority to the 150mg dose based off of the PASI and IGA scores. The study showed similar results as previous studies in relation to the measured scores.

Papp KA, Langley RG, Sigurgeirsson B, et al. Efficacy and safety of secukinumab in the treatment of moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. Br J Dermatol. 2013 Feb;168(2):412-21.

Study Design: Phase II, randomized, double-blind, placebo-controlled, parallel-group study.
Description of study: *Objective:* To assess the efficacy and safety of different doses of secukinumab in subjects with moderate to severe plaque psoriasis. *Methods:* The study was conducted at 19 centers in 6 different countries. 125 subjects were randomly assigned in a 1:1:1:1:1 ratio to receive placebo or subcutaneous injections of secukinumab (1 dose x 25mg, 3 x 25mg, 3 x 75mg or 3 x 150mg) at weeks 0, 4 and 8. Inclusion criteria include subjects diagnosed with chronic plaque psoriasis for at least 6 months, moderate to severe psoriasis with a PASI score of at least 12, an IGA score of at least 3 and 10% of body surface involvement and non-response of previous treatment. *Outcome measures:* Asses the efficacy of the previous mentioned doses in subjects with moderate to severe plaque psoriasis with respect to PASI reduction of 75% compared to placebo. *Results:* A total of 78 patients completed the study with most of the withdrawals coming from the placebo group due to lack of efficacy. After 12 weeks 57% of subjects from the 3x75mg group had statistically significant differences in PASI and 82% in the 3x150mg group compared to 9% with placebo. Higher PASI response rates were maintained through the follow up period (at 36 weeks) for the 3x75mg and 3x150mg groups compared to placebo. Throughout the study all groups except placebo and 1x25mg groups reported higher IGA response rates.
Limitations: The study did not mention whether or not the subjects who received 1 dose of secukinumab 25mg were given 2 placebo doses for blinding purposes. The study also had a very small sample size and short duration of treatment. The authors should have taken into account the inconvenience that would be associated with patients having to given themselves multiple injections at each dose.

Conclusion: Based off of the author's conclusions, they suggest that secukinumab 3x75mg and 3x150mg subcutaneous injections met the outcome measure of PASI 75% response and efficacy and safety in the treatment of moderate to severe plaque psoriasis. At the time of the study no dosing standards were established for secukinumab.

Contraindications[1,2,3]: Secukinumab is contraindication in patients with past hypersensitivity reactions to the drug or any components of the formulation. Anaphylaxis has been reported with an unknown incidence.

Precautions[1,2,3]:

Infections: Secukinumab may increase a patient's risk of infections therefore exercise caution when using the drug in patients who have chronic infections or history of recurrent infections.

Tuberculosis: Secukinumab should not be administered in patients who have active tuberculosis infections. Latent tuberculosis should be treated before therapy begins.

Crohn's disease: Close monitoring is required in patients with Crohn's disease due to increased exacerbation risks.

Latex allergy: The cap contains natural rubber latex.

Live vaccines: Avoid live vaccine administration during secukinumab use due to its immunosuppressive effects.

Adverse Effects[1,2,3]:

Dermatologic:
Urticaria (0.6% - 1.2%)

Gastrointestinal:
Diarrhea (2.6% - 4.1%)

Infectious Disease:
Mucocutaneous candidiasis (1.2%)
General infections (28.7% - 47.5%)

Respiratory:
Nasopharyngitis (11.4% - 12.3%)
Pharyngitis (1% - 1.2%)
Rhinitis (1.4%)
Upper respiratory infection (2.5% - 3.2%)

Drug Interactions[1,2,3]:

Belimumab: Monoclonal antibodies may enhance the adverse/toxic effect of this drug .

Denosumab, pimecrolimus, Tacrolimus (Topical): These drugs may enhance the adverse/toxic effect of immunosuppressants. Specifically, the risk for serious infections may be increased.

Echinacea, Sipuleucel-T: These drugs may diminish the therapeutic effect of immunosuppressants.

Leflunomide, natalizumab: Immunosuppressants may enhance the adverse/toxic effect of these drugs.

Roflumilast, tofacitinib: These drugs may enhance the immunosuppressive effect of immunosuppressants.

Trastuzumab: trastuzumab may enhance the neutropenic effect of immunosuppressants.

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of vaccines

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of vaccines.

Dosing/Administration[1,2,3]:

Adult dosing- plaque psoriasis (Moderate to Severe):
Initial dose: 300mg subcutaneous injections at weeks 0, 1, 2, 3 and 4.
Maintenance dose: 300mg subcutaneous injection every 4 weeks.
*Some patients may only require 150mg injections.

Geriatric dosing
Refer to adult dosing.

Renal Impairment
No dose adjustments provided in manufacturer's labeling due to no clinical study.

Hepatic Impairment
No dose adjustments provided in manufacturer's labeling due to no clinical study.

Use in special circumstances:

Pregnancy
Category B- There are no well controlled trials of Cosentyx in pregnant women.

Nursing Mothers

It is unknown whether or not secukinumab is absorbed systemically or excreted in human milk after administration. Use with caution in nursing mothers.

Conclusion: Secukinumab is an alternative for patients with moderate to severe plaque psoriasis who have failed other treatment therapies and would prefer the convenience of infrequent dosing schedules. However, theses conveniences come at a price that is not affordable to many patients. The current studies conducted on secukinumab and the efficacy seem to lack larger sample sizes and sufficient durations despite using randomized, controlled trials. If patients experience adverse effects, the extremely long half-life could be problematic. The increased risk of infections would be a major concern for patients as well. Overall, secukinumab should have a place in therapy for patients suffering from failed therapies to treat moderate to severe plaque psoriasis.

Recommended References:

1. Cosentyx [package insert]. DailyMed. East Hanover, NJ. Novartis. 2015.

2. Secukinumab. DRUGDEX® System [Internet Database]. Truven Health Analytics. Micromedex. Updated periodically. Accessed: September 23, 2015.

3. Secukinumab. Lexi-Drugs [database online]. Lexi-Comp, Inc; April 23, 2015.

4. 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. 2015Feb;172(2):484-93.

5. 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 Jun;29(6):1082-90.

6. Papp KA, Langley RG, Sigurgeirsson B, et al. Efficacy and safety of secukinumab in the treatment of moderate-to-severe plaque psoriasis: a randomized, double-blind, placebo-controlled phase II dose-ranging study. Br J Dermatol. 2013 Feb;168(2):412-21.

Prepared by: Nicole R. Simons, Doctor of Pharmacy Candidate