Media Backgrounder

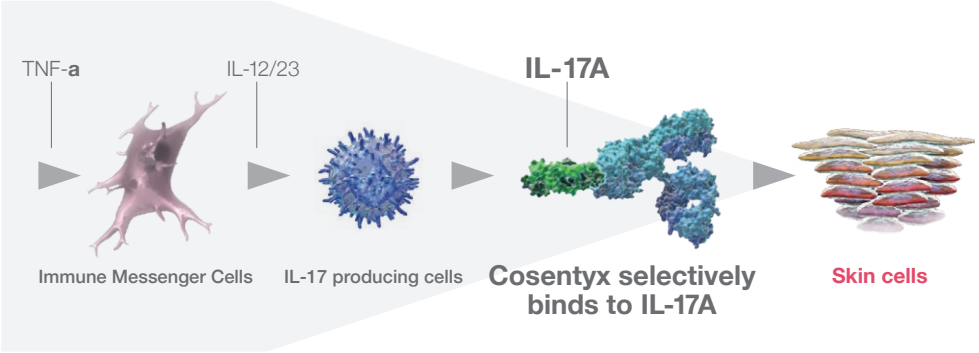
COSENTYX™ (SECUKINUMAB)

Cosentyx™ (secukinumab) is a treatment for psoriasis which selectively blocks interleukin-17A (IL-17A)[1,2].

High levels of IL-17A are present in skin affected by psoriasis and Cosentyx works by inhibiting the action of this protein[1-6].

Research shows that **IL-17A** plays a key role in driving the body's immune response in disorders such as **plaque psoriasis**, and is an optimal target for therapies[1-5], like Cosentyx.

High amounts of **IL-17A** can be found near skin cells compared to other proteins targeted by psoriasis therapies such as **TNF-α** and **IL-12/IL-23**. Consequently, **IL-17A inhibitors** such as Cosentyx are more effective at **achieving clear skin** as they specifically target the messenger protein nearest the affected skin cells[7,8].



Cosentyx was approved by the **European Commission (EC)** in January 2015, making it the first IL-17A inhibitor approved in Europe as a first-line systemic* treatment of moderate-to-severe plaque psoriasis in adults who are candidates for systemic therapy. The recommend dose approved is 300 mg, which is administered as two subcutaneous injections of 150 mg[9].

Additionally, the **US Food and Drug Administration (FDA)** approved Cosentyx for the treatment of moderate-to-severe plaque psoriasis in adult patients who are candidates for systemic therapy or phototherapy (light therapy). This follows the unanimous vote by the FDA Advisory Committee to recommend Cosentyx in October 2014. The recommend dose and administration approved in the US is the same as with EC approval[10].

***Systemic:** treatments or medication absorbed into the blood stream, allowing them to be carried where they are needed to work.

Date of preparation: January 2015 COSPR001-0115

NOVARTIS PHARMACEUTICALS

KEY CLINICAL TRIALS FOR COSENTYX

The approval of Cosentyx is based on the safety and efficacy outcomes from **10 Phase II and Phase III studies** which included over **3,990 adult patients** with moderate-to-severe plaque psoriasis. This included four pivotal Phase III trials:

- **ERASURE:** (**E**fficacy of **R**esponse **A**nd **S**afety of two fixed sec**U**kinumab **RE**gimens in psoriasis) was a randomized, double-blind, placebo-controlled, multicenter, parallel-group Phase III study involving 738 patients with moderate-to-severe plaque psoriasis[7].

- **FIXTURE:** (the **F**ull year **I**nvestigative e**X**amination of secukinumab vs. e**T**anercept **U**sing 2 dosing **R**egimens to determine **E**fficacy in psoriasis) was a randomized, double-blind, placebo and etanercept controlled, multicenter, parallel-group Phase III study involving 1,306 patients with moderate-to-severe plaque psoriasis[7].

- **FEATURE:** (**F**irst study of s**E**cukinum**A**b in prefilled syringes in subjec**T**s with chronic plaq**U**e-type psoriasis **RE**sponse) was a randomized double-blind, placebo-controlled, multicenter, Phase III study involving 177 patients with moderate-to-severe plaque psoriasis. In this study, prefilled syringes (PFS) for self administration were introduced into the Cosentyx clinical program[11].

- **JUNCTURE:** (**J**udging the efficacy of sec**U**kinumab in patients with psoriasis using autoi**N**jector: a **C**linical **T**rial eval**U**ating treatment **RE**sults) was a double-blind, placebo-controlled, multicenter, Phase III study involving 182 patients with moderate-to-severe plaque psoriasis. In this study, the autoinjector/pen (AI) for self administration was introduced into the Cosentyx clinical program[12].

ONGOING PHASE IIIB STUDIES

The second head-to-head study, Phase IIIb CLEAR study, for Cosentyx versus the IL-12/23 inhibitor Stelara®** (ustekinumab) is currently underway. Topline results show Cosentyx demonstrated superiority to this biologic treatment[8].

- **CLEAR** (**C**omparison to assess **L**ong-term **E**fficacy, s**A**fety and tole**R**ability of secukinumab vs. ustekinumab), a 52-week, multicenter, randomized, double-blind study, is the second head-to-head Phase III study initiated with Cosentyx, and compared the efficacy, long-term safety and tolerability of Cosentyx versus ustekinumab, in patients with moderate-to-severe plaque psoriasis. 24 countries across North America, Europe, Asia and Australia participated in the study, with enrollment reaching 679 patients in record time[8].

REFERENCES

1. Gaffen SL. “Structure and signaling in the IL-17 receptor family.” Nat Rev Immunol. 2009;9(8):556-67.
2. Ivanov S, Linden A. “Interleukin-17 as a drug target in human disease.” Trends Pharmacol Sci. 2009;30(2):95-103
3. Kopf M, Bachmann MF, Marsland BJ. “Averting inflammation by targeting the cytokine environment” Nat Rev Drug Discov. 2010; 9(9):703-18.
4. Onishi RM, Gaffen SL. “Interleukin-17 and its target genes: mechanisms of interleukin-17 function in disease.” Immunology. 2010;129(3):311-21.
5. Krueger J, Fretzin S, Suárez-Fariñas M, et al. “IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis.” J Allergy Clin Immunol. 2012;130(1):145-154.
6. Johansen C, Usher PA, Kjellerup RB, et al. “Characterization of the interleukin-17 isoforms and receptors in lesional psoriatic skin.” Brit J Dermatol.2009;160(2):319-24.
7. Langley RG, Elewski BE, Lebwohl M, et al. Secukinumab in plaque psoriasis--results of two phase 3 trials. N Engl J Med 2014;371:326-338.
8. Novartis, Data on file.
9. Novartis. Cosentyx (secukinumab) EU label. January 2015.
10. Novartis. Cosentyx (secukinumab) FDA label. January 2015.
11. Blauvelt A, Prinz J, Gottlieb AB, et al. Secukinumab Efficacy and Safety: Results From the First Study of Secukinumab in Prefilled Syringes in Subjects with Chronic Plaque-Type Psoriasis Response at 12 Weeks (FEATURE). E-poster presentation at: 72nd AAD Annual Meeting; Denver, Co.; 21-25 March 2014.
12. Paul C, Lacour JP, Cooper S. Secukinumab Efficacy and Safety: Results From the Judging the Efficacy of Secukinumab in Patients With Psoriasis Using Autoinjector: A Clinical Trial Evaluating Treatment Results (JUNCTURE). E-poster presentation at: 72nd AAD Annual Meeting; Denver, Co.; 21-25 March 2014.

NOVARTIS
PHARMACEUTICALS