

Key words

- ✓ Drug class: humanised monoclonal antibody
- ✓ Molecule: IgG1 kappa against Interleukin 17A
- ✓ Binding/inhibiting/MoA: binding of IL-17A prevents target cell activation and production of cytokines
- ✓ Originator brand name: Cosentyx® (Novartis)

Molecule

Secukinumab (Cosentyx®) is an IgG1 kappa fully human monoclonal antibody with a molecular weight of 147.9 kDa.

Mode of Action

Interleukin (IL)17A promotes inflammation when it binds to the IL17 receptors expressed on inflammatory cells such as keratinocytes, fibroblast-like synovocytes, endothelial cells, chondrocytes, and osteoblasts. Subsequently, inflammatory diseases as for example psoriasis may be caused. Secukinumab binds to IL17A. By attaching to IL17A, secukinumab blocks the subsequent pathway and thus reduces the activity of the immune system and symptoms of the diseases.

Indication

Cosentyx® is indicated for the treatment of moderate to severe plaque psoriasis, ankylosing spondylitis, psoriatic arthritis, juvenile idiopathic arthritis, and hidradenitis suppurativa. It is applied by subcutaneous injection and is sold in a pre-filled syringe or autoinjector.

Patent Situation

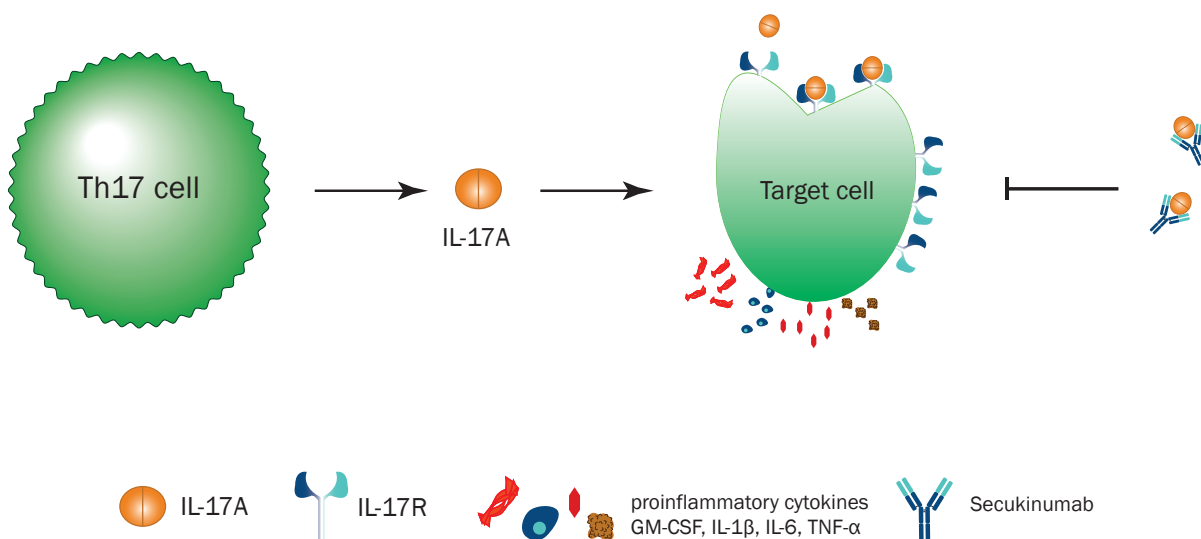
The patent protection for Cosentyx® will uphold until 2029. Other IL17A binding antibodies are marketed as well.

Market and Competitive Field

The originator product Cosentyx® of Novartis has been first approved in Europe and in US in 2015. In 2024, Cosentyx® had sales of 5.42 (2023: 4.63) billion € making it an attractive target for biosimilars. Biosimilars are currently only developed in China.

IL-17A binding to IL-17 receptors promotes inflammation, causing them to release pro-inflammatory cytokines like GM-CSF, IL-6, IL-1 β and TNF- α

Secukinumab binding to IL-17A prevents docking to IL-17R, therefore reducing the intracellular signaling and release of pro-inflammatory cytokines



Secukinumab: selected GMP, GLP, GCLP methods

Characterisation of the molecule & GxP techniques

CBA - CELL BASED ASSAYS



- Reporter gene assay
- Blocking of IL-17A activity
- ADCC (negative assay)
- ADCP (negative assay)
- CDC (negative assay)

PCM - PHYSICOCHEMICAL ASSAYS



- ✓ Size exclusion HPLC
- ✓ Ion exchange HPLC
- ✓ Reversed phase HPLC
- ✓ Peptide mapping HPLC
- ✓ HIC-HPLC
- ✓ Capillary electrophoresis
- ✓ cIEF (capillary isoelectric focusing)
- ✓ Western blot
- ✓ Polysorbate 20 (HPLC - ELSD)

LBA - LIGAND BINDING ASSAYS



- ✓ Cytokine, Chemokine (MSD)
- ✓ Immunology/Inflammation (MSD)
- Determination of binding kinetics & potency (SPR)
- IL-17A binding ELISA
- Fc Receptor affinity (SPR)
- Lectin Array Glycoprofiling

COMPENDIAL PCM METHODS (EP & USP)



- ✓ pH measurement (EP 2.2.3)
- ✓ Appearance (EP 2.2.1)
- ✓ Turbidity (EP 2.2.1)
- ✓ Colour of solution (EP 2.2.2)
- ✓ Osmolality (EP 2.2.35)
- ✓ Visible particles (2.9.20)
- ✓ Subvisible particles (2.9.19)
- ✓ Extractable volume (EP 2.9.17)
- ✓ Protein concentration by OD280 (EP 2.5.33)

(PRE-) CLINICAL ANALYTICS under G(C)LP



- PD - Pharmacodynamics
- PK - Pharmacokinetics
- ADA - Anti-Drug Antibody testing
- Biomarker studies

MICROBIOLOGY / SAFETY



- ✓ Sterility (EP 2.6.1)
- ✓ Endotoxin, gel-clot limit test (EP 2.6.14)
- ✓ Endotoxin, chromogenic LAL test (EP 2.6.14)
- ✓ Endotoxin, recombinant Factor C (EP 2.6.32)

✓ Installed at VelaLabs under GxP

○ Analytical concept exists/installed under R&D