

DrugB

1. Mechanism of action

DrugB is a human monoclonal IgG1 λ antibody that selectively binds to the p19 subunit of interleukin 23 (IL23A; UniProt Acc: Q9NPF7) and inhibits its interaction with the IL23 receptor. IL23 is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. DrugB inhibits the release of proinflammatory cytokines and chemokines.

2. Pharmacokinetics

DrugB exhibited linear pharmacokinetics in healthy subjects and subjects with psoriasis following subcutaneous injections. In subjects with psoriasis, following subcutaneous administration of 100 mg of DrugB at Weeks 0 and 4, and every 8 weeks thereafter, mean steady-state trough serum DrugB concentration was approximately 1.2 mcg/mL.

3. ADME

Absorption: Following a single 100 mg subcutaneous injection in healthy subjects, DrugB reached a mean (\pm SD) maximum serum concentration of 8.09 ± 3.68 mcg/mL by approximately 5.5 days post dose. The absolute bioavailability of DrugB following a single 100 mg subcutaneous injection was estimated to be approximately 49% in healthy subjects.

Elimination: Apparent clearance in subjects with plaque psoriasis was 0.516 L/day. Mean half-life of DrugB was approximately 15 to 18 days in subjects with plaque psoriasis across studies.

4. Biodistribution

Distribution: In subjects with plaque psoriasis, apparent volume of distribution was 13.5 L.

5. Target binding

High affinity, picomolar range binding affinity for IL-23.

DrugB is administered intravenously with an initial concentration of 200 mg.

Kon is 0.2246 (liter/picomole*day)

koff is 4.4928 (1/day)

Apparent volume is 3.43 L

6. Pharmacodynamics

DrugB reduced serum levels of IL-17A, IL-17F, and IL-22 relative to pretreatment levels in evaluated subjects with psoriasis based on exploratory analysis of the pharmacodynamic markers. The relationship between these pharmacodynamic markers and the mechanism(s) by which DrugB exerts its clinical effects is not fully understood.

7. Abbreviations

IL - Interleukin, AUC - Area Under the Curve, tmax - Time to Maximum Concentration, Cmax - Maximum Concentration, ADME - Absorption, Distribution, Metabolism, and Excretion, FDR -

False Discovery Rate, CRP - C-reactive Protein, ESR - Erythrocyte Sedimentation Rate, Ps - Psoriasis, RA - Rheumatoid Arthritis