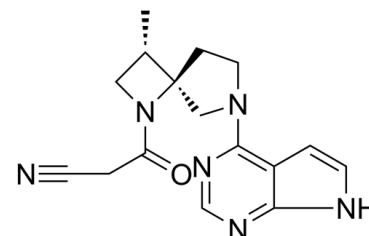


Data Sheet

Product Name:	Delgocitinib
Cat. No.:	CS-0031558
CAS No.:	1263774-59-9
Molecular Formula:	C ₁₆ H ₁₈ N ₆ O
Molecular Weight:	310.35
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt
Solubility:	DMSO : ≥ 58 mg/mL



BIOLOGICAL ACTIVITY:

Delgocitinib (JTE-052) is a specific **JAK** inhibitor with **IC₅₀s** of 2.8, 2.6, 13 and 58 nM for JAK1, JAK2, JAK3 and Tyk2, respectively^[1]. **IC₅₀ & Target:** IC₅₀: 2.8 nM (JAK1), 2.6 nM (JAK2), 13 nM (JAK3), 58 nM (Tyk2)^[1] **In Vitro:** In the enzymatic assays, Delgocitinib potently inhibits all of the JAK subtypes with IC₅₀ values of 2.8±0.6, 2.6±0.2, 13±0 and 58±9 nM for JAK1, JAK2, JAK3 and Tyk2, respectively. Lineweaver-Burk plots show that the inhibition mode of Delgocitinib toward all JAKs is competitive with ATP with K_i values of 2.1±0.3, 1.7±0.0, 5.5±0.3 and 14±1 nM for JAK1, JAK2, JAK3 and Tyk2, respectively. In these cell-based cytokine signaling assays, Delgocitinib inhibits the phosphorylation of Stat proteins induced by IL-2, IL-6, IL-23, GM-CSF, and IFN-α with IC₅₀ values of 40±9, 33±14, 84±11, 304±22 and 18±3 nM, respectively. Delgocitinib also inhibits IL-2-induced proliferation of T cells in a concentration-dependent manner (IC₅₀=8.9±3.6 nM), and its potency is similar to that of CP-690550 (IC₅₀=16 nM)^[1]. **In Vivo:** Delgocitinib decreases the IFN-γ production, but the potency of the 1-h prior administration is higher than that of the 6-h prior administration (ED₅₀=0.24 versus 1.3 mg/kg). In the administration from day 1, Delgocitinib prevents the development of hind paw swelling and histological changes of inflammatory cell infiltration and synovial cell hyperplasia. Delgocitinib inhibits radiographic and histological changes of bone destruction and cartilage destruction. In the administration from day 15, Delgocitinib decreases the paw swelling in a dose-dependent manner. In addition, Delgocitinib ameliorates the inflammatory cell infiltration, synovial cell hyperplasia, and cartilage/bone destructions in the histological and radiographic examinations at the end of the study^[1].

PROTOCOL (Extracted from published papers and Only for reference)

Cell Assay: For the *in vitro* experiments, Delgocitinib is dissolved in dimethyl sulfoxide (DMSO) and diluted with the buffer used in each experiment.^[1] For determination of IL-2-induced T cell proliferation, **human T cells** are precultured with 10 µg/mL PHA-M for 3 days and plated in 96-well plates at 1.0×10⁴ cells/well in the **presence or absence of various concentrations of Delgocitinib**. Following preincubation with Delgocitinib for 30 min at 37°C, the cells are stimulated by adding 20 ng/mL recombinant human IL-2 to each well and incubated for 3 days at 37°C under 5 % CO₂. After completion of the culture period, the cells are harvested with a 96-well harvester and counted in a scintillation counter^[1]. **Animal Administration:** ^[1]**Lewis rats** are used in this study. First, collagen-induced arthritis (CIA) is induced in rats. Lewis rats are immunized with 1 mL of the emulsion (1 mg of type II collagen) via ten intradermal injections on the back under anesthesia. The rats are then challenged with 0.2 mL of the emulsion injected into the base of the tail on day 8 under anesthesia. **Delgocitinib** is given **orally once daily** from day 1 to day 21 (preventive administration) or from day 15 to day 28 (therapeutic administration). After arthritis induction, the hind paw volume is measured by a water displacement method using a plethysmometer. On day 22 or day 29, the rats are euthanized, and their hind paws are excised and X-rayed or processed for histological evaluation^[1].

References:

[1]. Tanimoto A, et al. Pharmacological properties of JTE-052: a novel potent JAK inhibitor that suppresses various inflammatory responses in vitro and in vivo. Inflamm Res. 2015 Jan;64(1):41-51.

CAIndexNames:

1,6-Diazaspiro[3.4]octane-1-propanenitrile, 3-methyl- β -oxo-6-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)-, (3S,4R)-

SMILES:

O=C(N(C[C@@H]1C)[C@]21CN(C3=C(C=CN4)C4=NC=N3)CC2)CC#N

Caution: Product has not been fully validated for medical applications. For research use only.

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