

Baricitinib, Inhibitor

Baricitinib (LY3009104, INCB028050)

CATALOG #
AAA14579

PRODUCT SYNONYMS

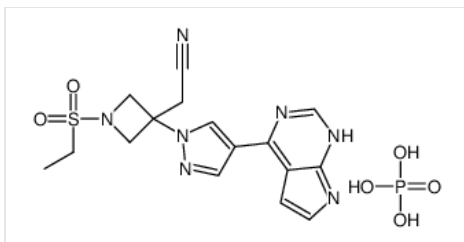
Baricitinib; Baricitinib (LY3009104; INCB028050); Baricitinib phosphate; inhibitor

PRODUCT SPECIFICATIONS

Purity/Purification	98.9%
Form/Format	POWDER
CAS	1187595-84-1
Formula	C ₁₆ H ₂₀ N ₇ O ₆ PS
Solubility	DMSO 200
Receptor (IC ₅₀)	JAK 1 5.9 nM JAK 2 5.7 nM JAK3 >400 nM Tyk 2 53 nM
Animal Experiment	Rats
Biological Activity	Baricitinib phosphate is a selective orally bioavailable JAK1/JAK2 inhibitor.
Smiles	OP(=O)(O)O.CCS(=O)(=O)N1CC(CC#N)(C1)n1cc(cn1)c1c2cc[nH]c2ncn1
In vitro Activity	In cell-based assays, Baricitinib (INCB028050) proves to be a potent inhibitor of JAK signaling and function. In PBMCs, Baricitinib inhibits IL-6-stimulated phosphorylation of the canonical substrate STAT3 (pSTAT3) and subsequent production of the chemokine MCP-1 with IC ₅₀ values of 44 nM and 40 nM, respectively. In isolated naive T-cells, INCB028050 also inhibits pSTAT3 stimulated by IL-23 (IC ₅₀ =20 nM). Importantly, this inhibition prevented the production of two pathogenic cytokines (IL- 17 and IL-22) produced by Th17 cells-a subtype of helper T cells with demonstrable inflammatory and pathogenic properties-with an IC ₅₀ value of 50 nM. In stark contrast, the structurally similar but ineffective JAK1/2 inhibitors INCB027753 and INCB029843 has no significant effect in any of these assays systems when tested at concentrations up to 10 μM[1].
In vivo Activity	Baricitinib (INCB028050) treatment, compares with vehicle, inhibits the increase in hind paw volumes during the 2 wk of treatment by 50% at a dose of 1 mg/kg and >95% at doses of 3 or 10 mg/kg. Because baseline paw volume measurements are taken on treatment day 0—in animals with significant signs of disease-it is possible to have >100% inhibition in animals showing marked improvement in swelling[1]. Baricitinib (0.7 mg/day) treated mice exhibits substantially reduced inflammation as assessed by H&E staining, reduced CD8 infiltration, and reduced MHC class I and class II expression when compared with vehicle-control treated mice. CD8+NKG2D+ cells, critical effectors of disease in murine and human alopecia areata (AA), are greatly diminished in Baricitinib treated mice compare with vehicle control treated mice[2].
Kinase Assay	Enzyme assays are performed using a homogeneous time-resolved fluorescence assay with recombinant epitope tagged kinase domains (JAK1, 837-1142; JAK2, 828- 1132; JAK3, 718-1124; Tyk2, 873-1187) or full-length enzyme (cMET and Chk2) and peptide substrate. Each enzyme reaction is performed with or without test compound (10-point dilution), JAK, cMET, or Chk2 enzyme, 500 nM (100 nM for Chk2) peptide, ATP (at the K _m specific for each kinase or 1 mM), and 2.0% DMSO in assay buffer. The calculated IC ₅₀ value is the compound concentration required for inhibition of 50% of the fluorescent signal. Additional kinase assays are performed at Cerep using standard conditions at 200 nM. Enzymes tested included: Abl, Aktl, AurA, AurB, CDC2, CDK2, CDK4, CHK2, c-kit, EGFR, EphB4, ERK1, ERK2, FLT-1, HER2, IGF1R, IKKo, IKK~, JNK1, Lck, MEK1, p380, p70S6K, PKA, PKCo, Src, and ZAP70[1].

Cell Assay	Baricitinib (INCB 028050) is dissolved in stock solutions, and then diluted with appropriate media before use[1]. Human PBMCs are isolated by leukapheresis followed by Ficoll-Hypaque centrifugation. For the determination of IL-6-induced MCP-1 production, PBMCs are plated at 3.3x 10 ⁵ cells per well in RPMI 1640+10% FCS in the presence or absence of various concentrations of INCB028050 (1 nM, 10 nM, 100 nM, 1 μ M, and 10 μ M). Following preincubation with compound for 10 min at room temperature, cells are stimulated by adding 10 ng/mL human recombinant IL-6 to each well. Cells are incubated for 48h at 37°C, 5% CO ₂ .
Preparation and Storage	2 years -80°C in solvent; 3 years -20°C in powder.

IMAGES



Structure

NCBI AND UNIPROT INFORMATION

Molecular Weight	469.41
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For Research Use Only. Not for use in diagnostic or therapeutic procedures. Small volumes of product may become entrapped in the seal of the vial during shipment and storage; if necessary, briefly centrifuge the vial on a tabletop centrifuge to dislodge any liquid in the cap.

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Online datasheet: <https://www.aaabiotech.com/inhibitor/baricitinib/14579>