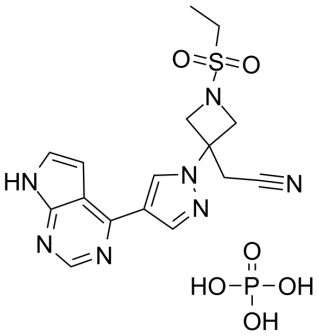
Baricitinib phosphate

Cat. No.:	HY-15315A
CAS No.:	1187595-84-1
Molecular Formula:	$C_{16}H_{20}N_7O_6PS$
Molecular Weight:	469.41
Target:	JAK
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 1 years; -20°C, 6 months (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 4.7 mg/mL (10.01 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.1303 mL	10.6517 mL	21.3033 mL
	5 mM	0.4261 mL	2.1303 mL	4.2607 mL
	10 mM	0.2130 mL	1.0652 mL	2.1303 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.08 mg/mL (4.43 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: 2.08 mg/mL (4.43 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.08 mg/mL (4.43 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Baricitinib phosphate (LY3009104 phosphate; INCB028050 phosphate) is a selective orally bioavailable JAK1/JAK2 inhibitor with IC_{50} of 5.9 nM and 5.7 nM, respectively.

IC_{50} & Target

JAK2	JAK1	Tyk2	JAK3
5.7 nM (IC_{50})	5.9 nM (IC_{50})	53 nM (IC_{50})	560 nM (IC_{50})

In Vitro

In cell-based assays, Baricitinib phosphate (INCB028050 phosphate) 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Baricitinib phosphate (INCB028050 phosphate) 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]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [1]	For the determination of IL-6-induced MCP-1 production, PBMCs are plated at 3.3×10^5 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 μM, and 10 μM). 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 48 h at 37°C, 5% CO_2. Supernatants are harvested and analyzed by ELISA for levels of human MCP-1. The ability of INCB028050 to inhibit IL-6-induced secretion of MCP-1 is reported as the concentration required for 50% inhibition (IC_{50}). Proliferation of Ba/F3-TEL-JAK3 cells is performed over 3 d using Cell-Titer Glo[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1][2]	Rats[1] Female rats (n=6 per gender per group) are given a dose of 10 mg/kg Baricitinib and given by oral gavage at 10 mL/kg. The first three rats are bled at 0 (predose), 2, 8, and 24 h, and the second three rats are bled 1, 4, and 12 h after dosing. EDTA is used as the anticoagulant, and samples are centrifuged to obtain plasma. An analytical method for the quantification of INCB028050 has been developed and used to analyze samples from toxicology studies. The method combines a protein precipitation extraction with 10% methanol in acetonitrile and LC/MS/MS analysis. The method has demonstrated a linear assay range 1-5000 nM using 0.1 mL of study samples. Data are processed using Analyst 1.3.1. A standard curve is determined from peak area ratio versus concentration using a weighted linear regression (1/x2). Mice[2] The C3H/HeJ graft-recipient mouse model of AA is used for these experiments. Briefly, alopecic skin from a C3H/HeJ mouse that spontaneously developed hair loss is grafted onto 8-10 week old C3H/HeJ mice free of disease. At the time of grafting, an osmotic pump that administered approximately 0.7 mg/day of Baricitinib or placebo is implanted. Osmotic pumps are changed monthly. A time-to-event survival analysis for interval censored data is performed. The survival and interval packages in R are used to perform log-rank tests. The hypothesis that the survival distributions are equal in the (n=10) Baricitinib-treated mice and (n=10) placebo-treated mice is rejected at the 5% level using Sun's score to perform an exact log-rank two-sample test with the p-value of 0.0035. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cell. 2021 Apr 15;184(8):2167-2182.e22.
- Science. 2017 Dec 1;358(6367):eaan4368.
- Signal Transduct Target Ther. 2021 Apr 24;6(1):165.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Nat Commun. 2023 Apr 24;14(1):2342.

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REFERENCES

[1]. Fridman JS, et al. Selective inhibition of JAK1 and JAK2 is efficacious in rodent models of arthritis: preclinical characterization of INCB028050. J Immunol. 2010 May 1;184(9):5298-307.

[2]. Jabbari A, et al. Reversal of Alopecia Areata Following Treatment With the JAK1/2 Inhibitor Baricitinib. EBioMedicine. 2015 Feb 26;2(4):351-5.

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

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