

Product Data Sheet

Product Name: Baricitinib phosphate

Cat. No.: GC13830

Chemical Properties

Cas. No. 1187595-84-1

Chemical Name 2-[1-ethylsulfonyl-3-[4-(7H-pyrrolo[2,3-d]pyrimidin-4-yl)pyrazol-1-yl]azetidin-3-yl]acetoneitrile;phosphoric acid

SMILES CCS(=O)(=O)N1CC(C1)(CC#N)N2C=C(C=N2)C3=C4C=CNC4=NC=N3.OP(=O)(O)O

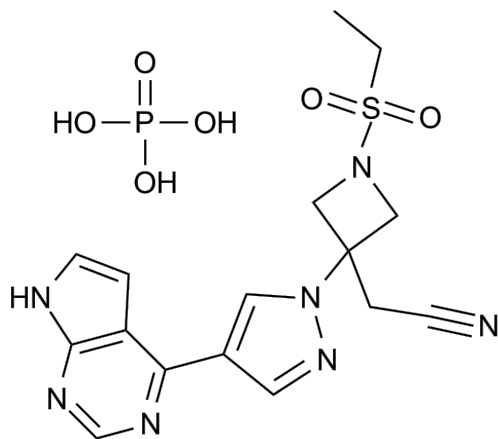
Formula $C_{16}H_{20}N_7O_6PS$ M.Wt 469.41

Solubility ≥ 172.6 mg/mL in DMSO Storage Store at $-20^{\circ}C$

General tips For obtaining a higher solubility , please warm the tube at $37^{\circ}C$ and shake it in the ultrasonic bath for a while. Stock solution can be stored below $-20^{\circ}C$ for several months.

Shipping Condition Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.

Structure



Protocol

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

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Cell experiment: 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 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 48 h at 37°C, 5% CO₂. 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 (IC₅₀). Proliferation of Ba/F3-TEL-JAK3 cells is performed over 3 d using Cell-Titer Glo[1].

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**Animal
experiment:**

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.

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.

Background

Direct and indirect inhibition of the JAKs has demonstrated rapid and sustained improvement in

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clinical measures of disease. Baricitinib phosphate (INCB 028050) is a selective JAK1 and JAK2 inhibitor.

In vitro: Baricitinib phosphate is a selective orally bioavailable JAK1/JAK2 inhibitor with nanomolar potency against JAK1 (5.9 nM) and JAK2 (5.7 nM) and ~10-fold selective versus JAK3 and Tyk2, no inhibition to c-Met and Chk2. INCB028050 inhibits intracellular signaling of multiple proinflammatory cytokines including IL-6 and IL-23 at concentrations, 50 nM [1].

In vivo: Significant efficacy was achieved in the rat adjuvant arthritis model with doses of Baricitinib phosphate providing partial and/or periodic inhibition of JAK1/JAK2 and no inhibition of JAK3. Baricitinib phosphate was also effective in multiple murine models of arthritis, with no evidence of suppression of humoral immunity or adverse hematologic effects [2].

Clinical trial: Several clinical trials have been conducted to investigate the PK, efficacy and DDI of Baricitinib phosphate in healthy people as well as in participants With Rheumatoid Arthritis.

Reference:

[1] Fridman JS, Scherle PA, Collins R, Burn TC, Li Y, Li J, Covington MB, Thomas B, Collier P, Favata MF, Wen X, Shi J, McGee R, Haley PJ, Shepard S, Rodgers JD, Yeleswaram S, Hollis G, Newton RC, Metcalf B, Friedman SM, Vaddi K. Selective inhibition of JAK1 and JAK2 is efficacious in rodent models of arthritis: preclinical characterization of INCB028050. J Immunol. 2010;184(9):5298-307.

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