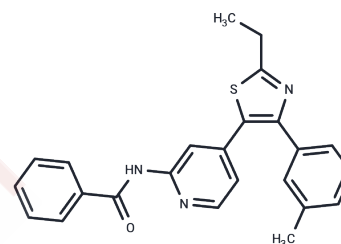


TAK-715

Chemical Properties

CAS No. :	303162-79-0
Formula:	C ₂₄ H ₂₁ N ₃ O ₅
Molecular Weight:	399.51
Storage:	Powder: -20°C for 3 years In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



Biological Description

Description	TAK-715 is a p38 MAPK inhibitor for p38α.
Targets(IC50)	Casein Kinase, JNK, p38 MAPK
In vitro	TAK 715 inhibits LPS-stimulated release of TNF-α from THP-1 with IC ₅₀ of 48 nM. [1] TAK 715 (10 μM) inhibits Wnt-3a-induced hDvl2 phosphorylation and the hDvl2 shift in U2OS-EFC cells. [2] The amide NH of TAK 715 is hydrogen bonded to the main-chain carbonyl of Met109 of p38 α. TAK 715 binds relatively high in the ATP pocket, occupying the hydrophobic back pocket, the adenine region and the front pocket of p38 as well as extending to most of the length of the Gly-rich loop. [3]
In vivo	TAK 715 (10 mg/kg, po) inhibits LPS-induced TNF-α production in mice with 87.6% inhibition. TAK 715 has a modest mouse bioavailability of 18.4% and a slightly improved rat bioavailability of 21.1%. TAK 715 has a modest mouse bioavailability of 18.4% and a slightly improved rat bioavailability of 21.1%. TAK 715 results in C _{max} of 0.19 μg/mL and AUC(0-24 hours) of 1.16 μg·h/mL in rats. TAK 715 (30 mg/kg, po) significantly reduces the secondary paw volume with 25 % inhibition in a rat adjuvant-induced arthritis (AA) model. [1]
Kinase Assay	Assay of PI3K enzyme inhibition: The inhibition of PI3Kβ, PI3Kα, PI3Kγ, and PI3Kδ is evaluated in an AlphaScreen based enzyme activity assay using human recombinant enzymes. The assay measures PI3K-mediated conversion of PIP ₂ to PIP ₃ . Biotinylated PIP ₃ , a GST-tagged pleckstrin homology (PH) domain and the two AlphaScreen beads form a complex that elicits a signal upon laser excitation at 680 nm. The PIP ₃ formed in the enzyme reaction competes with the biotinylated PIP ₃ for binding to the PH domain thus reducing the signal with increasing enzyme product. The AZD6482 is dissolved in DMSO and added to 384 well plates. PBKβ, PBKα, PBKγ, or PBKδ is added in a Tris buffer (50 mM Tris pH 7.6, 0.05% CHAPS, 5 mM DTT, and 24 mM MgCl ₂) and allowed to preincubate with AZD6482 for 20 minutes prior to the addition of substrate solution containing PIP ₂ and ATP. The enzyme reaction is stopped after 20 minutes by addition of stop solution containing EDTA and biotin-PIP ₃ , followed by addition of detection solution containing GST-grpl PH and AlphaScreen beads. Plates are left for a minimum of 5 hours in the dark prior to analysis. The final concentration of DMSO, ATP and PIP ₂ in the assay are, 0.8%, 4 μM, and 40 μM, respectively. IC ₅₀ values are calculated according to the equation, $y = \{a + [(b-a) / (1 + (x/IC_{50})^s)]\}$, where y = % inhibition; a = 0%; b = 100%; s =

Kinase Assay	the slope of the concentration-response curve; x = AZD6482 concentration.
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Solubility Information

Solubility	Ethanol: 20 mg/mL (50.06 mM),Sonication is recommended. DMSO: 122.5 mg/mL (306.63 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 10 mg/mL (25.03 mM),Solution. 10% DMSO+90% Saline: < 10 mg/mL (25.03 mM),Lower concentrations may be soluble, but exact solubility limit is unknown. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.5031 mL	12.5153 mL	25.0307 mL
5 mM	0.5006 mL	2.5031 mL	5.0061 mL
10 mM	0.2503 mL	1.2515 mL	2.5031 mL
50 mM	0.0501 mL	0.2503 mL	0.5006 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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Verkaar F, et al. Chem Biol, 2011, 18(4), 485-494.

Azevedo R, et al. Acta Crystallogr D Biol Crystallogr. 2012 Aug;68(Pt 8):1041-50.

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