Upadacitinib

Cat. No.: HY-19569

CAS No.: 1310726-60-3

Molecular Formula: $C_{17}H_{19}F_3N_6O$

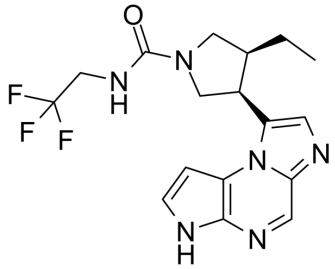
Molecular Weight: 380.37

Target: JAK

Pathway: Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 22 mg/mL (57.84 mM)

H_2O : < 0.1 mg/mL (insoluble)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	2.6290 mL	13.1451 mL	26.2902 mL
	5 mM	0.5258 mL	2.6290 mL	5.2580 mL
	10 mM	0.2629 mL	1.3145 mL	2.6290 mL

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

In Vivo

1. Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
   Solubility: ≥ 2.75 mg/mL (7.23 mM); Clear solution
2. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.75 mg/mL (7.23 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 1.67 mg/mL (4.39 mM); Clear solution
4. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 1.67 mg/mL (4.39 mM); Clear solution
5. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 1.67 mg/mL (4.39 mM); Clear solution
6. Add each solvent one by one: 1% DMSO >> 99% saline
   Solubility: ≥ 0.55 mg/mL (1.45 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Upadacitinib (ABT-494) is a potent, orally active and selective Janus kinase 1 (JAK1) inhibitor (IC_{50}=43 nM). Upadacitinib (ABT-494) displays approximately 74 fold selective for JAK1 over JAK2 (200 nM) in cellular assays dependent on specific, relevant cytokines. Upadacitinib (ABT-494) is used in development for the treatment of several autoimmune disorders[1][2].

IC_{50} & Target			
JAK1 0.043 μM (IC_{50})	JAK2 0.2 μM (IC_{50})	JAK3 2.3 μM (IC_{50})	Tyk2 4.7 μM (IC_{50})

In Vitro

In biochemical assays, Upadacitinib is 74-fold more selective for JAK-1 than for JAK-2 (which is involved in erythropoiesis) and 58-fold more selective for JAK-1 than for JAK-3 (which is involved in immunosurveillance)[1]. The enhanced selectivity of Upadacitinib for JAK-1 over JAK-2 and JAK-3 may offer an improved benefit–risk profile in patients with RA range[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Upadacitinib (0.1-10 mg/kg; oral gavage; twice a day for 10 days) demonstrates efficacy in rat arthritis models[3].

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Animal Model:	Female Lewis rats (Rat adjuvant-induced arthritis model)[3]
Dosage:	0.1, 0.3, 1, 3, 10 mg/kg
Administration:	Oral gavage; twice a day for 10 days
Result:	Inhibits disease pathology in rat adjuvant induced arthritis.

REFERENCES

[1]. Nakayamada S, et al. Recent Progress in JAK Inhibitors for the Treatment of Rheumatoid Arthritis. BioDrugs. 2016 Oct;30(5):407-419.

[2]. J. Voss, et al. THU0127 Pharmacodynamics of A Novel JAK1 Selective Inhibitor in Rat Arthritis and Anemia Models and in Healthy Human Subjects. doi 10.1136/annrheumdis-2014-eular.3823.

[3]. Parmentier JM, et al. In vitro and in vivo characterization of the JAK1 selectivity of upadacitinib (ABT-494). BMC Rheumatol. 2018 Aug 28;2:23.

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