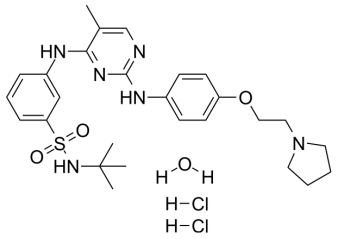
Fedratinib hydrochloride hydrate

Cat. No.:	HY-10409A
CAS No.:	1374744-69-0
Molecular Formula:	$C_{27}H_{40}Cl_2N_6O_4S$
Molecular Weight:	615.62
Target:	JAK; Apoptosis
Pathway:	Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Apoptosis
Storage:	4°C, sealed storage, away from moisture * In solvent : -80°C, 2 years; -20°C, 1 year (sealed storage, away from moisture)



SOLVENT & SOLUBILITY

In Vitro

DMSO : 100 mg/mL (162.44 mM; Need ultrasonic)

H_2O : 100 mg/mL (162.44 mM; Need ultrasonic)

Preparing Stock Solutions	Mass / Solvent / Concentration	1 mg	5 mg	10 mg
	1 mM	1.6244 mL	8.1219 mL	16.2438 mL
	5 mM	0.3249 mL	1.6244 mL	3.2488 mL
	10 mM	0.1624 mL	0.8122 mL	1.6244 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: ≥ 2.5 mg/mL (4.06 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (4.06 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fedratinib hydrochloride hydrate (TG-101348 hydrochloride hydrate) is a potent, selective, ATP-competitive and orally active JAK2 inhibitor with IC_{50}s of 3 nM for both JAK2 and JAK2V617F kinase. Fedratinib hydrochloride hydrate shows 35- and 334-fold selectivity over JAK1 and JAK3, respectively. Fedratinib hydrochloride hydrate induces cancer cell apoptosis and has the potential for myeloproliferative disorders research[1][2].

IC_{50} & Target	JAK2	JAK2(V617F)	Flt3	Ret
	3 nM (IC_{50})	3 nM (IC_{50})	15 nM (IC_{50})	48 nM (IC_{50})

In Vitro	Fedratinib (TG101348) inhibits proliferation of a human erythroblast leukemia (HEL) cell line that harbors the JAK2V617F mutation, as well as a murine pro-B cell line expressing human JAK2V617F (Ba/F3 JAK2V617F), with an IC_{50} value of approximately 300 nM for either line. Proliferation of parental Ba/F3 cells was inhibited to a comparable level, with an IC_{50} value of ~420 nM[1]. Exposure of these cells to Fedratinib (TG101348) (0.1 μM, 0.3 μM, 1 μM, 3 μM, and 10 μM) reduces STAT5 phosphorylation at concentrations that parallel the concentrations required to inhibit cell proliferation[1]. Fedratinib (TG101348) (0.1 μM, 0.3 μM, 1 μM, 3 μM, and 10 μM) induces apoptosis in both HEL and Ba/F3 JAK2V617F cells in a dose-dependent manner[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Fedratinib (TG101348; 60-120 mg/kg; oral gavage; twice daily; for 42 days; C57Bl/6 mice) trewatment shows a dose-dependent reduction in polycythemia and a marked dose-dependent reduction in splenomegaly of treated animals[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	C57Bl/6 mice induced by the JAK2V617F mutation[1]
Dosage:	60 mg/kg, 120 mg/kg
Administration:	Oral gavage; twice daily; for 42 days
Result:	Showed a statistically significant reduction in hematocrit and leukocyte count, a dose-dependent reduction/elimination of extramedullary hematopoiesis.

CUSTOMER VALIDATION

- Nature. 2023 Jun;618(7963):151-158.
- Signal Transduct Target Ther. 2022 Feb 23;7(1):52.
- Signal Transduct Target Ther. 2020 Dec 26;5(1):295.
- Mol Cancer. 2023 May 20;22(1):86.
- Mol Cancer. 2021 May 29;20(1):80.

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REFERENCES

[1]. Wernig G, et al. Efficacy of TG101348, a selective JAK2 inhibitor, in treatment of a murine model of JAK2V617F-induced polycythemia vera. Cancer Cell. 2008 Apr;13(4):311-20.

[2]. Geron I, et al. Selective inhibition of JAK2-driven erythroid differentiation of polycythemia vera progenitors. Cancer Cell. 2008 Apr;13(4):321-30.

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