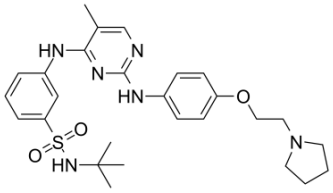
Fedratinib

Cat. No.:	HY-10409
CAS No.:	936091-26-8
Molecular Formula:	$C_{27}H_{36}N_6O_3S$
Molecular Weight:	524.68
Target:	JAK; Apoptosis
Pathway:	Epigenetics; JAK/STAT Signaling; Stem Cell/Wnt; Apoptosis
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 : 250 mg/mL (**476.48 mM;** Need ultrasonic)
H_2O : < 0.1 mg/mL (insoluble)

Preparing Stock Solutions	Concentration / Solvent / Mass	1 mg	5 mg	10 mg
	1 mM	1.9059 mL	9.5296 mL	19.0592 mL
	5 mM	0.3812 mL	1.9059 mL	3.8118 mL
	10 mM	0.1906 mL	0.9530 mL	1.9059 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 (4.76 mM); Clear solution
2. Add each solvent one by one: **10% DMSO >> 90% (20% SBE-β-CD in saline)**
   Solubility: 2.5 mg/mL (4.76 mM); Suspended solution; Need ultrasonic
3. Add each solvent one by one: **10% DMSO >> 90% corn oil**
   Solubility: ≥ 2.5 mg/mL (4.76 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Fedratinib (TG-101348) 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 shows 35- and 334-fold selectivity over JAK1 and JAK3, respectively. Fedratinib 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

- **Sci Transl Med**. 2018 Jul 18;10(450). pii: eaaq1093.
- **Cell Syst**. 2018 Apr 25;6(4):424-443.e7.
- **EMBO Rep**. 2019 Jun;20(6):e47202.
- **Mol Ther Nucleic Acids**. 2020 Sep 4;21:900-915.
- **Am J Clin Nutr**. 2020 Jan 1;111(1):110-121.

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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.

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

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