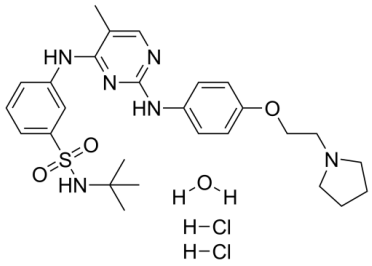
Data Sheet

Product Name:	Fedratinib (hydrochloride hydrate)
Cat. No.:	CS-0028556
CAS No.:	1374744-69-0
Molecular Formula:	$C_{27}H_{40}Cl_2N_6O_4S$
Molecular Weight:	615.62
Target:	Apoptosis; JAK
Pathway:	Apoptosis; Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt
Solubility:	DMSO : 100 mg/mL (ultrasonic);H_2O : 100 mg/mL (ultrasonic)



BIOLOGICAL ACTIVITY:

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]. ***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]. ***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].

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.

CAIndexNames:

Benzenesulfonamide, N-(1,1-dimethylethyl)-3-[[5-methyl-2-[[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]amino]-4-pyrimidinyl]amino]-, hydrochloride, hydrate (1:2:1)

SMILES:

[H]Cl.[H]O[H].[H]Cl.O=S(C1=CC=CC(NC2=NC(NC3=CC=C(C=C3)OCCN4CCCC4)=NC=C2C)=C1)(NC(C)(C)C)=O

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

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