

# Fedratinib

**Catalog No: tcsc0052**



## Available Sizes

**Size:** 5mg

**Size:** 10mg

**Size:** 50mg

**Size:** 100mg



## Specifications

**CAS No:**

936091-26-8

**Formula:**

$C_{27}H_{36}N_6O_3S$

**Pathway:**

Epigenetics;Stem Cell/Wnt;JAK/STAT Signaling

**Target:**

JAK;JAK;JAK

**Purity / Grade:**

>98%

**Solubility:**

DMSO :  $\geq$  42 mg/mL (80.05 mM)

**Alternative Names:**

TG-101348;SAR 302503

**Observed Molecular Weight:**

524.68

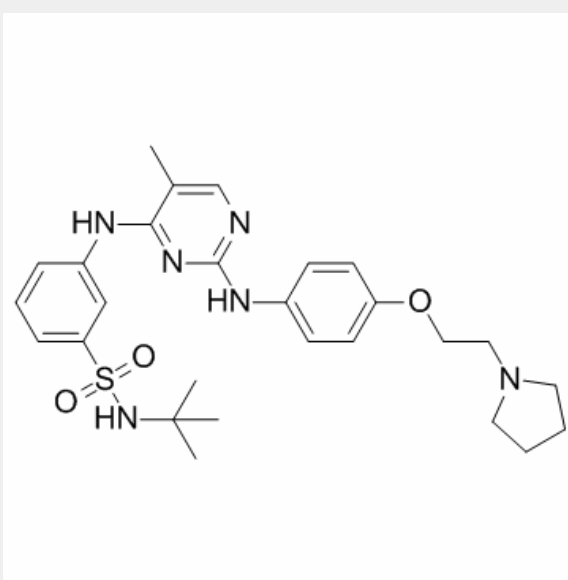
## Product Description

Fedratinib (TG-101348) is a selective inhibitor of **JAK2** with an **IC<sub>50</sub>** of 3 nM, showing 35- and 334-fold selectivity over JAK1 and JAK3, respectively.

IC50 & Target: IC50: 3 nM (JAK2)<sup>[1]</sup>

**In Vitro:** Fedratinib (TG-101348) significantly inhibits JAK2 V617F, Flt3, and Ret with IC<sub>50</sub> of 3 nM, 15 nM, and 48 nM, respectively. TG101348 has an IC<sub>50</sub> appr 300-fold higher for the closely related JAK3 and is a less potent inhibitor of the JAK1 and TYK2 family members. Fedratinib (TG-101348) 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 IC<sub>50</sub> of 305 nM and 270 nM, respectively. Fedratinib (TG-101348) also inhibits proliferation of parental Ba/F3 cells to a comparable level, with IC<sub>50</sub> of appr 420 nM. Fedratinib (TG-101348) treatment reduces STAT5 phosphorylation at concentrations that parallel the concentrations required to inhibit cell proliferation. Fedratinib (TG-101348) induces apoptosis in both HEL and Ba/F3 JAK2V617F cells in a dose-dependent manner. Fedratinib does not show proapoptotic activity in control normal human dermal fibroblasts at concentrations up to 10 μM, and the antiproliferative IC<sub>50</sub> against fibroblasts is >5 μM<sup>[1]</sup>. Fedratinib (TG-101348) treatment decreases GATA-1 expression, which is associated with erythroid-skewing of JAK2V617F+ progenitor differentiation, and inhibits STAT5 as well as GATA S310 phosphorylation<sup>[2]</sup>. Fedratinib (TG-101348) inhibits the proliferation of HMC-1.1 (KITV560G) cells, with somewhat lower potency than HMC-1.2 (KITD816V, KITV560G) cells, with IC<sub>50</sub> of 740 nM and 407 nM, respectively<sup>[3]</sup>.

**In Vivo:** Fedratinib (TG-101348) has potential for efficacious treatment of JAK2V617F-associated myeloproliferative diseases (MPD). In treated animals, there is a statistically significant reduction in hematocrit and leukocyte count, a dose-dependent reduction/elimination of extramedullary hematopoiesis, and, at least in some instances, evidence for attenuation of myelofibrosis, correlated with surrogate endpoints, including reduction/elimination of JAK2V617F disease burden, suppression of endogenous erythroid colony formation, and in vivo inhibition of JAK-STAT signal transduction. There are no apparent toxicities and no effect on T cell number<sup>[1]</sup>. Oral administration of Fedratinib (TG-101348) (120 mg/kg) significantly inhibits PV progenitor erythroid differentiation in vivo<sup>[2]</sup>.



All products are for RESEARCH USE ONLY. Not for diagnostic & therapeutic purposes!