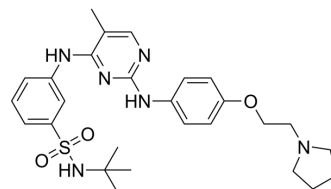


Fedratinib

| | | | | | | | | | | | | | |
|---------------------------|--|---------|-------|---------|--|-----|---------|------------|-------|---------|--|-------|--------|
| Cat. No.: | HY-10409 | | | | | | | | | | | | |
| CAS No.: | 936091-26-8 | | | | | | | | | | | | |
| Molecular Formula: | C ₂₇ H ₃₆ N ₆ O ₃ S | | | | | | | | | | | | |
| Molecular Weight: | 524.68 | | | | | | | | | | | | |
| Target: | JAK; Apoptosis | | | | | | | | | | | | |
| Pathway: | Epigenetics; JAK/STAT Signaling; Protein Tyrosine Kinase/RTK; Stem Cell/Wnt; Apoptosis | | | | | | | | | | | | |
| Storage: | <table border="0"> <tr> <td>Powder</td> <td>-20°C</td> <td>3 years</td> </tr> <tr> <td></td> <td>4°C</td> <td>2 years</td> </tr> <tr> <td>In solvent</td> <td>-80°C</td> <td>2 years</td> </tr> <tr> <td></td> <td>-20°C</td> <td>1 year</td> </tr> </table> | Powder | -20°C | 3 years | | 4°C | 2 years | In solvent | -80°C | 2 years | | -20°C | 1 year |
| Powder | -20°C | 3 years | | | | | | | | | | | |
| | 4°C | 2 years | | | | | | | | | | | |
| In solvent | -80°C | 2 years | | | | | | | | | | | |
| | -20°C | 1 year | | | | | | | | | | | |



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (238.24 mM; Need ultrasonic)

| Preparing Stock Solutions | Solvent Concentration | 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

- Add each solvent one by one: 50% PEG300 >> 50% saline
Solubility: 10 mg/mL (19.06 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 5% DMSO >> 40% PEG300 >> 5% Tween-80 >> 50% saline
Solubility: ≥ 2.87 mg/mL (5.47 mM); Clear solution
- Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
Solubility: 2.87 mg/mL (5.47 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 2.08 mg/mL (3.96 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 2.08 mg/mL (3.96 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 2.08 mg/mL (3.96 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]} . | | | | | | | | | | | |
| IC₅₀ & Target | JAK2 3 nM (IC ₅₀) | JAK2(V617F) 3 nM (IC ₅₀) | Flt3 15 nM (IC ₅₀) | Ret 48 nM (IC ₅₀) | | | | | | | | |
| In Vitro | <p>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 IC₅₀ value of approximately 300 nM for either line. Proliferation of parental Ba/F3 cells was inhibited to a comparable level, with an IC₅₀ value of 420 nM^[1].</p> <p>?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].</p> <p>?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].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> | | | | | | | | | | | |
| In Vivo | <p>Fedratinib (TG101348; 60-120 mg/kg; oral gavage; twice daily; for 42 days; C57Bl/6 mice) shows a dose-dependent reduction in polycythemia and a marked dose-dependent reduction in splenomegaly of treated animals^[1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 30%;">Animal Model:</td> <td>C57Bl/6 mice induced by the JAK2V617F mutation^[1]</td> </tr> <tr> <td>Dosage:</td> <td>60 mg/kg, 120 mg/kg</td> </tr> <tr> <td>Administration:</td> <td>Oral gavage; twice daily; for 42 days</td> </tr> <tr> <td>Result:</td> <td>Showed a statistically significant reduction in hematocrit and leukocyte count, a dose-dependent reduction/elimination of extramedullary hematopoiesis.</td> </tr> </table> | | | | 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. |
| Animal Model: | C57Bl/6 mice induced by the JAK2V617F mutation ^[1] | | | | | | | | | | | |
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| 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.

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

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