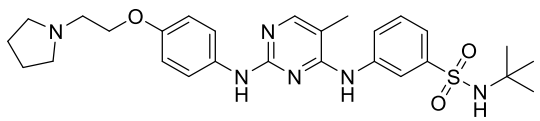
Product data sheet

MedKoo Cat#: 202893 Name: Fedratinib CAS#: 936091-26-8 (free base) Chemical Formula: $C_{27}H_{36}N_6O_3S$ Exact Mass: 524.25696 Molecular Weight: 524.67814	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:

Fedratinib, also known as TG101348 and SAR302503, is a JAK2 inhibitor, is also an orally bioavailable, small-molecule, ATP-competitive inhibitor of Janus-associated kinase 2 (JAK2) with potential antineoplastic activity. JAK2 inhibitor TG101348 competes with JAK2 as well as the mutated form AK2V617F for ATP binding, which may result in inhibition of JAK2 activation, inhibition of the JAK-STAT signaling pathway, and the induction of tumor cell apoptosis. JAK2 is the most common mutated gene in bcr-abl-negative myeloproliferative disorders (MPDs); the mutated form JAK2V617F has a valine-to-phenylalanine modification at position 617 and plays a key role in tumor cell proliferation and survival.

2. CoA, QC data, SDS, and handling instruction

SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	126.67	241.42
Ethanol	0.5	0.95

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.91 mL	9.53 mL	19.06 mL
5 mM	0.38 mL	1.91 mL	3.81 mL
10 mM	0.19 mL	0.95 mL	1.91 mL
50 mM	0.04 mL	0.19 mL	0.38 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator

Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study

In vitro study

1. AlMuraikhi N, Alaskar H, Binhamdan S, Alotaibi A, Kassem M, Alfayez M. JAK2 Inhibition by Fedratinib Reduces Osteoblast Differentiation and Mineralisation of Human Mesenchymal Stem Cells. Molecules. 2021 Jan 25;26(3):606. doi: 10.3390/molecules26030606. PMID: 33503825; PMCID: PMC7866227.
2. Pitroda SP, Stack ME, Liu GF, Song SS, Chen L, Liang H, Parekh AD, Huang X, Roach P, Posner MC, Weichselbaum RR, Khodarev NN. JAK2 Inhibitor SAR302503 Abrogates PD-L1 Expression and Targets Therapy-Resistant Non-small Cell Lung Cancers. Mol Cancer Ther. 2018 Apr;17(4):732-739. doi: 10.1158/1535-7163.MCT-17-0667. Epub 2018 Feb 21. PMID: 29467274.

In vivo study

1. Tang Y, Liu W, Wang W, Fidler T, Woods B, Levine RL, Tall AR, Wang N. Inhibition of JAK2 Suppresses Myelopoiesis and Atherosclerosis in Apoe-/- Mice. Cardiovasc Drugs Ther. 2020 Apr;34(2):145-152. doi: 10.1007/s10557-020-06943-9. PMID: 32086626; PMCID: PMC7125070.

2. Zhang L, Wang Y, Wu G, Rao L, Wei Y, Yue H, Yuan T, Yang P, Xiong F, Zhang S, Zhou Q, Chen Z, Li J, Mo BW, Zhang H, Xiong W, Wang CY. Blockade of JAK2 protects mice against hypoxia-induced pulmonary arterial hypertension by repressing pulmonary arterial smooth muscle cell proliferation. Cell Prolif. 2020 Feb;53(2):e12742. doi: 10.1111/cpr.12742. Epub 2020 Jan 14. PMID: 31943454; PMCID: PMC7046303.

7. Bioactivity

Biological target:

Fedratinib (TG-101348) is an ATP-competitive JAK2 inhibitor with IC50s of 3 nM for both JAK2 and JAK2V617F kinase.

In vitro activity

Fedratinib-treated hMSC-TERT cells (3 μM) exhibited a significant reduction in ALP production, as evidenced by reduced cytochemical staining intensity (Figure 2B) compared with DMSO-vehicle treated control cells (Figure 2A). Moreover, the measurement of ALP activity at day 10 post-osteoblast differentiation induction was reduced compared with DMSO-vehicle treated control cells (Figure 2C). Fedratinib did not exert significant effects on hMSC-TERT cells viability at day 10 post-osteoblast differentiation induction (Figure 2D). Fedratinib-treated hMSC-TERT cells (3 μM) exhibited a significant decrease in mineralised matrix formation, as demonstrated by Alizarin red staining (Figure 3B), compared with DMSO-vehicle treated control cells (Figure 3A), which was associated with the significant downregulation of several osteoblast gene markers: ALP, ON, OC, RUNX2, OPN, and COL1A1 (Figure 4B).

Reference: Molecules. 2021 Feb; 26(3): 606. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7866227/

In vivo activity

These studies demonstrate that TG101348 decreases atherosclerosis in Apoe$^{-/-}$ mice, likely by selective inhibition of hematopoietic JAK2 that results in suppression of excessive myelopoiesis driven by enhanced cell proliferation signaling in HSPCs and myeloid progenitors and reversal of HSPC expansion and leukocytosis. This suggests the possible translation of TG101348 therapy in reducing the risk of ACD in association with moderate myeloproliferation with or without JAK2 mutations.

Reference: Cardiovasc Drugs Ther. 2020; 34(2): 145–152. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7125070/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.