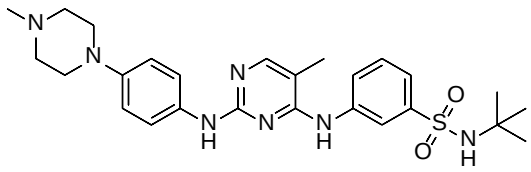
Product data sheet

MedKoo Cat#: 406190 Name: TG101209 CAS#: 936091-14-4 Chemical Formula: $C_{26}H_{35}N_7O_2S$ Exact Mass: 509.2573 Molecular Weight: 509.67	
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:
TG101209 is a novel and potent JAK2 inhibitor, which induced dose- and time-dependent cytotoxicity in a variety of multiple myeloma (MM) cell lines. The induction of cytotoxicity was associated with inhibition of cell cycle progression and induction of apoptosis in myeloma cell lines and patient-derived plasma cells. Exploring the mechanism of action of TG101209 indicated downregulation of pJak2, pStat3, and Bcl-xl levels with upregulation of pErk and pAkt levels indicating cross talk between signaling pathways. TG101209 , when used in combination with the PI3K inhibitor LY294002, demonstrated synergistic cytotoxicity against myeloma cells.

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	29.17	57.23
DMF	16.0	31.39
DMF:PBS (pH 7.2) (1:1)	0.50	0.98
Ethanol	0.12	0.24

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	**1 mg**	**5 mg**	**10 mg**
1 mM	1.96 mL	9.81 mL	19.62 mL
5 mM	0.39 mL	1.96 mL	3.92 mL
10 mM	0.20 mL	0.98 mL	1.96 mL
50 mM	0.04 mL	0.20 mL	0.39 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. Ramakrishnan V, Kimlinger T, Haug J, Timm M, Wellik L, Halling T, Pardanani A, Tefferi A, Rajkumar SV, Kumar S. TG101209, a novel JAK2 inhibitor, has significant in vitro activity in multiple myeloma and displays preferential cytotoxicity for CD45+ myeloma cells. Am J Hematol. 2010 Sep;85(9):675-86. doi: 10.1002/ajh.21785. PMID: 20652971; PMCID: PMC2940994.
2. Cheng Z, Yi Y, Xie S, Yu H, Peng H, Zhang G. The effect of the JAK2 inhibitor TG101209 against T cell acute lymphoblastic leukemia (T-ALL) is mediated by inhibition of JAK-STAT signaling and activation of the crosstalk between apoptosis and autophagy signaling. Oncotarget. 2017 Oct 23;8(63):106753-106763. doi: 10.18632/oncotarget.22053. PMID: 29290986; PMCID: PMC5739771.

In vivo study

Product data sheet

1. Pardanani A, Hood J, Lasho T, Levine RL, Martin MB, Noronha G, Finke C, Mak CC, Mesa R, Zhu H, Soll R, Gilliland DG, Tefferi A. TG101209, a small molecule JAK2-selective kinase inhibitor potently inhibits myeloproliferative disorder-associated JAK2V617F and MPLW515L/K mutations. Leukemia. 2007 Aug;21(8):1658-68. doi: 10.1038/sj.leu.2404750. Epub 2007 May 31. PMID: 17541402.
2. Sun Y, Moretti L, Giacalone NJ, Schleicher S, Speirs CK, Carbone DP, Lu B. Inhibition of JAK2 signaling by TG101209 enhances radiotherapy in lung cancer models. J Thorac Oncol. 2011 Apr;6(4):699-706. doi: 10.1097/JTO.0b013e31820d9d11. PMID: 21325979; PMCID: PMC3104103.

7. Bioactivity

Biological target: TG101209 is a JAK2 inhibitor with IC50 of 6 nM.

In vitro activity

The DU 528, HSD2, PEER, MOLT-4 and Jurkat T-ALL cell lines were treated with TG101209, and cell proliferation was analysed using MTT assay. The IC50s of the cell lines were 2.542 μM (DU528), 0.329 μM (HSD2), 0.612 μM (PEER), 2.893 μM (MOLT-4) and 1.794 μM (Jurkat) (Supplementary Figure 2). Apoptosis was increased in the HSD2 and PEER cell lines in a TG101209 concentration-dependent manner, according to the flow cytometry analysis. The expression of apoptosis-related proteins (Bax, Cleaved PARP, caspase-3 and caspase-9) was determined by Western blotting. The expression levels of Bax and Cleaved PARP were up-regulated by TG101209, while caspase-3 and caspase-9 were down-regulated in both HSD2 and PEER cell lines (Figure 3A). The cell cycle of each cell line was analysed using flow cytometry. After treatment, the cell cycle was arrested mainly at the G2/M phase. The expression of the indicated cell cycle-related proteins (P21, P27, CDK4 and CDK6) was determined by Western blotting. The expression levels of P21 and P27 were up-regulated by TG101209, while those of CDK4 and CDK6 were down-regulated by TG101209 in both the HSD2 and PEER cell lines (Figure 3B). Primary bone marrow cells from T-ALL patients and healthy controls were treated with TG101209 (0, 1, 2, 4, 6, 8, or 10 μM), and cell proliferation was analysed using MTT assay. The IC50s were 0.755um and 1.565 um respectively. (Supplementary Figure 2). Apoptosis was increased in the cells in a TG101209 concentration-dependent manner, according to the flow cytometry analysis. (Figure 3A).

Reference: Oncotarget. 2017 Oct 23;8(63):106753-106763. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5739771/

In vivo activity

To test the in vivo efficacy of TG101209 in inhibiting JAK2V617F, a mouse model of JAK2V617F-induced hematopoietic disease was used. All the animals in the control group died due to disease progression by day 11. In striking contrast, TG101209 at the highest dose level (100 mg/kg b.i.d.) was effective in treating JAK2V617F-induced disease as there was a statistically significant prolongation of survival in this group (10 days; $P<0.02$), and the animals in this group were still alive at the previously defined study end point of 10 days past the time of death of the final placebo-treated animal (Figure 6a). The animals at the lower dose levels (that is, 10 or 30 mg/kg b.i.d.) developed disease with the same latency and penetrance as the placebo-treated animals, without evidence of prolongation of survival (Figure 6a). Compared with placebo-treated animals, TG101209-treated animals exhibited a statistically significant, dose-dependent reduction in the circulating tumor cell burden at day +11 (75% GFP+ cells in placebo-treated versus 15% GFP+ cells in 100 mg/kg b.i.d. TG101209-treated animals; $P<0.02$) (Figure 6b). The clinical benefit of TG101209 in this model correlated with inhibition of JAK2V617F activity in vivo, evident in the marked decrease in STAT-5 phosphorylation demonstrable in splenic tumors, as early as 7 h after administration of a single dose of TG101209 (100 mg/kg) to the affected mice (Figure 6c).

Reference: Leukemia. 2007 Aug;21(8):1658-68. https://www.nature.com/articles/2404750