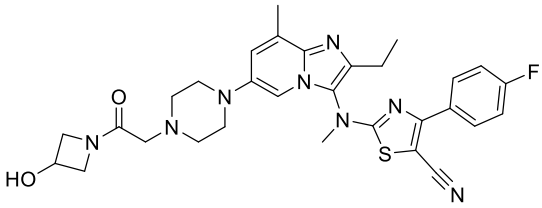
Product data sheet

MedKoo Cat#: 522696 Name: Ziritaxestat (GLPG-1690) CAS#: 1628260-79-6 Chemical Formula: $C_{30}H_{33}FN_8O_2S$ Exact Mass: 588.2431 Molecular Weight: 588.71	
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:
Ziritaxestat, also known as GLPG1690, is a selective autotaxin inhibitor discovered by Galapagos, with potential application in idiopathic pulmonary disease (IPF). In a Phase 1 study in healthy human volunteers, GLPG1690 demonstrated favorable safety and tolerability, as well as a strong pharmacodynamic signal implying target engagement.

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	70.84	120.32
Ethanol	4.0	6.79

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.70 mL	8.49 mL	16.99 mL
5 mM	0.34 mL	1.70 mL	3.40 mL
10 mM	0.17 mL	0.85 mL	1.70 mL
50 mM	0.03 mL	0.17 mL	0.34 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. Feng Y, Mischler WJ, Gurung AC, Kavanagh TR, Androsov G, Sadow PM, Herbert ZT, Priolo C. Therapeutic Targeting of the Secreted Lysophospholipase D Autotaxin Suppresses Tuberous Sclerosis Complex-Associated Tumorigenesis. Cancer Res. 2020 Jul 1;80(13):2751-2763. doi: 10.1158/0008-5472.CAN-19-2884. Epub 2020 May 11. PMID: 32393662; PMCID: PMC7335343.

In vivo study

1. Tang X, Wuest M, Benesch MGK, Dufour J, Zhao Y, Curtis JM, Monjardet A, Heckmann B, Murray D, Wuest F, Brindley DN. Inhibition of Autotaxin with GLPG1690 Increases the Efficacy of Radiotherapy and Chemotherapy in a Mouse Model of Breast Cancer. Mol Cancer Ther. 2020 Jan;19(1):63-74. doi: 10.1158/1535-7163.MCT-19-0386. Epub 2019 Sep 23. PMID: 31548293.

7. Bioactivity
Biological target:

Ziritaxestat (GLPG1690) is a first-in-class autotaxin (ATX) inhibitor, with an IC50 of 131 nM.

In vitro activity

Product data sheet

To assess GLPG1690-induced cell signaling changes, this study screened 43 P-kinase sites and 2 related proteins in the LAM patient-derived TSC2-deficient cells and the TSC2 add-back control cells treated with GLPG1690 (6 μM, 6 hr) or DMSO. Twenty-four of these P-kinase sites (or proteins) showed greater than 25% suppression by GLPG1690 treatment specifically in the TSC2-deficient cells; 8 of them showed greater than 50% change with the inhibitor, including Erk1/2 (T202/Y204, T185/Y187) and Akt1/2/3 (S473) (Supplementary Figure 5A), which are known to mediate signaling downstream of LPAR/S1PR 28–34. This study confirmed the effect of GLPG1690 on Akt and Erk phosphorylation by immunoblotting: 6 hr-treatment with GLPG1690 (6 μM) led to a decrease in P-Akt (S473) by 68 ± 10% and in P-Erk (T202/Y204) by 56 ± 12% in the human TSC2-deficient cells (Figure 4A–B). P-S6 (S235/236), a direct target of mTORC1, was not affected under this condition. Consistent results were obtained in Tsc2−/− MEFs (Supplementary Figure 5B).

Reference: Cancer Res. 2020 Jul 1; 80(13): 2751–2763. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7335343/

In vivo activity

Chronic inflammation is widely recognized as one of the “hallmarks” of cancer, and inflammation is augmented by irradiation, which may be associated with irradiation-induced fibrosis. Blocking ATX with GLPG1690 decreased the concentrations of CCL11, IL9, IL12 p40, M-CSF, and IFNγ in tumors or tumor-adjacent adipose tissue of irradiated mice. Importantly, these proinflammatory cytokines are closely related to the pathogenesis of pulmonary fibrosis. Activation of LPA1 receptors drives fibrosis in several fibrotic conditions, and consequently, blocking LPA formation with GLPG1690 should theoretically attenuate the development of irradiation-induced fibrosis as it does in the case of idiopathic pulmonary fibrosis.

Reference: Mol Cancer Ther. 2020 Jan; 19(1): 63-74. https://mct.aacrjournals.org/content/19/1/63.long