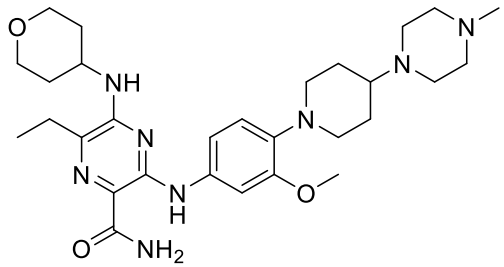
Product data sheet

MedKoo Cat#: 206139 Name: Gilteritinib CAS#: 1254053-43-4 (free base) Chemical Formula: $C_{29}H_{44}N_8O_3$ Exact Mass: 552.35364 Molecular Weight: 552.71	
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:

Gilteritinib, also known as ASP2215, is a potent FLT3/AXL inhibitor, which showed potent antileukemic activity against AML with either or both FLT3-ITD and FLT3-D835 mutations. In invitro, among the 78 tyrosine kinases tested, ASP2215 inhibited FLT3, LTK, ALK, and AXL kinases by over 50% at 1 nM with an IC50 value of 0.29 nM for FLT3, approximately 800-fold more potent than for c-KIT, the inhibition of which is linked to a potential risk of myelosuppression. ASP2215 inhibited the growth of MV4-11 cells, which harbor FLT3-ITD, with an IC50 value of 0.92 nM, accompanied with inhibition of pFLT3, pAKT, pSTAT5, pERK, and pS6. ASP2215 decreased tumor burden in bone marrow and prolonged the survival of mice intravenously transplanted with MV4-11 cells. ASP2215 may have potential use in treating AML.

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	10	18.09
Ethanol	6	10.86

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.81 mL	9.05 mL	18.09 mL
5 mM	0.36 mL	1.81 mL	3.62 mL
10 mM	0.18 mL	0.90 mL	1.81 mL
50 mM	0.04 mL	0.18 mL	0.36 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. Mori M, Kaneko N, Ueno Y, Yamada M, Tanaka R, Saito R, Shimada I, Mori K, Kuromitsu S. Gilteritinib, a FLT3/AXL inhibitor, shows antileukemic activity in mouse models of FLT3 mutated acute myeloid leukemia. Invest New Drugs. 2017 Oct;35(5):556-565. doi: 10.1007/s10637-017-0470-z. Epub 2017 May 17. PMID: 28516360; PMCID: PMC5613053.

2. Li L, Lin L, Li M, Li W. Gilteritinib induces PUMA-dependent apoptotic cell death via AKT/GSK-3β/NF-κB pathway in colorectal cancer cells. J Cell Mol Med. 2020 Feb;24(3):2308-2318. doi: 10.1111/jcmm.14913. Epub 2019 Dec 27. PMID: 31881122; PMCID: PMC7011145.

In vivo study

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1. Mori M, Kaneko N, Ueno Y, Yamada M, Tanaka R, Saito R, Shimada I, Mori K, Kuromitsu S. Gilteritinib, a FLT3/AXL inhibitor, shows antileukemic activity in mouse models of FLT3 mutated acute myeloid leukemia. Invest New Drugs. 2017 Oct;35(5):556-565. doi: 10.1007/s10637-017-0470-z. Epub 2017 May 17. PMID: 28516360; PMCID: PMC5613053.

2. Li L, Lin L, Li M, Li W. Gilteritinib induces PUMA-dependent apoptotic cell death via AKT/GSK-3β/NF-κB pathway in colorectal cancer cells. J Cell Mol Med. 2020 Feb;24(3):2308-2318. doi: 10.1111/jcmm.14913. Epub 2019 Dec 27. PMID: 31881122; PMCID: PMC7011145.

7. Bioactivity

Biological target:

Gilteritinib (ASP2215) is a potent and ATP-competitive FLT3/AXL inhibitor with IC50s of 0.29 nM/0.73 nM, respectively.

In vitro activity

Gilteritinib inhibits the activity of eight of the 78 tested kinases by over 50% at concentrations of either 1 nM (FLT3, LTK, ALK, and AXL) or 5 nM (TRKA, ROS, RET, and MER). The IC50s are 0.29 nM for FLT3 and 0.73 nM for AXL. Gilteritinib inhibits FLT3 at an IC50 that is approximately 800-fold more potent than the concentration required to inhibit c-KIT (230 nM). The antiproliferative activity of Gilteritinib is evaluated against MV4-11 and MOLM-13 cells, which endogenously express FLT3-ITD. After 5 days of treatment, Gilteritinib inhibits the growth of MV4-11 and MOLM-13 cells with mean IC50s of 0.92 nM (95% CI: 0.23-3.6 nM) and 2.9 nM (95% CI: 1.4-5.8 nM), respectively. Growth suppression of MV4-11 cells is accompanied by inhibition of FLT3 phosphorylation. Relative to vehicle control cells, phosphorylated FLT3 levels are 57%, 8%, and 1% after 2 h of treatment with 0.1 nM, 1 nM, and 10 nM Gilteritinib, respectively. In addition, doses as low as 0.1 nM or 1 nM result in the suppression of phosphorylated ERK, STAT5, and AKT, all of which are downstream targets of FLT3 activation. To investigate the effects of Gilteritinib on AXL inhibition, MV4-11 cells that expressed exogenous AXL are treated with Gilteritinib. At concentrations of 1 nM, 10 nM, and 100 nM for 4 h, Gilteritinib treatment decreases phosphorylated AXL levels by 38%, 29%, and 22%, respectively.

Reference: Invest New Drugs. 2017 Oct;35(5):556-565. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/28516360/

In vivo activity

The maximal plasma concentrations of gilteritinib were observed 2 h after a single oral administration of gilteritinib at 1 mg/kg, 6 mg/kg, and 10 mg/kg to MV4–11 xenografted mice. By contrast, the maximal intratumor concentrations were observed 4 h (1 mg/kg) or 8 h (6 mg/kg and 10 mg/kg) after dosing. Cmax and AUCt in plasma and tumors increased with increasing doses between 1 mg/kg and 10 mg/kg. The concentration in tumors was higher than that in plasma at each time point (Fig. 2a–b, Table S3). Gilteritinib dose ranges for cell viability studies are presented in the online resource (Table S4). Phosphorylated FLT3 decreased by approximately 40% compared with control phosphorylation levels in tumor samples within 1 h after single oral administration of 1–10 mg/kg gilteritinib (Fig. 2c), indicating target inhibition by gilteritinib. The effect on tumor burden of inhibiting FLT3 phosphorylation was assessed following 28 days of once-daily oral administration of gilteritinib. Significant growth inhibition of MV4–11 tumors was observed at 1 mg/kg/day (63% inhibition; $P < 0.05$) and 3 mg/kg/day (80% inhibition; $P < 0.01$), and near-complete tumor regression was seen at 6 mg/kg/day (93%; $P < 0.001$) and 10 mg/kg/day (100%; $P < 0.001$) (Fig. 2e). Four of the six mice in the 6 mg/kg/day group experienced complete tumor regression; all six mice in the 10 mg/kg/day group experienced complete tumor regression. Body weight was not affected by treatment with gilteritinib at any tested dose (Fig. 2f).

Reference: Invest New Drugs. 2017 Oct;35(5):556-565. https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/28516360/

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.