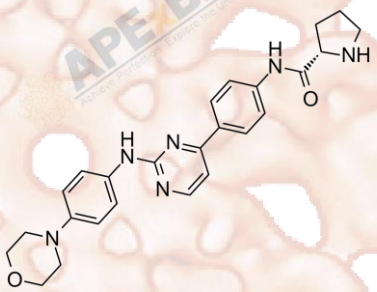
Product Data Sheet

XL019



Cat. No.:	A3937
CAS No.:	945755-56-6
Formula:	C25H28N6O2
M.Wt:	444.53
Synonyms:	XL-019;XL 019
Target:	Chromatin/Epigenetics
Pathway:	JAK
Storage:	Store at -20°C

Solvent & Solubility

In Vitro

insoluble in EtOH; insoluble in H2O; ⩾11.125 mg/mL in DMSO

Preparing Stock Solutions

Mass / Solvent / Concentration	1mg	5mg	10mg
1 mM	2.2496 mL	11.2478 mL	22.4957 mL
5 mM	0.4499 mL	2.2496 mL	4.4991 mL
10 mM	0.2250 mL	1.1248 mL	2.2496 mL

Please refer to the solubility information to select the appropriate solvent.

Biological Activity

Shortsummary	JAK2 inhibitor,potent and selective
IC_{50} & Target	2.2 nM (JAK2)

In Vitro

Cell Viability Assay

Cell Line:	HEL92.1.7 and KG-1 tumor cell lines, primary human erythroid cells
Preparation method:	The solubility of this compound in DMSO is > 11.1 mg/mL. General tips for obtaining a higher concentration: Please warm the tube at 37 °C for 10 minutes and/or shake it in the ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.
Reacting conditions:	24h

	Applications:	XL019 downregulated STAT signaling in cell lines expressing both wild type and activated forms of JAK2. IC50s for inhibition of STAT5 phosphorylation by XL019 ranged from 623 nM (HEL92.1.7) to 3398 nM (KG-1) in tumor cell lines. XL019 showed increased potency in primary human erythroid cells, where the IC50 for inhibition of EPO-stimulated phospho-STAT5 was 64 nM. XL019 inhibited proliferation in cell lines harboring activated or overexpressed JAK2, including certain lines derived from patients with Hodgkin's Lymphoma (L-1236, 928 nM IC50), AML (MV4-11, 992 nM IC50), essential thrombocythemia (SET-2, 386 nM IC50), and erythroleukemia (HEL92.1.7, 6777 nM IC50).
In Vivo	**Animal experiment**	
	Animal models:	Mice bearing HEL92.1.7, CFPAC-1 and DU 145 xenograft tumors
	Dosage form:	Oral administration, 30, 100, and 300 mg/kg.
	Applications:	Oral administration of XL019 (30, 100, and 300 mg/kg) significantly inhibited downstream markers pSTAT1 and pSTAT3 with an ED50 of 42 mg/kg (pSTAT1) and 210 mg/kg (pSTAT3). XL019 demonstrated 60% and 70% inhibition when dosed orally at 200 mg/kg and 300 mg/kg respectively twice a day for 14 days. XL019 showed a superior pharmacodynamic profile and exhibited good oral absorption, and modest clearance and halflife across species. XL019 inhibited HEL.92.1.7 xenograft tumors growth in mice. XL019 showed potent effect on JAK-STAT signaling in HEL92.1.7, CFPAC-1 and DU 145 xenograft tumors. Twice daily dosing (bid) led to substantial tumor growth inhibition in the DU145 and HEL models (maximum tumor growth inhibition of 86% and 60%, respectively), accompanied by increases in tumor cell apoptosis (4 – 4.4 fold increase) and decreases in tumor microvasculature (44% reduction in DU 145 xenograft tumors).
	Other notes:	Please test the solubility of all compounds indoor, and the actual solubility may slightly differ with the theoretical value. This is caused by an experimental system error and it is normal.

Product Citations

See more customer validations on www.apexbt.com.

References

[1]. Verstovsek S, Pardanani A D, Shah N P, et al. A Phase I Study of XL019, a Selective JAK2 Inhibitor, in Patients with Primary

Myelofibrosis and Post-Polycythemia Vera/Essential Thrombocythemia Myelofibrosis[J]. 2007.
[2]. Forsyth T, Kearney P C, Kim B G, et al. SAR and in vivo evaluation of 4-aryl-2-aminoalkylpyrimidines as potent and selective Janus kinase 2 (JAK2) inhibitors[J]. Bioorganic & medicinal chemistry letters, 2012, 22(24): 7653-7658.

Caution

FOR RESEARCH PURPOSES ONLY.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE.

Specific storage and handling information for each product is indicated on the product datasheet. Most APExBIO products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. Shortterm storage of many products are stable in the short-term at temperatures that differ from that required for long-term storage. We ensure that the product is shipped under conditions that will maintain the quality of the reagents. Upon receipt of the product, follow the storage recommendations on the product data sheet.

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