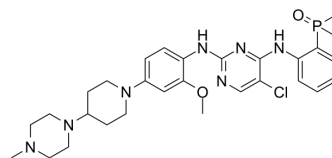


Brigatinib

Cat. No.:	HY-12857		
CAS No.:	1197953-54-0		
Molecular Formula:	C ₂₉ H ₃₉ ClN ₇ O ₂ P		
Molecular Weight:	584.09		
Target:	Anaplastic lymphoma kinase (ALK)		
Pathway:	Protein Tyrosine Kinase/RTK		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	2 years
		-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

Ethanol : 10 mg/mL (17.12 mM; Need ultrasonic and warming)
 DMSO : 2 mg/mL (3.42 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.7121 mL	8.5603 mL	17.1206 mL
	5 mM	0.3424 mL	1.7121 mL	3.4241 mL
	10 mM	0.1712 mL	0.8560 mL	1.7121 mL

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

In Vivo

- Add each solvent one by one: 10% EtOH >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 1 mg/mL (1.71 mM); Clear solution
- Add each solvent one by one: 10% EtOH >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 1 mg/mL (1.71 mM); Clear solution
- Add each solvent one by one: 10% EtOH >> 90% corn oil
Solubility: ≥ 1 mg/mL (1.71 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
Solubility: ≥ 0.5 mg/mL (0.86 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
Solubility: ≥ 0.5 mg/mL (0.86 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
Solubility: ≥ 0.5 mg/mL (0.86 mM); Clear solution

BIOLOGICAL ACTIVITY

Description	Brigatinib (AP-26113) is a highly potent, selective and orally active ALK inhibitor, with an IC ₅₀ of 0.6 nM. Brigatinib can be used for research of NSCLC ^[1] .
IC₅₀ & Target	IC ₅₀ : 0.6 nM (ALK) ^[1]
In Vitro	<p>Brigatinib potently inhibits the in vitro kinase activity of ALK (IC₅₀, 0.6 nM) and all five mutant variants tested, including G1202R (IC₅₀, 0.6-6.6 nM).</p> <p>Brigatinib demonstrates a high degree of selectivity, only inhibiting 11 additional native or mutant kinases with IC₅₀ <10 nM. These include ROS1, FLT3, and mutant variants of FLT3 (D835Y) and EGFR (L858R; IC₅₀, 1.5-2.1 nM).</p> <p>Brigatinib exhibits more modest activity against EGFR with a T790M resistance mutation (L858R/T790M), native EGFR, IGF1R, and INSR (IC₅₀, 29-160 nM) and does not inhibit MET (IC₅₀ >1000 nM).</p> <p>In cellular assays, brigatinib inhibits ALK and ROS1 with IC₅₀s of 14 and 18 nM, respectively.</p> <p>Brigatinib inhibits FLT3 and IGF-1R with about 11-fold lower potency (IC₅₀, 148-158 nM) and inhibits mutant variants of FLT3 and EGFR with 15- to 35-fold lower potency (IC₅₀, 211-489 nM).</p> <p>Brigatinib inhibits cell growth with GI₅₀ values ranging from 503 to 2,387 nM in three ALK-negative ALCL and NSCLC cell lines^[1].</p> <p>Brigatinib inhibits ALK activity and abrogates proliferation of ALK addicted neuroblastoma cell lines, with IC₅₀ of 75.27 ± 8.89 nM.</p> <p>Brigatinib inhibits both the ALK-I1171N and the ALK-G1269A mutant receptors at 10 and 4 nM levels, respectively^[3].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
In Vivo	<p>Brigatinib (10, 25, or 50 mg/kg once daily, p.o.) leads to a dose-dependent inhibition of tumor growth in ALK⁺ Karpas-299 (ALCL) and H2228 (NSCLC) xenograft mouse models. Brigatinib markedly enhances survival of mice bearing ALK⁺ brain tumors compared with PF-02341066^[1].</p> <p>Brigatinib (10, 25, 50 mg/kg, p.o.) results in dose-dependent antitumor activity, with tumor regressions in a mouse model of NSCLC^[2].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

PROTOCOL

Kinase Assay ^[1]	<p>In vitro HotSpotSM kinase profiling of 289 kinases is performed. The assay is conducted in the presence of 10 μM [³³P]-ATP, using brigatinib concentrations ranging from 0.05 nM to 1 μM.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Cell Assay ^[3]	<p>Cells are seeded at 15,000 per well with serial dilutions of the indicated inhibitors. After 72 hours cell viability is assessed by resazurin. IC₅₀ values are calculated with GraphPad Prism 6.0 by fitting data to a log (inhibitor concentration) vs. normalized response (variable slope) equation. Each experiment is performed in duplicate and repeated at least three times.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>
Animal Administration ^[2]	<p>Mice: (1) Eight- to 10-week-old female SCID/beige mice are injected intravenously with 5×10⁶ H3122 cells per mouse and are randomly selected into treatment groups (n=10) when the average tumor size reaches appr 300 mm³ (day zero). Treatments are administered orally for up to 21 consecutive days at a 10 mL/kg dose volume. Subcutaneous tumors are measured two or three times weekly. Tumor volume (in mm³) is calculated using the formula (L×W²)/2. When a tumor reaches 10% of the body weight of the host, the animal is euthanized via CO₂ asphyxiation. (2) Eight- to 10-week old female SCID/beige mice are injected subcutaneously with 2.5×10⁶ Karpas-299 cells per mouse and are randomly selected into treatment groups (n=10) when the average tumor size reached appr 180 mm³ (day zero). Treatments are administered orally for 14 consecutive days at a 10 mL/kg dose volume. Tumor volume is measured and calculated as described for the H3122 model.</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p>

CUSTOMER VALIDATION

- Cancer Discov. 2018 Jun;8(6):714-729.
- Nat Cancer. 2022 Jun 20.
- Sci Transl Med. 2018 Jul 18;10(450):eaaq1093.
- Cell Rep Med. 2023 Jan 10;100911.
- Theranostics. 2019 Jul 9;9(17):4878-4892.

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REFERENCES

- [1]. Zhang S, et al. The Potent ALK Inhibitor Brigatinib (AP26113) Overcomes Mechanisms of Resistance to First- and Second-Generation ALK Inhibitors in Preclinical Models. Clin Cancer Res. 2016 Nov 15;22(22):5527-5538
- [2]. Huang WS, et al. Discovery of Brigatinib (AP26113), a Phosphine Oxide-Containing, Potent, Orally Active Inhibitor of Anaplastic Lymphoma Kinase. J Med Chem. 2016 May 26;59(10):4948-64.
- [3]. Siaw JT, et al. Brigatinib, an anaplastic lymphoma kinase inhibitor, abrogates activity and growth in ALK-positive neuroblastoma cells, Drosophila and mice. Oncotarget. 2016 May 17;7(20):29011-22
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Caution: Product has not been fully validated for medical applications. For research use only.

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