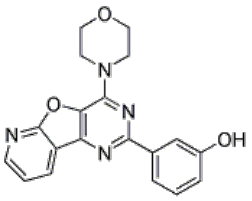
PI-103 Datasheet

Technical Data

Molecular Weight (MW)	348.36
Formula	$C_{19}H_{16}N_4O_3$
CAS No.	371935-74-9, 371935-79-4 (HCl)
Synonyms	N/A

Solubility (25°C)	DMSO 24 mg/mL		
	Water <1 mg/mL		
	Ethanol <1 mg/mL		
Storage	2 years	-20°C	Powder
	2 weeks	4°C	in DMSO
	6 months	-80°C	in DMSO

PI-103 Chemical Structure



Biological Activity

Description	PI-103 is a potent, ATP-competitive PI3K inhibitor of **DNA-PK**, **p110α**, mTORC1, PI3-KC2β, p110δ, mTORC2, p110β, and p110γ with **IC50** of 2 nM, 8 nM, 20 nM, 26 nM, 48 nM, 83 nM, 88 nM and 150 nM, respectively.					
Targets	DNA-PK	p110α	mTORC1	PI3-KC2β	p110δ	
IC50	2 nM	8 nM	20 nM	26 nM	48 nM [1]	
In vitro	PI-103 potently inhibits both the rapamycin-sensitive (mTORC1) and rapamycin-insensitive (mTORC2) complexes of the protein kinase mTOR. [1] PI-103 inhibits constitutive and growth factor-induced PI3K/Akt, as well as mTORC1 activation. [2] In blast cells, PI-103 inhibits leukemic proliferation, the clonogenicity of leukemic progenitors and induces mitochondrial apoptosis, especially in the compartment containing leukemic stem cells. PI-103 inhibits p110α >200-fold more potently than p110β. PI-103 also potently blocks production of PI(3,4)P2 and PIP3 in adipocytes and PIP3 in myotubes. [2] PI-103 inhibits phosphorylation of Akt with an IC95 100-fold lower than that for LY294002. Strikingly, PI-103 completely protects animals from insulin-stimulated decline in blood glucose. PI-103 has additive proapoptotic effects with etoposide in blast cells and in immature leukemic cells. [2]					
In vivo	When tumors reach 50-100 mm^3, animals are randomized and treated with vehicle or PI-103. PI-103 exhibits significant activity, decreasing average tumor size by 4-fold after 18 days. [2] Mice treated with PI-103 have no obvious signs of toxicity premorbidly (based on body weight, food and water intake, activity, and general exam) or at necropsy. Treated tumors display decreased levels of phosphorylated Akt and S6, consistent with blockade of p110α and mTOR. PI-103 treatment is cytostatic to glioma xenografts. [2]					
Clinical Trials						
Features	PI-103 represents the first potent, synthetic mTOR inhibitor.					

Protocol (Only for Reference)

Kinase Assay: [1]

Assay of p110 kinase	Reactions are initiated by the addition of ATP containing 10 μCi of γ- ^{32}P-ATP to a final concentration 10 or 100 μM, and allowed to proceed for 20 minutes at room temperature. For TLC analysis, reactions are then terminated by the addition of 105 μL 1 N HCl followed by 160μL $CHCl_3$:MeOH (1:1). The biphasic mixture is vortexed, briefly centrifuged, and the organic phase transferred to a new tube using a gel loading pipette tip precoated with $CHCl_3$. This extract is spotted on TLC plates and developed for 3-4 hours in a 65:35 solution of n-propanol:1 M acetic acid. The TLC plates are then dried, exposed to a phosphorimager screen, and quantitated. For PI-103, kinase activity is typically measured at 10-12 inhibitor concentrations representing two-fold dilutions from the highest concentration tested (100 μM). For PI-103 showing significant activity, IC50 determinations are repeated two to four times, and the reported value is the average of these independent measurements.

Cell Assay: [2]

Cell Lines	U87MG cells
Concentrations	0.5 μM
Incubation Time	24 hours
Methods	U87MG cells are treated with PI-103 for 24 hours. Cell death is quantified by colorimetric determination of LDH activity using a cytotoxicity detection kit. Percentage of cell death (mean of three 12-well plates per experimental point) is calculated [(experimental value- low control)/(high control -low control) × 100], where the low-control cells are DMSO treated and high-control cells are Triton treated (1% Triton X-100, 30 min, 37 °C).

Animal Study: [2]

Animal Models	6- to 12-week-old Balbc nu/nu mice bearing U87MG:ΔEGFR cells
Formulation	50% DMSO
Doses	5 mg/kg

Return Policy

Selleck Chemicals wishes you the best possible online shopping experience with our 365 day unconditional Return Policy. If you are not satisfied with your purchase, either for protocol related or product related problems, you may return any item(s) within 365 days from the original purchase date. Please see the following instructions when you return products.

1. All requests for returns should be communicated to Selleck Chemicals prior to shipping. Any items returned to Selleck Chemicals should be in the original packaging and in the same condition as originally purchased.
2. When returning purchased goods, please inform us of the purchase order number or package tracking number.
3. Return shipping is absolutely FREE.
4. This offer is only valid for products purchased directly from Selleck and its authorized distributors.
5. Once your return request is received and approved, your refund will be processed or automatically applied to your credit card within 7 days. Please note that depending on your credit card company, it may take additional 2-10 business days for us to post the refund to your account.

Toll Free:

(877) 796-6397

-- USA and Canada only --

Fax:

+1-713-796-9816

Orders:

+1-832-582-8158

sales@selleckchem.com

Tech Support:

tech@selleckchem.com
(chemistry support)

techbio@selleckchem.com
(biology support)

Website:

www.selleckchem.com

Administration	Administered via i.p.

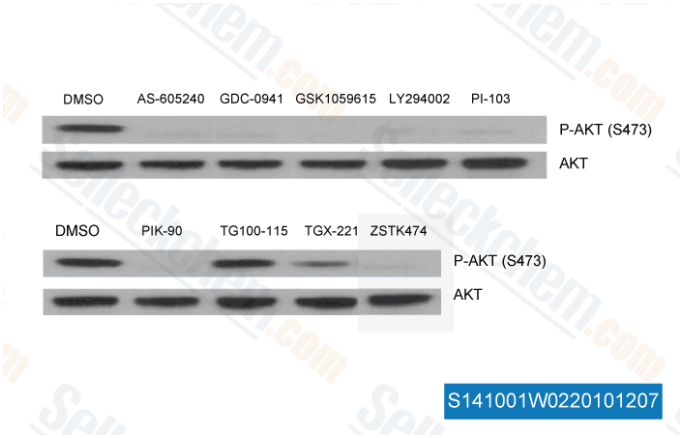
References

[1] Knight ZA, et al. Cell, 2006, 125(4), 733-747.
[2] Fan QW, et al. Cancer Cell, 2006, 9(5), 341-349.

Customer Reviews

S103801W0220120307

Data from [**Mol Carcinog**, 2012.April, ahead of print] **PI-103** purchased from **Selleck**
(A) MCF7 cells pre-treated with 100 nM siRNA for 72 h were re-seeded with normal growth media and grown overnight, then further transfected by 100nM of fresh siRNA. Twenty-(A) four hours after transfection, the cells were further treated with PI-103 for 24 h and the cell lysates were immunoblotted with the indicated antibodies. (B) Breast cancer cells carrying BRCA1 mutations were treated with 1 mM of PI-103 for 24h (left) or increasing amounts of PI-103 for 24 h (right). Cell lysates were analyzed by Western blotting with the indicated antibodies.



S141001W0220101207

Data independently produced by Saraswati Sukumar of Johns Hopkins University School of Medicine---PI-103 purchased from Selleck, **PI-103** purchased from **Selleck**
We treated all of drugs in T47D which has a PI3KCA H1044R mutation with the concentration shown below for 1 hour and performed western blot analysis using antibodies to phospho-AKT(SERINE 472), and total AKT.

PLEASE KEEP THE PRODUCT UNDER -20°C FOR LONG-TERM STORAGE.

NOT FOR HUMAN, VETERINARY DIAGNOSTIC OR THERAPEUTIC USE

Specific storage and handling information for each product is indicated on the product datasheet. Most Selleck products are stable under the recommended conditions. Products are sometimes shipped at a temperature that differs from the recommended storage temperature. 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, but save your shipping charges by using the most economical storage conditions for an overnight shipment. Upon receipt of the product, follow the storage recommendations on the product datasheet.