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Produktinformation

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Lieferung & Zahlungsart

siehe unsere Liefer- und Versandbedingungen

Zuschläge

- Mindermengenzuschlag
- Trockeneiszuschlag
- Gefahrgutzuschlag
- Expressversand

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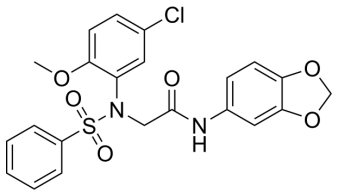
LX2343

Cat. No.:	HY-111383
CAS No.:	333745-53-2
Molecular Formula:	$C_{22}H_{19}ClN_2O_6S$
Molecular Weight:	474.91
Target:	Beta-secretase; PI3K; Amyloid-β; Autophagy
Pathway:	Neuronal Signaling; PI3K/Akt/mTOR; Autophagy
Storage:	Powder -20°C 3 years 4°C 2 years In solvent -80°C 2 years -20°C 1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 100 mg/mL (210.57 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Solvent / Mass / Concentration	1 mg	5 mg	10 mg
1 mM	2.1057 mL	10.5283 mL	21.0566 mL
5 mM	0.4211 mL	2.1057 mL	4.2113 mL
10 mM	0.2106 mL	1.0528 mL	2.1057 mL

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

In Vivo

1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
   Solubility: ≥ 2.5 mg/mL (5.26 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.26 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

LX2343 is a BACE1 enzyme inhibitor with an IC_{50} value of 11.43±0.36 μM. LX2343 acts as a non-ATP competitive PI3K inhibitor with an IC_{50} of 15.99±3.23 μM. LX2343 stimulates autophagy in its promotion of Aβ clearance.

IC_{50} & Target

BACE1	PI3K	Aβ	Autophagy
11.43 μM (IC_{50})	15.99 μM (IC_{50})		

In Vitro

LX2343 (5-20 μM) dose-dependently decreased Aβ accumulation in HEK293-APPsw and CHO-APP cells, and promotes Aβ clearance in SH-SY5Y cells and primary astrocytes. LX2343 ameliorates cognitive dysfunction in APP/PS1 transgenic mice via both Aβ production inhibition and clearance promotion, which highlights the potential of LX2343 in the treatment of AD.

	Western blot results in both HEK293-APP_{sw} cells and CHO-APP cells demonstrate that LX2343 fails to regulate BACE1 protein levels, while in vitro BACE1 enzymatic activity assays indicated that LX2343 dose-dependently decreases BACE1 activity (TDC as a positive control) with an IC_{50} of 11.43±0.36 μM. To test whether competition exists between LX2343 and ATP, we investigated the effects of ATP at different concentrations on the inhibitory activity of LX2343. The result demonstrated that the inhibition of LX2343 against PI3K is virtually unaffected by ATP. Thus, this result suggested that LX2343 is a non-ATP competitive inhibitor of PI3K. In the presence of 10 μM of ATP, the IC_{50} of LX2343 is 13.11±1.47 μM, in the presence of 50 μM ATP, the IC_{50} of LX2343 is 13.86±1.12 μM, in the presence of 100 μM ATP, the IC_{50} of LX2343 is 15.99±3.23 μM [1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	APP/PS1 mice express chimeric human Swedish mutant APP and a mutant human presenilin 1 protein and are widely used as an effective animal model for AD dementia. The amelioration of memory impairment by LX2343 is evaluated t in this model using the MWM test. In 8-d training trials, the path lengths and escape latencies used to find the platform for APP/PS1 transgenic mice are remarkably longer than those for non-transgenic mice, while 10 mg/kg LX2343 administration obviously antagonizes the prolonged path lengths and escape latencies at d 7 and 8. In the probe trial assay, the LX2343-administered transgenic mice cross over the hidden location of the platform more frequently compared with the vehicle-administered transgenic mice[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Kinase Assay [1]	Inhibition of BACE1 enzyme by LX2343 is assayed using BACE1 activity kits in vitro. Briefly, BACE1 substrate (250 nM), BACE1 enzyme (0.35 U/mL), and varied concentrations of LX2343 (5, 10, and 20 μM) are sequentially incubated for 1 h at 37°C in the dark. Fluorescence intensity is measured with excitation and emission wavelengths at 545 and 585 nm, respectively[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Cell Assay [1]	SH-SY5Y cells are transfected with mRFP-GFP-LC3 plasmids via an adenovirus. The cells are treated without or with Streptozotocin (0.8 mM) in combination with 5 or 20 μM LX2343 for 4 h and then fixed with 4% paraformaldehyde and observed using an Olympus Fluoview FV1000 confocal microscope[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [1]	Mice[1] APP/PS1 [B6C3-Tg(APP_{swe}, $PS1^{dE9}$)] transgenic mice are used. Genotyping to confirm APP/PS1 DNA sequences in their offspring is performed by assaying the DNA from tail biopsies, with Tg-negative mice as a negative control. Twenty male APP/PS1 mice are divided into two groups with ten non-transgenic mice in one group to serve as a negative control. The two 6-month transgenic groups are administered 10 mg/kg per day of LX2343 or vehicle, and the 6-month non-transgenic group is administered the vehicle for 100 d via intraperitoneal injection. After 100 d of administration, MWM assays are applied to evaluate the cognitive abilities of the mice for 8 d under continuous LX2343 treatment. Upon completion of the MWM test, the mice are euthanized, and the brains are removed and bisected at the mid-sagittal plane. The right hemispheres are frozen and stored at -80°C, and the left hemispheres are fixed in 4% paraformaldehyde[1]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Guo XD, et al. Small molecule LX2343 ameliorates cognitive deficits in AD model mice by targeting both amyloid β production and clearance. Acta Pharmacol Sin. 2016 Sep;37(10):1281-1297.

Caution: Product has not been fully validated for medical applications. For research use only.

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