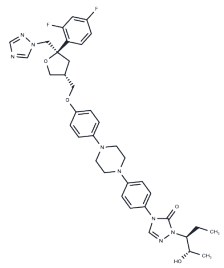
Data Sheet (Cat.No.T6211)

TargetMol

Posaconazole

Chemical Properties



CAS No. : 171228-49-2

Formula: C37H42F2N8O4

Molecular Weight: 700.78

Storage: Keep away from direct sunlight,Keep away from moisture,Store at low temperature
Powder: -20°C for 3 years | In solvent: -80°C for 1 year
Actual storage temperature shall be subject to the COA.

Biological Description

Description	Posaconazole (POS) is a sterol C14 demethylase inhibitor (IC50: 0.25 nM).
Targets(IC50)	Parasite,Antifungal
In vitro	The bioavailability of Posaconazole is significantly increased by food intake, especially a high-fat diet. When consumed with high-fat and non-fat meals, the systemic exposure to Posaconazole is respectively quadrupled and increased by 2.6 times. Administration of Posaconazole (≥15 mg/kg, b.i.d) can extend the lifespan of mice and reduce tissue burden. Used alone in infected animals, Amiodarone reduces parasitemia and increases the survival rate to 60% at 60 days (compared to 0% in untreated controls), demonstrating this effect. When used in combination, Posaconazole and Amiodarone can delay the progression of parasitemia. This suggests that Posaconazole and Amiodarone may offer an effective, low-side-effect treatment against T. cruzi. When Posaconazole is taken fasting with Boost Plus, there is an increase in drug exposure.
In vivo	Posaconazole exhibits enhanced efficacy against clinically relevant intracellular, non-flagellated parasitic forms. Its minimum inhibitory concentration (MIC) and IC50 are 3 nM and 0.25 nM, respectively. Posaconazole is active against strains of Candida and Aspergillus that are resistant to fluconazole, voriconazole, and amphotericin B, showing superior effectiveness compared to other triazole antifungal agents. It synergizes with amiodarone and disrupts the internal calcium (Ca2+) homeostasis in T. cruzi. Additionally, posaconazole demonstrates a dose-dependent effect on the proliferation of the extracellular (pre-flagellar) stage, with an MIC of 20 nM and an IC50 of 14 nM.
Kinase Assay	In vitro Aβ reduction assays : Human embryonic kidney cells (American Type Culture Collection CRL-1573), transfected with the gene for APP751 (HEK 293) are used for routine Aβ reduction assays. Cells are plated in 96-well plates and allowed to adhere overnight in Dulbecco's modified Eagle medium (DMEM) supplemented with 10% heat-inactivated fetal bovine serum. DAPT are diluted from stock solutions in dimethylsulfoxide (DMSO) to yield a final concentration equal to 0.1% DMSO in media. Cells are pre-treated for 2 hours at 37 °C with DAPT, media are aspirated off and fresh compound solutions applied. After an additional 2-hour treatment period, conditioned media is drawn off and analyzed by a sandwich ELISA (266-3D6) specific for total Aβ.

Kinase Assay	Reduction of Aβ production is measured relative to control cells treated with 0.1% DMSO and expressed as a percentage inhibition. Data from at least six doses in duplicate are fitted to a four-parameter logistical model using XLfit software in order to determine potency. Human and PDAPP mouse neuronal cultures are grown in serum-free media to enhance their neuronal characteristics, and appeared to be greater than 90% neurons after maturation prior to use. Conditioned media to establish baseline Aβ values are collected by adding fresh media to each well and incubated for 24 hours at 37 °C in the absence of DAPT. Cultures are then treated with fresh media containing DAPT at the desired range of concentrations for an additional 24 hours at 37 °C, and conditioned media collected. For the measurement of total Aβ, samples are analyzed with the same ELISA (266-3D6) as used for the HEK 293 cell assays. Analyses of samples for Aβ42 production are performed by a separate ELISA (21F12-3D6) that utilizes a capture antibody specific for the Aβ42 C-terminus. Inhibition of production for both total Aβ and Aβ42 are determined by the difference between the values for the compound treatment and baseline periods.After plotting percentage inhibition versus DAPT concentration, data are analyzed with XLfit software, as above, to determine potency.
Cell Research	The epimastigote form of the parasite is cultivated in liver infusion tryptose medium, supplemented with 10% new born calf serum at 28 °C with strong (120 rpm) agitation. Cultures are initiated at a cell density of 2 × 106 epimastigotes/mL,and Posaconazole is added at a cell density of 0.5–1.0 × 107 epimastigotes/mL.Cell densities are measured by using an electronic particle counter as well as by direct counting with a hemocytometer.Cell viability is followed by Trypan blue exclusion,using light microscopy.Amastigotes are cultured in Vero cells maintained in minimal essential medium supplemented with 1% fetal calf serum in a humidified atmosphere (95% air–5% CO2) at 37 °C.Cells are infected with 10 tissue culture-derived trypomastigotes per cell for 2 hours and then washed three times with phosphate-buffered saline (PBS) to remove nonadherent parasites.Fresh medium with and without Posaconazole is added,and the cells are incubated for 96 hours with a medium change at 48 hours.The percent of infected cells and the numbers of parasites per cell are determined directly using light microscopy,and a statistical analysis of the results is carried out.IC50 values are calculated by nonlinear regression,using the program GraFit.Fractional inhibitory concentrations (FIC) are calculated.Cytoplasmic free Ca2+ concentrations in control and drug-treated extracellular epimastigotes are determined by fluorimetric methods using Fura-2.Subcellular Ca2+ levels and mitochondrial membrane potentials are monitored on individual Vero cells infected with T.cruzi amastigotes by using time-scan confocal microscopy.Briefly,Vero cells heavily infected (72 hours) with T.cruzi amastigotes are plated onto 22 × 40 mm glass coverslips (0.15 mm thickness) and incubated simultaneously with 10 μM cell-permeant Rhod-2 and 10 μg/mL Rhodamine-123 for 50 minutes at 37 °

Solubility Information

Solubility	Ethanol: < 1 mg/mL (insoluble or slightly soluble), DMSO: 245 mg/mL (349.61 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	1.427 mL	7.1349 mL	14.2698 mL
5 mM	0.2854 mL	1.427 mL	2.854 mL
10 mM	0.1427 mL	0.7135 mL	1.427 mL
50 mM	0.0285 mL	0.1427 mL	0.2854 mL

Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

Reference

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