Temanogrel

Cat. No.: HY-10560

CAS No.: 887936-68-7

Molecular Formula: $C_{24}H_{28}N_4O_4$

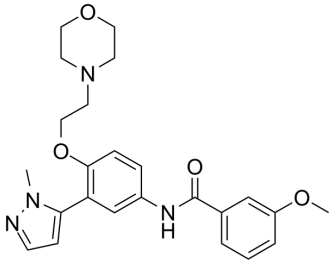
Molecular Weight: 436.5

Target: 5-HT Receptor

Pathway: GPCR/G Protein; Neuronal Signaling

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	6 months
	-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : 125 mg/mL (286.37 mM; Need ultrasonic)

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.2910 mL	11.4548 mL	22.9095 mL
	5 mM	0.4582 mL	2.2910 mL	4.5819 mL
	10 mM	0.2291 mL	1.1455 mL	2.2910 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: ≥ 6.25 mg/mL (14.32 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 6.25 mg/mL (14.32 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 6.25 mg/mL (14.32 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Temanogrel is a highly selective 5-HT_{2A} receptor antagonist with a K_i of 4.9 nM.

IC_{50} & Target

5-HT_{2A} Receptor
4.9 nM (Ki)

In Vitro

Temanogrel is a highly selective 5-HT_{2A} receptor antagonist with a K_i of 4.9 nM. Temanogrel inhibits inositol phosphate accumulation with an IC_{50} of 5.2 nM. Temanogrel exhibits potent inhibition of serotonin mediated amplification of ADP-

	stimulated human and dog platelet aggregation (IC_{50}=8.7 and 23.1 nM, respectively)[1]. Pretreatment of aortic rings with Temanogrel prevents the vasoconstriction caused by 20 μM 5-HT in a concentration-dependent manner. Preincubation with Temanogrel also significantly inhibits the 5-HT-stimulated DNA synthesis with an IC_{50} of 13±7 nM[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	There are no differences in heart rate or mean arterial pressure between saline-treated and Temanogrel-treated groups at any time during the experiment (that is, for mean arterial pressure, P=0.508 between groups, and P=0.540 for group-time interaction). In dogs assigned to receive Temanogrel, plasma Temanogrel levels show a rapid and sustained increase, averaging 25.5±4.1, 28.7±4.6 and 31.2±4.5 ng/mL, respectively, at 10 min, 1.25 h and 2.25 h after the start of treatment[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	To provide further insights into the effect of Temanogrel on platelet-dependent clot formation in models devoid of vascular smooth muscle, two in vitro post hoc experiments are performed. Paired aliquots of heparinized whole blood are incubated with Temanogrel (100 nM) or vehicle for 10 min at 37°C, and then placed in a thromboelastogram (TEG) pin-and-cup system with 10 μm serotonin, reptilase, and activated factor XIII (n=3 paired samples). The maximum amplitude of torsion is quantified for all samples. Aliquots of citrated blood (n=3 pairs) are incubated with Temanogrel (100 nM) or vehicle for 10 min at 37°C, and then pipetted into collagen-ADP cartridges. For each sample, the time (in seconds) required for the complete platelet-mediated thrombotic occlusion of the membrane aperture is recorded[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
Animal Administration [3]	Adult male beagle dogs (n=3) are used and receive a single oral gavage dose of Temanogrel at 10 mg/kg. Temanogrel is formulated in sterile water at 5 mL/kg. Animals are fasted before Temanogrel delivery. Serial sampling is used to obtain plasma concentration versus time profiles. Whole blood samples are collected via jugular vein venipuncture over a 24-h period. Plasma is prepared by centrifugation from sodium heparin-treated whole blood, frozen, and stored at approximately -20°C until bioanalytical analysis[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Xiong Y, et al. Discovery and structure-activity relationship of 3-methoxy-N-(3-(1-methyl-1H-pyrazol-5-yl)-4-(2-morpholinoethoxy)phenyl)benzamide (APD791): a highly selective 5-hydroxytryptamine2A receptor inverse agonist for the treatment of arterial thr

[2]. Przyklenk K, et al. Targeted inhibition of the serotonin 5HT2A receptor improves coronary patency in an in vivo model of recurrent thrombosis. J Thromb Haemost. 2010 Feb;8(2):331-40.

[3]. Adams JW, et al. APD791, 3-methoxy-n-(3-(1-methyl-1h-pyrazol-5-yl)-4-(2-morpholinoethoxy)phenyl)benzamide, a novel 5-hydroxytryptamine 2A receptor antagonist: pharmacological profile, pharmacokinetics, platelet activity and vascular biology. J Pharmacol E

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

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