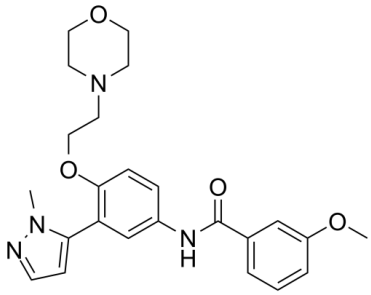
Data Sheet

Product Name:	Temanogrel
Cat. No.:	CS-0002653
CAS No.:	887936-68-7
Molecular Formula:	$C_{24}H_{28}N_4O_4$
Molecular Weight:	436.50
Target:	5-HT Receptor
Pathway:	GPCR/G Protein; Neuronal Signaling
Solubility:	DMSO : 125 mg/mL (286.37 mM; Need ultrasonic)



BIOLOGICAL ACTIVITY:

Temanogrel is a highly selective **5-HT$_{2A}$ receptor** antagonist with a **K$_i$** of 4.9 nM. IC50 & Target: Ki: 4.9 nM (5-HT$_{2A}$ receptor) **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]. **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].

PROTOCOL (Extracted from published papers and Only for reference)

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]. **Animal Administration:** Temanogrel is dissolved in water for in vivo study.[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].

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 thrombosis. J Med Chem. 2010 Jun 10;53(11):4412-21.

[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 Exp Ther. 2009 Oct;331(1):96-103.

CAIndexNames:

Benzamide, 3-methoxy-N-[3-(1-methyl-1H-pyrazol-5-yl)-4-[2-(4-morpholinyl)ethoxy]phenyl]-

SMILES:

CN1C(C2=C(OCCN3CCOCC3)C=CC(NC(C4=CC=CC(OC)=C4)=O)=C2)=CC=N1

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