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产品名称：IPSU
产品别名：IPSU

生物活性：

Description	IPSU is a selective, orally available and brain penetrant OX2R antagonist with a pKi of 7.85.
IC_{50} & Target	pKi: 7.85 (OX2R), 6.29 (OX1R)[1]
In Vitro	Orexin receptor antagonists represent attractive targets for the development of drugs for the treatment of insomnia. IPSU binds rapidly and reaches equilibrium very quickly in binding and/or functional assays[2].
In Vivo	IPSU has low blood clearance, shows high maximal blood exposure and AUC after oral dosing. It exhibits an acceptable absolute oral bioavailability and a brain/blood concentration ratio that indicated favorable brain penetration. IPSU increases sleep when dosed during the mouse active phase (lights off); IPSU induces sleep primarily by increasing NREM sleep. IPSU shows a fast onset of action, with a clear increase in total sleep time during the first hour afterdosing. The effect lasts 4-5 h, after which time the total sleep time per hour is the same as on vehicle day [1].
Solvent&Solubility	***In Vitro:*** **DMSO : ≥ 30 mg/mL (73.98 mM)** * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent / Mass / Concentration	1 mg	5 mg	10 mg
	1 mM	2.4662 mL	12.3308 mL	24.6615 mL
	5 mM	0.4932 mL	2.4662 mL	4.9323 mL
	10 mM	0.2466 mL	1.2331 mL	2.4662 mL

*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液；一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。

储备液的保存方式和期限：-80°C, 6 months; -20°C, 1 month。-80°C 储存时，请在 6 个月内使用，-20°C 储存时，请在 1 个月内使用。

References	[1]. Betschart C, et al. Identification of a novel series of orexin receptor antagonists with a distinct effect on sleeparchitecture for the treatment of insomnia. J Med Chem. 2013 Oct 10;56(19):7590-607. [2]. Callander GE, et al. Kinetic properties of "dual" orexin receptor antagonists at OX1R and OX2R orexin receptors. Front Neurosci. 2013 Dec 3;7:230. [3]. Hoyer D, et al. Distinct effects of IPSU and suvorexant on mouse sleep architecture.

实验参考：

Animal Administration	Mice: Freely moving C57Bl/6 mice with chronically implanted electrodes are well abituated to the experiment boxes and had access to food and ater ad libitum. The test compounds (IPSU) or vehicle are administered per os as a suspension in 0.5% methylcellulose immediately prior to lights off and start of recording. Movement is recorded using infrared sensors in the roof of the box. EEG/EMG signals and motility data are used to score 10 s epochs into wake, NREM sleep, and REM sleep. Each animal served as its own control by application and recording of vehicle the day before compound (IPSU) dosing[1].

Kinase Assay	Competition experiments are performed with a single concentration of radioligand and six concentrations of competitor (unlabeled ligands; BBAC, almorexant, SB-649868, suvorexant, filorexant or IPSU). 4.6 nM [^{3}H]-BBAC is added simultaneously with various concentrations of unlabeled ligand (0.1 nM-10 μM) to membranes (150 μL/well) in 50 μL/well of assay buffer with a total volume of 250 μL/well. The amount of [^{3}H]-BBAC bound to receptors is determined at room temperature at different time points (ranging from 15 min to 4 h) and terminated by rapid vacuum filtration and liquid scintillation counting[2].
References	[1]. Betschart C, et al. Identification of a novel series of orexin receptor antagonists with a distinct effect on sleeparchitecture for the treatment of insomnia. J Med Chem. 2013 Oct 10;56(19):7590-607. [2]. Callander GE, et al. Kinetic properties of "dual" orexin receptor antagonists at OX1R and OX2R orexin receptors. Front Neurosci. 2013 Dec 3;7:230. [3]. Hoyer D, et al. Distinct effects of IPSU and suvorexant on mouse sleep architecture.