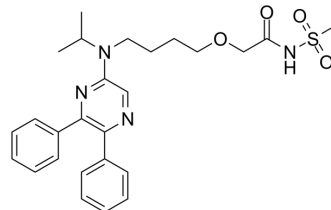


## Selexipag

<b>Cat. No.:</b>	HY-14870		
<b>CAS No.:</b>	475086-01-2		
<b>Molecular Formula:</b>	C <sub>26</sub> H <sub>32</sub> N <sub>4</sub> O <sub>4</sub> S		
<b>Molecular Weight:</b>	496.62		
<b>Target:</b>	Prostaglandin Receptor		
<b>Pathway:</b>	GPCR/G Protein		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

#### In Vitro

DMSO : ≥ 50 mg/mL (100.68 mM)  
 \* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	2.0136 mL	10.0681 mL	20.1361 mL
	5 mM	0.4027 mL	2.0136 mL	4.0272 mL
	10 mM	0.2014 mL	1.0068 mL	2.0136 mL

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

#### In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline  
 Solubility: ≥ 2.5 mg/mL (5.03 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)  
 Solubility: 2.5 mg/mL (5.03 mM); Suspended solution; Need ultrasonic
- Add each solvent one by one: 10% DMSO >> 90% corn oil  
 Solubility: ≥ 2.5 mg/mL (5.03 mM); Clear solution

### BIOLOGICAL ACTIVITY

#### Description

Selexipag (NS-304) is an orally available and potent agonist for the Prostacyclin (PGI<sub>2</sub>) receptor (IP receptor).

#### IC<sub>50</sub> & Target

IP Receptor

#### In Vitro

Selexipag (NS-304) is an orally available and long-acting IP receptor agonist prodrug, and its active form, MRE-269, is highly selective for the IP receptor. Selexipag (NS-304) inhibits the binding of [<sup>3</sup>H]Iloprost to the human and rat IP receptors in a

concentration-dependent manner. The  $K_i$  is 260 nM for the human IP receptor and 2100 nM for the rat IP receptor. The intracellular cAMP levels in hIP-CHO cells are increased in a concentration-dependent manner by treatment with Selexipag (NS-304) with  $EC_{50}$  of 177 nM. Selexipag (NS-304) also inhibits platelet aggregation in humans and monkeys with  $IC_{50}$  values of 5.5 and 3.4  $\mu$ M, respectively, but it shows no inhibition in dogs ( $IC_{50}$  of  $>100 \mu$ M)<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

The  $C_{max}$  of MRE-269 after oral administration of NS-304 is 1.1  $\mu$ g/mL in rats and 9.0  $\mu$ g/mL in dogs. Selexipag (NS-304) at 1 or 3 mg/kg increases FSBF in anesthetized rats for more than 4 h after intraduodenal administration in a dose-dependent manner. In particular, Selexipag (NS-304) at 3 mg/kg causes a sustained increase in FSBF and exhibits a maximal increase of 93% in FSBF 1 h after administration<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## PROTOCOL

#### Cell Assay <sup>[1]</sup>

CHO cells expressing the human IP receptor (hIP-CHO cells) are seeded at  $1 \times 10^5$  cells/well in a 24-well plate and cultured for 48 h. The cells are washed with Dulbecco's phosphate-buffered saline without divalent cations, preincubated in the medium for 1 h at 37°C, and then incubated for 15 min at 37°C with medium containing each drug in the presence of 500  $\mu$ M 3-isobutyl-1-methylxanthine. The medium is removed, and perchloric acid solution is added to terminate the reaction. Intracellular cAMP levels are measured by enzymelinked immunosorbent assay<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### Animal Administration <sup>[1]</sup>

Mice<sup>[1]</sup>  
Male Sprague-Dawley rats, cynomolgus monkeys, and male beagle dogs are used. Selexipag (NS-304) is orally administered to rats at 10 mg/kg and to dogs at 3 mg/kg, and blood samples are collected at various times and centrifuged to obtain plasma. The plasma concentrations of Selexipag (NS-304) and MRE-269 after oral administration of Selexipag (NS-304) to each animal are determined by high performance liquid chromatography coupled to mass spectrometry (LC/MS), and their pharmacokinetic parameters are calculated. Rats are orally administered Selexipag (NS-304) at 3 mg/kg twice daily for 1, 2, 3, or 4 weeks as a pretreatment. On the day after the final administration in the pretreatment, rats are anesthetized with urethane, and the FSBF is measured with a laser Doppler flowmeter after intraduodenal administration of Selexipag (NS-304) at 3 mg/kg<sup>[1]</sup>. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## CUSTOMER VALIDATION

- Am J Physiol Lung Cell Mol Physiol. 2018 Aug 1;315(2):L276-L285.
- Erasmus Universiteit Rotterdam. 2017, November 30.

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## REFERENCES

- [1]. Kuwano K, et al. 2-[4-[(5,6-diphenylpyrazin-2-yl)(isopropyl)amino]butoxy]-N-(methylsulfonyl)acetamide (NS-304), an orally available and long-acting prostacyclin receptor agonist prodrug. J Pharmacol Exp Ther. 2007 Sep;322(3):1181-8.
- [2]. Mous DS, et al. Treatment of rat congenital diaphragmatic hernia with sildenafil and NS-304, selexipag's active compound, at the pseudoglandular stage improves lung vasculature. Am J Physiol Lung Cell Mol Physiol. 2018 May 10.

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

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