# Selexipag

**Cat. No.:** HY-14870

**CAS No.:** 475086-01-2

**Molecular Formula:** $C_{26}H_{32}N_4O_4S$

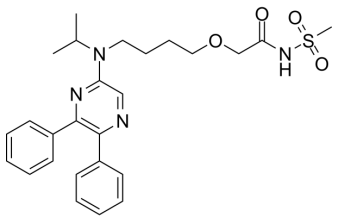
**Molecular Weight:** 496.62

**Target:** Prostaglandin Receptor

**Pathway:** GPCR/G Protein

**Storage:**

| | | |
|---|---|---|
| Powder | -20°C | 3 years |
| | 4°C | 2 years |
| In solvent | -80°C | 2 years |
| | -20°C | 1 year |



## SOLVENT & SOLUBILITY

**In Vitro**

DMSO : ≥ 50 mg/mL (100.68 mM)

* "≥" means soluble, but saturation unknown.

**Preparing Stock Solutions**

| Solvent / Mass / Concentration | 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**

1. 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
2. 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
3. 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 ($PGI_2$) receptor (IP receptor).

**$IC_{50}$ & Target**

hIP
260 nM (Ki)

**In Vitro**

Selexipag (NS-304) is an orally available and long-acting IP receptor agonist prodrug, and its active form, MRE-269, is highly

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|---|---|
| | selective for the IP receptor. Selexipag (NS-304) inhibits the binding of [$^3$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 177nM. Selexipag (NS-304) also inhibits platelet aggregation in humans and monkeys with $IC_{50}$ values of 5.5 and 3.4 μM, respectively, but it shows no inhibition in dogs ($IC_{50}$ of >100 μM)[1].<br>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 μg/mL in rats and 9.0 μg/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[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |

## PROTOCOL

| | |
|---|---|
| **Cell Assay** [1] | CHO cells expressing the human IP receptor (hIP-CHO cells) are seeded at $1\times10^5$ 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 μM 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[1].<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only. |
| **Animal Administration** [1] | Mice[1]<br>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[1].<br>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.

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

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