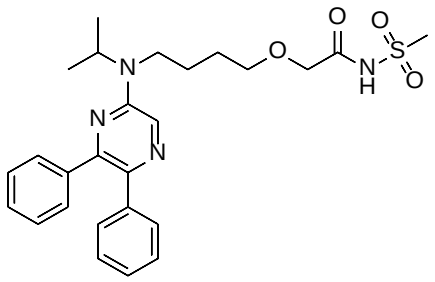
Product data sheet

MedKoo Cat#: 317125 Name: Selexipag CAS#: 475086-01-2 Chemical Formula: $C_{26}H_{32}N_4O_4S$ Exact Mass: 496.2144 Molecular Weight: 496.62	
Product supplied as:	Powder
Purity (by HPLC):	≥ 98%
Shipping conditions	Ambient temperature
Storage conditions:	Powder: -20°C 3 years; 4°C 2 years.
	In solvent: -80°C 3 months; -20°C 2 weeks.

1. Product description:
Selexipag, also known as ACT-293987 and NS-304, is a a first-in-class orally available selective non-prostanoid IP receptor agonist, which is currently in development by Actelion as a treatment of pulmonary arterial hypertension. Selexipag and its active metabolite, ACT-333679, are agonists at the prostacyclin receptor, which leads to vasodilation in the pulmonary circulation.

2. CoA, QC data, SDS, and handling instruction
SDS and handling instruction, CoA with copies of QC data (NMR, HPLC and MS analytical spectra) can be downloaded from the product web page under "QC And Documents" section. Note: copies of analytical spectra may not be available if the product is being supplied by MedKoo partners. Whether the product was made by MedKoo or provided by its partners, the quality is 100% guaranteed.

3. Solubility data

Solvent	Max Conc. mg/mL	Max Conc. mM
DMSO	57.17	115.12
Ethanol	34.50	69.47
DMF	30.0	60.41
PBS (pH 7.2)	1.0	2.01

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.01 mL	10.07 mL	20.14 mL
5 mM	0.40 mL	2.01 mL	4.03 mL
10 mM	0.20 mL	1.01 mL	2.01 mL
50 mM	0.04 mL	0.20 mL	0.40 mL

5. Molarity Calculator, Reconstitution Calculator, Dilution Calculator
Please refer the product web page under section of "Calculator"

6. Recommended literature which reported protocols for in vitro and in vivo study
In vitro study

1. Gatfield J, Menyhart K, Wanner D, Gnerre C, Monnier L, Morrison K, Hess P, Iglarz M, Clozel M, Nayler O. Selexipag Active Metabolite ACT-333679 Displays Strong Anticontractile and Antiremodeling Effects but Low β-Arrestin Recruitment and Desensitization Potential. J Pharmacol Exp Ther. 2017 Jul;362(1):186-199. doi: 10.1124/jpet.116.239665. Epub 2017 May 5. PMID: 28476928.

In vivo study

1. Kuwano K, Kosugi K, Fuchikami C, Funaki S. [Pharmacological characteristics and clinical study results of Selexipag (Uptravi® tablets), a selective prostacyclin receptor agonist]. Nihon Yakurigaku Zasshi. 2021;156(3):178-186. Japanese. doi: 10.1254/fpj.20092. PMID: 33952848.

7. Bioactivity
Biological target: Selexipag (NS-304) is an agonist for the Prostacyclin (PGI2) receptor (IP receptor) with Ki of 260 nM.

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In vitro activity

Prostacyclin (PGI2) receptor (IP receptor) agonists, which are indicated for the treatment of pulmonary arterial hypertension (PAH), increase cytosolic cAMP levels and thereby inhibit pulmonary vasoconstriction, pulmonary arterial smooth muscle cell (PASMC) proliferation, and extracellular matrix synthesis. Selexipag is an IP receptor agonist. The active metabolite of selexipag, ACT-333679, behaved as a full agonist in multiple PAH-relevant receptor-distal-or downstream-cellular assays with a maximal efficacy (Emax) comparable to that of the prototypic PGI2 analog iloprost. In PASMC, ACT-333679 potently induced cellular relaxation (EC50 4.3 nM) and inhibited cell proliferation (IC50 4.0 nM) as well as extracellular matrix synthesis (IC50 8.3 nM). In contrast, ACT-333679 displayed partial agonism in receptor-proximal-or upstream-cAMP accumulation assays (Emax 56%) when compared with iloprost and the PGI2 analogs beraprost and treprostinil (Emax ~100%). Partial agonism of ACT-333679 also resulted in limited β-arrestin recruitment (Emax 40%) and lack of sustained IP receptor internalization, whereas all tested PGI2 analogs behaved as full agonists in these desensitization-related assays.

Reference: J Pharmacol Exp Ther. 2017 Jul;362(1):186-199. https://jpet.aspetjournals.org/content/362/1/186.long

In vivo activity

Selexipag is a novel prostacyclin receptor (IP receptor) agonist approved for the treatment of pulmonary arterial hypertension (PAH). Selexipag is converted to MRE-269 in vivo, and the plasma concentration of MRE-269 is maintained at a therapeutic level for a long time. MRE-269 has selective IP receptor agonist activity and exerts vasodilatory and anti-proliferative effects on pulmonary arterial smooth muscle cells. In a Sugen 5416/hypoxia rat model of PAH, selexipag significantly improved pulmonary artery obstruction, decreased right ventricular systolic pressure, decreased right ventricular hypertrophy and improved survival rate.

Reference: Nihon Yakurigaku Zasshi. 2021;156(3):178-186. https://www.jstage.jst.go.jp/article/fpj/156/3/156_20092/_article/-char/ja/