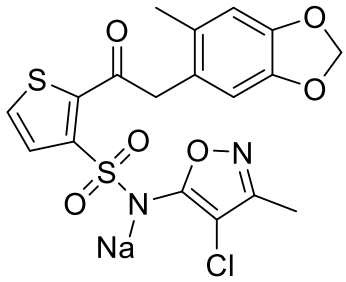
Product data sheet

MedKoo Cat#: 317137 Name: Sitaxentan sodium CAS#: 210421-74-2 (sodium salt) Chemical Formula: $C_{18}H_{14}ClN_2NaO_6S_2$ Molecular Weight: 476.88	
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:

Sitaxentan, also known as TBC-11251 and IPI 1040, is a medication for the treatment of pulmonary arterial hypertension (PAH). It was marketed as Thelin. In 2010, Pfizer voluntarily removed sitaxentan from the market due to concerns about liver toxicity. Sitaxentan is a small molecule that blocks the action of endothelin (ET) on the endothelin-A (ETA) receptor selectively (by a factor of 6000 compared with the ETB).

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
DMF	10	20.97
DMSO	15	31.45
Ethanol	5	10.48

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.10 mL	10.48 mL	20.97 mL
5 mM	0.42 mL	2.10 mL	4.19 mL
10 mM	0.21 mL	1.05 mL	2.10 mL
50 mM	0.04 mL	0.21 mL	0.42 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. Burbank MG, Sharanek A, Burban A, Mialanne H, Aerts H, Guguen-Guillouzo C, Weaver RJ, Guillouzo A. From the Cover: MechanisticInsights in Cytotoxic and Cholestatic Potential of the Endothelial Receptor Antagonists Using HepaRG Cells. Toxicol Sci. 2017 Jun 1;157(2):451-464. doi: 10.1093/toxsci/kfx062. PMID: 28369585.
2. Erve JC, Gauby S, Maynard JW Jr, Svensson MA, Tonn G, Quinn KP. Bioactivation of sitaxentan in liver microsomes, hepatocytes, and expressed human P450s with characterization of the glutathione conjugate by liquid chromatography tandem mass spectrometry. Chem Res Toxicol. 2013 Jun 17;26(6):926-36. doi: 10.1021/tx4001144. Epub 2013 May 30. PMID: 23721565.

In vivo study

1. Duthie KM, Hadoke PW, Kirkby NS, Miller E, Ivy JR, McShane JF, Lim WG, Webb DJ. Selective endothelin A receptor antagonism with sitaxentan reduces neointimal lesion size in a mouse model of intraluminal injury. Br J Pharmacol. 2015 Jun;172(11):2827-37. doi: 10.1111/bph.13086. Epub 2015 Apr 23. PMID: 25598351; PMCID: PMC4439878.

2. Cross DM, Horsley E, Derzi M, Owen K, Stavros FL. An evaluation of reproductive and developmental toxicity of sitaxentan (thelin) in rats. Birth Defects Res B Dev Reprod Toxicol. 2012 Oct;95(5):327-36. doi: 10.1002/bdrb.21021. Epub 2012 Aug 13. PMID: 22890981.

7. Bioactivity

Biological target:

Sitaxentan is a potent nonpeptide ETA receptor antagonist (IC50 = 1.4 nM). It is selective for ETA over ETB receptors (IC50 = 9,800 nM).

In vitro activity

The study provides insights into sitaxentan's hepatotoxicity, rationalizing its withdrawal from the market in 2010. Sitaxentan formed a reactive ortho-quinone metabolite, detected in vitro using liver microsomes and hepatocytes from various species. Human liver microsomes showed time-dependent inhibition of P450 3A4. The quinone metabolite reacted with glutathione, forming a conjugate. Computational modeling suggested that the 2-position on the phenyl ring is the likely site of glutathione conjugation.

Reference: Chem Res Toxicol. 2013 Jun 17;26(6):926-36. https://pubmed.ncbi.nlm.nih.gov/23721565/

In vivo activity

Sitaxentan reduces neointimal lesion formation. Sitaxentan produced a selective, concentration-dependent parallel rightward shift of ET-1-mediated contraction in isolated femoral arteries from adult, male C57Bl6 mice. Sitaxentan reduced neointimal lesion size, whereas ETB and combined ETA / B receptor antagonism did not. Macrophage and α-smooth muscle actin content were unaltered by ET receptor antagonism but sitaxentan reduced the amount of collagen in lesions.

Reference: Br J Pharmacol. 2015 Jun;172(11):2827-37. https://pubmed.ncbi.nlm.nih.gov/25598351/

Note: The information listed here was extracted from literature. MedKoo has not independently retested and confirmed the accuracy of these methods. Customer should use it just for a reference only.