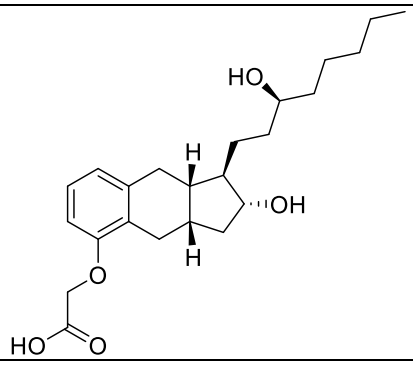
Product data sheet

MedKoo Cat#: 318899 Name: Treprostinil free acid CAS#: 81846-19-7 (free acid) Chemical Formula: $C_{23}H_{34}O_5$ Exact Mass: 390.2406 Molecular Weight: 390.52	
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:
Treprostinil is a vasodilator that is used for the treatment of pulmonary arterial hypertension. Treprostinil is a synthetic analog of prostacyclin (PGI2). The inhaled form of treprostinil was approved by the FDA in July 2009 and is marketed as the trade name Tyvaso.

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	125.0	320.09

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	2.56 mL	12.80 mL	25.61 mL
5 mM	0.51 mL	2.56 mL	5.12 mL
10 mM	0.26 mL	1.28 mL	2.56 mL
50 mM	0.05 mL	0.26 mL	0.51 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. Themanns M, Koban F, Bergmayr C, Chrzan A, Strohmaier W, Haybaeck J, Freissmuth M, Zebedin-Brandl E. Treprostinil reduces endothelial damage in murine sinusoidal obstruction syndrome. J Mol Med (Berl). 2019 Feb;97(2):201-213. doi: 10.1007/s00109-018-1726-6. Epub 2018 Dec 7. PMID: 30535954; PMCID: PMC6348071.
2. Lambers C, Roth M, Jaksch P, Muraközy G, Tamm M, Klepetko W, Ghanim B, Zhao F. Treprostinil inhibits proliferation and extracellular matrix deposition by fibroblasts through cAMP activation. Sci Rep. 2018 Jan 18;8(1):1087. doi: 10.1038/s41598-018-19294-1. PMID: 29348469; PMCID: PMC5773699.

In vivo study

1. Nikam VS, Schermuly RT, Dumitrascu R, Weissmann N, Kwapiszewska G, Morrell N, Klepetko W, Fink L, Seeger W, Voswinckel R. Treprostinil inhibits the recruitment of bone marrow-derived circulating fibrocytes in chronic hypoxic pulmonary hypertension. Eur Respir J. 2010 Dec;36(6):1302-14. doi: 10.1183/09031936.00028009. Epub 2010 Jun 4. PMID: 20525716.
2. Wang L, Halliday G, Huot JR, Satoh T, Baust JJ, Fisher A, Cook T, Hu J, Avolio T, Goncharov DA, Bai Y, Vanderpool RR, Considine RV, Bonetto A, Tan J, Bachman TN, Sebastiani A, McTiernan CF, Mora AL, Machado RF, Goncharova EA, Gladwin MT, Lai YC. Treatment With Treprostinil and Metformin Normalizes Hyperglycemia and Improves Cardiac Function in Pulmonary Hypertension Associated With Heart Failure With Preserved Ejection Fraction. Arterioscler Thromb Vasc Biol. 2020 Jun;40(6):1543-1558. doi: 10.1161/ATVBAHA.119.313883. Epub 2020 Apr 9. PMID: 32268788; PMCID: PMC7255946.

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7. Bioactivity

Biological target:

Treprostinil (LRX-15) is a potent DP1 and EP2 agonist with EC50 values of 0.6±0.1 and 6.2±1.2 nM, respectively.

In vitro activity

The effect of Treprostinil on TGF-ß1 and PDGF-induced fibroblast proliferation and ECM deposition was investigated. Human peripheral lung fibroblasts of seven IPF patients and five lung donors were stimulated by PDGF, or TGF-β1, or the combination. Cells were pre-incubated (30 min) with either Treprostinil, forskolin, di-deoxyadenosine (DDA), or vehicle. Treprostinil time dependently activated cAMP thereby preventing PDGF-BB induced proliferation and TGF-β1 secretion. Cell counts indicated proliferation; α-smooth muscle actin (α-SMA) indicted differentiation, and collagen type-1 or fibronectin deposition remodeling. Myo-fibroblast indicating α-SMA expression was significantly reduced and its formation was altered by Treprostinil. Collagen type-I and fibronectin deposition were also reduced by Treprostinil. The effect of Treprostinil on collagen type-I deposition was cAMP sensitive as it was counteracted by DDA, while the effect on fibronectin was not cAMP mediated. Treprostinil antagonized the pro-fibrotic effects of both PDGF-BB and TGF-β1 in primary human lung fibroblasts. The data presented propose a therapeutic relevant anti-fibrotic effect of Treprostinil in IPF (idiopathic pulmonary fibrosis).

Reference: Sci Rep. 2018 Jan 18;8(1):1087. https://pubmed.ncbi.nlm.nih.gov/29348469/

In vivo activity

To evaluate the preventative effect of treprostinil on metabolic syndrome-associated PH-HFpEF, treprostinil (40 ng/kg/min, the effective dose for PAH therapy with similar average infusion rate achieved in clinical trials, on a ng/m2 basis) was given through osmotic minipumps for 16 weeks in mice fed with a HFD (Figure 1A), which has been shown to induce PH and/or HFpEF phenotype in mice. Consistent with previous studies, HFD-exposed mice had significantly higher body weights, hyperglycemia and glucose intolerance when compared to RD-treated mice (Figure 1B through 1D). Additionally, HFD-exposed mice developed mild PH and/or HFpEF phenotype as evidenced by elevated right ventricular systolic pressure (RVSP), higher left ventricular end diastolic pressure (LVEDP), preserved left ventricular ejection fraction (LVEF) and both LV and RV hypertrophy (Figure 1E through 1I). In contrast, chronic treprostinil treatment significantly lowered HbA1c levels and improved glucose intolerance independent of changes in body weight (Figure 1B through 1D). Furthermore, a tendency for treprostinil to lower pulmonary pressures was observed in HFD-exposed mice (P = 0.058; Figure 1E), although treprostinil caused no significant differences in LVEDP and biventricular hypertrophy (Figure 1F,1H and 1I). Collectively, these data demonstrate that chronic treprostinil treatment improves glucose metabolism and lowers pulmonary hypertension in a mild mouse model of PH-HFpEF induced by HFD.

Reference: Arterioscler Thromb Vasc Biol. 2020 Jun;40(6):1543-1558. https://pubmed.ncbi.nlm.nih.gov/32268788/