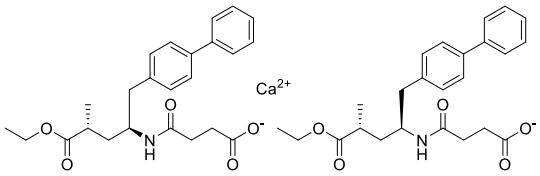
Product data sheet

MedKoo Cat#: 314262 Name: Sacubitril calcium salt CAS#: 1369773-39-6 (hemi-calcium) Chemical Formula: $C_{48}H_{56}CaN_2O_{10}$ Molecular Weight: 861.06	
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:

Sacubitril, also known as AHU377, is angiotensin receptor neprilysin inhibitor being studied for use in combination with valsartan for heart failure. Sacubitril is a prodrug that is activated to LBQ657 by de-ethylation via esterases. LBQ657 inhibits the enzyme neprilysin, which is responsible for the degradation of atrial and brain natriuretic peptide, two blood pressure lowering peptides that work mainly by reducing blood volume.

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	72.01	83.63
DMSO:PBS (pH 7.2) (1:3)	0.25	0.29
DMF	20.0	23.23
Ethanol	6.81	7.91

4. Stock solution preparation table:

Concentration / Solvent Volume / Mass	1 mg	5 mg	10 mg
1 mM	1.16 mL	5.81 mL	11.61 mL
5 mM	0.23 mL	1.16 mL	2.32 mL
10 mM	0.12 mL	0.58 mL	1.16 mL
50 mM	0.02 mL	0.12 mL	0.23 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. Burke RM, Lighthouse JK, Mickelsen DM, Small EM. Sacubitril/Valsartan Decreases Cardiac Fibrosis in Left Ventricle Pressure Overload by Restoring PKG Signaling in Cardiac Fibroblasts. Circ Heart Fail. 2019 Apr;12(4):e005565. doi: 10.1161/CIRCHEARTFAILURE.118.005565. PMID: 30998392; PMCID: PMC6530564.
2. Shi J, Wang X, Nguyen J, Wu AH, Bleske BE, Zhu HJ. Sacubitril Is Selectively Activated by Carboxylesterase 1 (CES1) in the Liver and the Activation Is Affected by CES1 Genetic Variation. Drug Metab Dispos. 2016 Apr;44(4):554-9. doi: 10.1124/dmd.115.068536. Epub 2016 Jan 27. PMID: 26817948; PMCID: PMC4810765.

In vivo study

1. Ushijima K, Ando H, Arakawa Y, Aizawa K, Suzuki C, Shimada K, Tsuruoka SI, Fujimura A. Prevention against renal damage in rats with subtotal nephrectomy by sacubitril/valsartan (LCZ696), a dual-acting angiotensin receptor-neprilysin inhibitor. Pharmacol Res Perspect. 2017 Aug;5(4):e00336. doi: 10.1002/prp2.336. PMID: 28805977; PMCID: PMC5684857.

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2. Seki T, Goto K, Kansui Y, Ohtsubo T, Matsumura K, Kitazono T. Angiotensin II Receptor-Neprilysin Inhibitor Sacubitril/Valsartan Improves Endothelial Dysfunction in Spontaneously Hypertensive Rats. J Am Heart Assoc. 2017 Oct 17;6(10):e006617. doi: 10.1161/JAHA.117.006617. PMID: 29042424; PMCID: PMC5721864.

7. Bioactivity

Biological target:

Sacubitril hemicalcium salt (AHU-377 hemicalcium salt) is a potent NEP inhibitor with an IC50 of 5 nM.

In vitro activity

In vitro incubation studies revealed that sacubitril is hydrolyzed by the liver, but not by the intestines, kidneys, or plasma, indicating that sacubitril is selectively activated by hepatic CES1. This conclusion is further supported by the observations that sacubitril was efficiently activated by purified recombinant CES1, but not CES2.

Reference: Drug Metab Dispos. 2016 Apr;44(4):554-9. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4810765/

In vivo activity

LCZ696 (sacubitril/valsartan) and valsartan dose dependently prolonged the survival of these animals, and the effect of LCZ696-(30 mg/kg) was significantly greater than that of valsartan-(15 mg/kg). In this study, LCZ696 and valsartan dose dependently reduced urinary protein excretion in rats with subtotal nephrectomy, and the effect of LCZ696-(30 mg/kg) was significantly greater than that of valsartan-(15 mg/kg). In addition, compared to the vehicle group, glomerular sclerosis was significantly alleviated in the LCZ696-(30 mg/kg), but not the valsartan-(15 mg/kg) groups at 8 weeks in Experiment 2.

Reference: Pharmacol Res Perspect. 2017 Aug; 5(4): e00336. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5684857/

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.