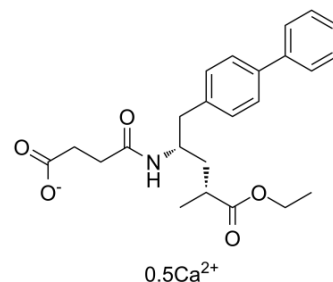


## Sacubitril hemicalcium salt

<b>Cat. No.:</b>	HY-15407A		
<b>CAS No.:</b>	1369773-39-6		
<b>Molecular Formula:</b>	C <sub>24</sub> H <sub>28</sub> Ca <sub>0.5</sub> NO <sub>5</sub>		
<b>Molecular Weight:</b>	430.52		
<b>Target:</b>	Neprilysin		
<b>Pathway:</b>	Metabolic Enzyme/Protease		
<b>Storage:</b>	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



### SOLVENT & SOLUBILITY

<b>In Vitro</b>	DMSO : 125 mg/mL (290.35 mM; Need ultrasonic)				
		Solvent Concentration	Mass 1 mg	5 mg	10 mg
	<b>Preparing Stock Solutions</b>	1 mM	2.3228 mL	11.6139 mL	23.2277 mL
		5 mM	0.4646 mL	2.3228 mL	4.6455 mL
10 mM		0.2323 mL	1.1614 mL	2.3228 mL	
Please refer to the solubility information to select the appropriate solvent.					
<b>In Vivo</b>	<ol style="list-style-type: none"> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 40% PEG300 &gt;&gt; 5% Tween-80 &gt;&gt; 45% saline Solubility: ≥ 6.25 mg/mL (14.52 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% (20% SBE-β-CD in saline) Solubility: ≥ 6.25 mg/mL (14.52 mM); Clear solution</li> <li>Add each solvent one by one: 10% DMSO &gt;&gt; 90% corn oil Solubility: ≥ 6.25 mg/mL (14.52 mM); Clear solution</li> </ol>				

### BIOLOGICAL ACTIVITY

<b>Description</b>	Sacubitril hemicalcium salt (AHU-377 hemicalcium salt) is a potent NEP inhibitor with an IC <sub>50</sub> of 5 nM. Sacubitril hemicalcium salt is a component of the heart failure medicine LCZ696.
<b>IC<sub>50</sub> &amp; Target</b>	IC <sub>50</sub> : 5 nM (NEP) <sup>[1]</sup>
<b>In Vitro</b>	Sacubitril (AHU-377) is a single molecule that is comprised of molecular moieties of valsartan, an ARB, and Sacubitril hemicalcium salt, a neprilysin inhibitor (1:1 ratio). Sacubitril (AHU-377) is converted by enzymatic cleavage of the ethyl ester

into the active neprilysin inhibiting metabolite LBQ657<sup>[2]</sup>. The inactive NEPI precursor, Sacubitril hemicalcium salt, does not inhibit collagen accumulation in fibroblasts nor cardiac myocyte hypertrophy. In cardiac fibroblasts, the active NEPI LBQ657 had no discernible effects. In contrast, LBQ657 modestly inhibits cardiac myocyte hypertrophy<sup>[3]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

#### In Vivo

In humans, Sacubitril (AHU-377)( $t_{max}$  0.5-1.1 h) are absorbed quickly. Sacubitril hemicalcium salt is converted rapidly into LBQ657 with its  $t_{max}$  being reached in 1.9-3.5 h. Mean  $t_{1/2}$  values for the biologically active LBQ657 is 9.9-11.1 h<sup>[2]</sup>. In vehicle-treated dogs, ANF increases urinary sodium excretion from  $17.3 \pm 3.6$  to  $199.5 \pm 18.4$   $\mu\text{equiv/kg/min}$ . This effect is potentiated significantly in animals which receive Sacubitril (AHU-377). Urinary volume is also potentiated in animals which receive an iv administration of Sacubitril (AHU-377)<sup>[1]</sup>.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

## REFERENCES

[1]. Ksander GM, et al. Dicarboxylic acid dipeptide neutral endopeptidase inhibitors. J Med Chem. 1995 May 12;38(10):1689-700.

[2]. Voors AA, et al. The potential role of valsartan + AHU377 ( LCZ696 ) in the treatment of heart failure. Expert Opin Investig Drugs. 2013 Aug;22(8):1041-7.

[3]. von Lueder TG, et al. Angiotensin receptor neprilysin inhibitor LCZ696 attenuates cardiac remodeling and dysfunction after myocardial infarction by reducing cardiac fibrosis and hypertrophy. Circ Heart Fail. 2015 Jan;8(1):71-8.

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

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