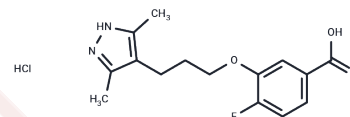


## Acoramidis hydrochloride

## Chemical Properties

CAS No. :	2242751-53-5
Formula:	C <sub>15</sub> H <sub>18</sub> ClFN <sub>2</sub> O <sub>3</sub>
Molecular Weight:	328.77
Storage:	Powder: -20°C for 3 years   In solvent: -80°C for 1 year Actual storage temperature shall be subject to the COA.



## Biological Description

Description	Acoramidis hydrochloride (Alxn2060 hydrochloride) is an orally active and selective kinetic stabilizer of WT and V122I- TTR (transthyretin) . Acoramidis hydrochloride is used in the study for transthyretin amyloidosis.
Targets(IC50)	Others
In vitro	Acoramidis (AG10, 0.1-10 $\mu$ M for TTR $\sim$ 5 $\mu$ M) stabilizes V122I- and WT-TTR effectively, outperforming their efficacy in whole serum [1]. Acoramidis (AG10) stimulates mitochondrial QO2 concentration-dependently between 10 and 100 $\mu$ M [3]. It exhibits minimal inhibition of the potassium ion channel hERG (IC <sub>50</sub> > 100 $\mu$ M) and several cytochrome P450 isozymes (IC <sub>50</sub> > 50 $\mu$ M) [low toxicity] [1]. Western Blot Analysis [1], using human serum (TTR $\sim$ 5 $\mu$ M), at concentrations of 0.1 and 10 $\mu$ M, with a 72-hour incubation, shows AG10 is significantly more effective than tafamidis in stabilizing TTR, with 10 $\mu$ M stabilizing almost all TTR in serum.
In vivo	Animal Model: Wistar rats [1] . Dosage: 50 mg/kg/d (Toxicity Analysis). Administration: Oral gavage, daily for 28 d. Result: Showed the plasma C max of $\sim$ 40 $\mu$ M and histopathological evaluation of liver, kidney, heart, spleen, thymus, and lung showed no signs of pathologic processes in the Acoramidis-treated animals

## Solubility Information

Solubility	DMSO: 60 mg/mL (182.5 mM),Sonication is recommended. (< 1 mg/ml refers to the product slightly soluble or insoluble)
In vivo Formulation	10% DMSO+40% PEG300+5% Tween 80+45% Saline: 2 mg/mL (6.08 mM),Sonication is recommended. <i>Please add the solvents sequentially, clarifying the solution as much as possible before adding the next one. Dissolve by heating and/or sonication if necessary. Working solution is recommended to be prepared and used immediately. The formulation provided above is for reference purposes only. In vivo formulations may vary and should be modified based on specific experimental conditions.</i>

### Preparing Stock Solutions

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	1mg	5mg	10mg
1 mM	3.0416 mL	15.2082 mL	30.4164 mL
5 mM	0.6083 mL	3.0416 mL	6.0833 mL
10 mM	0.3042 mL	1.5208 mL	3.0416 mL
50 mM	0.0608 mL	0.3042 mL	0.6083 mL

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Please select the appropriate solvent to prepare the stock solution, according to the solubility of the product in different solvents. Please use it as soon as possible.

Note: The dilution table applies only to solid products. For liquid products, please calculate the stock solution based on the stated concentration and/or density.

### Reference

- Sravan C Penchala, et al. AG10 inhibits amyloidogenesis and cellular toxicity of the familial amyloid cardiomyopathy-associated V122I transthyretin. *Proc Natl Acad Sci U S A*. 2013 Jun 11;110(24):9992-7.
- Jonathan C Fox, et al. First-in-Human Study of AG10, a Novel, Oral, Specific, Selective, and Potent Transthyretin Stabilizer for the Treatment of Transthyretin Amyloidosis: A Phase 1 Safety, Tolerability, Pharmacokinetic, and Pharmacodynamic Study in Healthy Adult Volunteers. *Clin Pharmacol Drug Dev*. 2020 Jan;9(1):115-129.
- Stephen P Soltoff, et al. Evidence that tyrphostins AG10 and AG18 are mitochondrial uncouplers that alter phosphorylation-dependent cell signaling. *J Biol Chem*. 2004 Mar 19;279(12):10910-8.

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