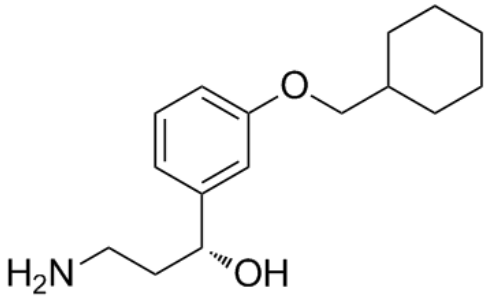
Product Data Sheet

Product Name: Emixustat (ACU-4429)
Cat. No.: GC31373

Chemical Properties

Cas. No.	1141777-14-1		
SMILES	O[C@H](CCN)C1=CC(OCC2CCCCC2)=CC=C1		
Formula	$C_{16}H_{25}NO_2$	M.Wt	263.38
Solubility	DMSO : ≥ 43 mg/mL (163.26 mM)	Storage	Store at -20°C
General tips	For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the ultrasonic bath for a while.Stock solution can be stored below -20°C for several months.		
Shipping Condition	Evaluation sample solution : ship with blue ice All other available size: ship with RT , or blue ice upon request.		
Structure			



Protocol

Animal experiment [1]:	
Animal models	BALB/c mice (8 weeks)

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Preparation method	Dark-adapted (12 hours) BALB/c mice (8 weeks, n = 4/group) were orally dosed with emixustat (0.01-3.0 mg/kg) or vehicle (water). At 4 hours post-dose, animals were photobleached (5000 lux white light, 10 min) without anesthesia or mydriatics, returned to the dark for 2 hours, and then euthanized under red light.
Dosage form	0.01-3.0 mg/kg; p.o
Applications	Emixustat was found to reduce the production of visual chromophore (11-cis retinal) in wild-type mice following a single oral dose (ED_{50} = 0.18 mg/kg).

References:

[1]. Bavik C, Henry SH,et,al. Visual Cycle Modulation as an Approach toward Preservation of Retinal Integrity. PLoS One. 2015 May 13;10(5):e0124940. doi: 10.1371/journal.pone.0124940. PMID: 25970164; PMCID: PMC4430241.

Background

Emixustat(ACU-4429) is a first in class small-molecule visual cycle modulator that inhibits the isomerase complex. As an inhibitor of visual cycle isomerase, the IC50 value is 4.4 nM[1].

Emixustat strongly inhibits 11-cis-retinol production with an IC50 value of 232±3 nM[2]. A concentration-dependent reduction of 11-cis-ROL production (i.e., inhibition of RPE65 isomerase activity) by emixustat(10-5 to 10-10 M)[1].

Emixustat(0.01-3.0 mg/kg; p.o) was found to reduce the production of visual chromophore (11-cis retinal) in wild-type mice following a single oral dose (ED50 = 0.18 mg/kg) [1]. In 40 subjects (mean age, 38 years) Emixustat (n = 30) (5, 10, 20, 30, or 40 mg; 14-day) was rapidly absorbed (median T(max), 3.0-5 hours) and readily eliminated (mean t(1/2), 4.6-7.9 hours), and mean C(max) generally increased in proportion to dose. Systemic adverse events were minimal[3]. Emixustat significantly abates permeability after Ischemia Reperfusion(IR) on vascular permeability in mice[4].

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References:

[1]. Bavik C, Henry SH, et,al.Visual Cycle Modulation as an Approach toward Preservation of Retinal Integrity. PLoS One. 2015 May 13;10(5):e0124940. doi: 10.1371/journal.pone.0124940. PMID: 25970164; PMCID: PMC4430241.

[2]. Kiser PD, Zhang J, et,al.Catalytic mechanism of a retinoid isomerase essential for vertebrate vision. Nat Chem Biol. 2015 Jun;11(6):409-15. doi: 10.1038/nchembio.1799. Epub 2015 Apr 20. PMID: 25894083; PMCID: PMC4433804.

[3].Kubota R, Al-Fayoumi S, et,al. Phase 1, dose-ranging study of emixustat hydrochloride (ACU-4429), a novel visual cycle modulator, in healthy volunteers. Retina. 2014 Mar;34(3):603-9. doi: 10.1097/01.iae.0000434565.80060.f8. PMID: 24056528.

[4].Dreffs A, Lin CM, et,al. All-trans-Retinaldehyde Contributes to Retinal Vascular Permeability in Ischemia Reperfusion. Invest Ophthalmol Vis Sci. 2020 Jun 3;61(6):8. doi: 10.1167/iovs.61.6.8. PMID: 32492112; PMCID: PMC7415894.

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

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