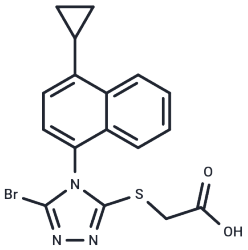
Data Sheet (Cat.No.T6875)

TargetMol

Lesinurad

Chemical Properties



CAS No. : 878672-00-5

Formula: C17H14BrN3O2S

Molecular Weight: 404.28

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	Lesinurad (RDEA594) is a selective inhibitor of uric acid reabsorption which is used in combination with other agents in the therapy of gout. Lesinurad has had a limited clinical use but has not been associated with serum enzyme elevations during therapy or with instances of clinically apparent liver injury.
Targets(IC50)	OAT
In vitro	Lesinurad inhibits the uric acid transport activity of human URAT1 (hURAT1) at a 20-fold higher potency compared to rat URAT1 (rURAT1), with IC50's of 3.36 and 74.84 μM, respectively. Lesinurad inhibits hURAT1 through an interaction that involves a critical residue, Phe365[1].
In vivo	Lesinurad (RDEA594) exhibits better pharmacokinetics than its pro-drug RDEA806. The 100 mg dose of Lesinurad exhibits a pharmacological effect in the range of that produced by 300 mg to 800 mg single doses of RDEA806[2].
Cell Research	Lesinurad is solubilized in DMSO and stored, and then diluted with appropriate media before use[1]. Validated oocytes, HEK293, MDCK-II, Caco-2 or MDCK-MDR1 cell systems are used to study the interaction of Lesinurad with membrane transporters localized to the kidney (OAT1, OAT3, OCT2, MATE1, and MATE2K) or liver (P-gp, BCRP, OATP1B1, OATP1B3, and OCT1). Xenopus laevis oocytes are injected with OAT1 or OAT3 cRNA or control (water) while HEK293 cells are stably transfected with MATE1, MATE2K, or vector and MDCK-II cells with hOATP1B1, hOATP1B3, hOCT1, hOCT2, or vector. The MDCKII cell line is stably transfected with the human MDR1 gene to create a P-gp cell line. The interaction of Lesinurad with BCRP relied on the endogenous expression in Caco-2 cells. All cells are cultured with growth medium according to standard methodology. In order to determine whether Lesinurad is a substrate for a transporter, cells are incubated with [14C]-labeled Lesinurad at various concentrations and the amount of Lesinurad taken up by the cells determined by subtracting the uptake in vector cells from that in the transfected cells. The uptake of a [3H]-labeled known substrate of the transporter served as the positive control. Inhibition of a transporter by Lesinurad is determined by incubating cells with a fixed concentration of [3H]-labeled known substrate and various concentrations of unlabeled Lesinurad. Inhibition by a known inhibitor of each transporter served as the positive control. Cells are incubated for the appropriate amount of time. All reactions are terminated by the addition of ice-cold medium. The cells are then rinsed with medium and lysed[1].

Solubility Information

Solubility	DMSO: 50 mg/mL (123.68 mM),Sonication is recommended. Ethanol: 50 mg/mL (123.68 mM),Sonication is recommended. H2O: < 1 mg/mL (insoluble or slightly soluble), (< 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 (4.95 mM),Sonication is recommended. *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.*

Preparing Stock Solutions

	1mg	5mg	10mg
1 mM	2.4735 mL	12.3677 mL	24.7353 mL
5 mM	0.4947 mL	2.4735 mL	4.9471 mL
10 mM	0.2474 mL	1.2368 mL	2.4735 mL
50 mM	0.0495 mL	0.2474 mL	0.4947 mL

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

L.Yeh, et al. RDEA594, a potential uric acid lowering agent througn inhibition of uric acid reuptake ,shows better pharmacokinetics rhan its prodrug RDEA806. 2008 ACR/ARHP Annual Scientific Meeting, 24-29 October 2008, USA.