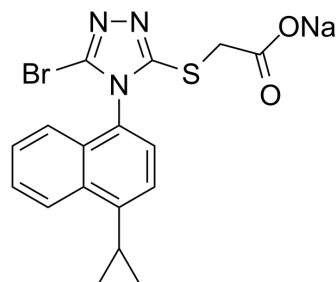


Lesinurad sodium

Cat. No.:	HY-15258A
CAS No.:	1151516-14-1
Molecular Formula:	C ₁₇ H ₁₃ BrN ₃ NaO ₂ S
Molecular Weight:	426.26
Target:	URAT1
Pathway:	Membrane Transporter/Ion Channel
Storage:	4°C, stored under nitrogen * In solvent : -80°C, 6 months; -20°C, 1 month (stored under nitrogen)



SOLVENT & SOLUBILITY

In Vitro	DMSO : 100 mg/mL (234.60 mM; Need ultrasonic)						
	Preparing Stock Solutions	Solvent Concentration	Mass	1 mg	5 mg	10 mg	
				1 mM	2.3460 mL	11.7299 mL	23.4599 mL
				5 mM	0.4692 mL	2.3460 mL	4.6920 mL
				10 mM	0.2346 mL	1.1730 mL	2.3460 mL
Please refer to the solubility information to select the appropriate solvent.							
In Vivo	1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline Solubility: 2.5 mg/mL (5.86 mM); Clear solution; Need ultrasonic						
	2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline) Solubility: 2.5 mg/mL (5.86 mM); Clear solution; Need ultrasonic						
	3. Add each solvent one by one: 10% DMSO >> 90% corn oil Solubility: 2.5 mg/mL (5.86 mM); Clear solution; Need ultrasonic						

BIOLOGICAL ACTIVITY

Description	Lesinurad sodium is a URAT1 and OAT inhibitor, is determined to be a substrate for the kidney transporters OAT1 and OAT3 with K _m values of 0.85 and 2 μM, respectively.
IC ₅₀ & Target	Km: 0.85 μM (OAT1), 2 μM (OAT3) ^[1]
In Vitro	Lesinurad is a novel selective uric acid reabsorption inhibitor (SURI). Lesinurad is determined to be a substrate for the kidney transporters organic anion transporter (OAT1) and OAT3 with K _m values of 0.85 and 2 μM, respectively ^[1] . Lesinurad (RDEA594) is a URAT1 and OAT inhibitor, which increases proximal renal tubule urate excretion ^[2] . Lesinurad (RDEA594) is a potential uric acid lowering agent through inhibition of uric acid reuptake, and exhibits favorable p450 profiles, inhibits

CYP2C9 and CYP2C8 with IC₅₀ of 14.4 μM and 16.2 μM, respectively. IC₅₀s of Lesinurad are all above 100 μM for CYP1A2, CYP2C19, and CYP2D6^[3].

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

In Vivo

Lesinurad (RDEA594) shows 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^[3].

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PROTOCOL

Cell Assay ^[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].

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CUSTOMER VALIDATION

- Food Funct. 2019 Aug 1;10(8):5215-5227.

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REFERENCES

- [1]. Shen Z, et al. In Vitro and In Vivo Interaction Studies Between Lesinurad, a Selective Urate Reabsorption Inhibitor, and Major Liver or Kidney Transporters. Clin Drug Investig. 2016 Jun;36(6):443-52
- [2]. Sattui SE, et al. Treatment of hyperuricemia in gout: current therapeutic options, latest developments and clinical implications. Ther Adv Musculoskelet Dis. 2016 Aug;8(4):145-59.
- [3]. L.Yeh, et al. RDEA594, a potential uric acid lowering agent through inhibition of uric acid reuptake, shows better pharmacokinetics than its prodrug RDEA806. 2008 ACR/ARHP Annual Scientific Meeting, 24-29 October 2008, USA.

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

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