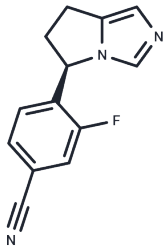
Data Sheet (Cat.No.T4277)

TargetMol

Osilodrostat

Chemical Properties



CAS No. : 928134-65-0

Formula: C13H10FN3

Molecular Weight: 227.24

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	Osilodrostat (LCI699) is a potent inhibitor of human 11β-hydroxylase (CYP11B1) and aldosterone synthase (CYP11B2) with IC50 values of 2.5 and 0.7 nM, respectively, and has been approved by the FDA for the treatment of Cushing's disease.
Targets(IC50)	Glucocorticoid Receptor,Hydroxylase
In vitro	**METHODS**: V79 or HEK-293 cell lines were treated with Osilodrostat (LCI699) (0-1000 nM). Aliquots of culture medium were removed after 5 hours, and steroids were extracted and analyzed by LC-MS/MS. **RESULTS** In V79 cells expressing CYP11B1, osilodrostat (LCI699) inhibited the conversion of 11-deoxycortisol to cortisol with an IC50 of 9.5 ± 0.5 nM. In contrast, in V79 cells expressing CYP11B2, LCI699 inhibited the conversion of corticosterone to aldosterone with an IC50 of 0.28 ± 0.06 nM. In V79 cells expressing CYP11A1, osilodrostat (LCI699) partially (<25%) inhibited pregnenolone formation at 1000 nM. In HEK-293 cells stably expressing CYP17A1 or CYP21A2, LCI699 showed negligible inhibition of activity (<1%) at concentrations up to 1000 nM. [5]
In vivo	**METHODS**: Rats were randomly divided into single-sex groups and received daily doses of pasireotide (0.3 mg/kg/day, subcutaneous injection), Osilodrostat (LCI699) (20 mg/kg/day, oral), Osilodrostat (LCI699)/Pasireotide combination (low dose, 1.5/0.03 mg/kg/day; medium dose, 5/0.1 mg/kg/day; or high dose, 20/0.3 mg/kg/day) or vehicle for 13 weeks. Different doses of Osilodrostat (LCI699) and pasireotide alone and in combination were evaluated. **RESULTS** Mean weight gain from baseline to week 13 was significantly lower in the pasireotide and combination treatment groups, whereas it was significantly higher in female rats treated with osilodrostat (LCI699) monotherapy; osilodrostat (LCI699) and pasireotide monotherapy were associated with significant changes in histology and mean weights of the pituitary and adrenal glands, liver, and ovaries/fallopian tubes; osilodrostat (LCI699) alone was associated with adrenal cortical hypertrophy and hepatocyte hypertrophy. [1] **METHODS**: Osilodrostat (LCI699) was evaluated after oral administration (0.1-3 mg/kg for the Ang II model and 1-100 mg/kg for the ACTH model). **RESULTS** Osilodrostat (LCI699) was rapidly absorbed (time to maximum plasma concentration [tmax] 0.3-2.4 hours) with a terminal elimination half-life (t½) of 2-5 hours. The pharmacokinetics of LCI699 were dose proportional over the dose range tested. Plasma protein binding was 35.9%.[4]

Animal Research	Sixty male and 60 female rats are randomized into single-sex groups to receive daily doses of pasireotide (0.3 mg/kg/day, s.c.), osilodrostat (20 mg/kg/day, p.o.), osilodrostat/pasireotide in combination (low dose, 1.5/0.03 mg/kg/day; mid-dose, 5/0.1 mg/kg/day; or high dose, 20/0.3 mg/kg/day), or vehicle for 13 weeks.

Solubility Information

Solubility	DMSO: 50 mg/mL (220.03 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 (8.8 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	4.4006 mL	22.0032 mL	44.0063 mL
5 mM	0.8801 mL	4.4006 mL	8.8013 mL
10 mM	0.4401 mL	2.2003 mL	4.4006 mL
50 mM	0.088 mL	0.4401 mL	0.8801 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

Li L, et al. Osilodrostat (LCI699), a potent 11β-hydroxylase inhibitor, administered in combination with the multireceptor-targeted somatostatin analog pasireotide: A 13-week study in rats. Toxicol Appl Pharmacol. 2015 Aug 1;286(3):224-33.

Fleseriu M, et al. Osilodrostat, a potent oral 11β-hydroxylase inhibitor: 22-week, prospective, Phase II study in Cushing's disease. Pituitary. 2016 Apr;19(2):138-48.

Creemers SG, et al. Osilodrostat Is a Potential Novel Steroidogenesis Inhibitor for the Treatment of Cushing Syndrome: An In Vitro Study. J Clin Endocrinol Metab. 2019 Aug 1;104(8):3437-3449.

Ménard J, et al. Aldosterone synthase inhibition: cardiorenal protection in animal disease models and translation of hormonal effects to human subjects. J Transl Med. 2014 Dec 10;12:340.

Valentín-Goyco J, et al. Selectivity of osilodrostat as an inhibitor of human steroidogenic cytochromes P450. J Steroid Biochem Mol Biol. 2023 Jul;231:106316.