Merimepodib

Cat. No.: HY-13986

CAS No.: 198821-22-6

Molecular Formula: $C_{23}H_{24}N_4O_6$

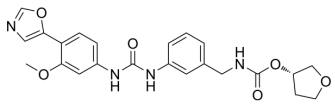
Molecular Weight: 452.46

Target: HBV; HCV; Flavivirus; Dengue virus

Pathway: Anti-infection

Storage:

Powder	-20°C	3 years
	4°C	2 years
In solvent	-80°C	2 years
	-20°C	1 year



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 31 mg/mL (68.51 mM)

* "≥" means soluble, but saturation unknown.

Preparing Stock Solutions

Concentration \ Solvent, Mass	1 mg	5 mg	10 mg
1 mM	2.2101 mL	11.0507 mL	22.1014 mL
5 mM	0.4420 mL	2.2101 mL	4.4203 mL
10 mM	0.2210 mL	1.1051 mL	2.2101 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 (5.53 mM); Clear solution
2. Add each solvent one by one: 10% DMSO >> 90% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.53 mM); Clear solution
3. Add each solvent one by one: 10% DMSO >> 90% corn oil
   Solubility: ≥ 2.5 mg/mL (5.53 mM); Clear solution
4. Add each solvent one by one: 5% DMSO >> 95% (20% SBE-β-CD in saline)
   Solubility: ≥ 2.5 mg/mL (5.53 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Merimepodib (VX-497) is a noncompetitive and oral inhibitor of inosine monophosphate dehydrogenase (IMPDH) with broad spectrum antiviral activities.

In Vitro

VX-497 has antiproliferative effect on lymphoid and keratinocyte cells. The antiproliferative effect of VX-497 in cells is

	reversed within 48 h of its removal[1]. VX-497 has intermediate antiviral activity against a second group of viruses, which includes HSV-1, parainfluenza-3 virus, BVDV, VEEV, and dengue virus, with IC_{50}s ranging from 6 to 19 μM. VX-497 is 100-fold more potent, with an IC_{50} of 380 nM and a corresponding CC_{50} of 5.2 μM, for a therapeutic index of 14. The antiviral activity of VX-497 in HepG2.2.2.15 cells is reversed threefold by the addition of guanosine[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Oral administration of VX-497 inhibits the primary IgM antibody response in a dose-dependent manner, with an ED_{50} value of appr 30-35 mg/kg in mice. Single daily dosing of VX-497 is observed to be as effective as twice-daily dosing in this model of immune activation[1]. GVHD developed in the vehicle-treated allografted F1 mice and treatment with VX-497 improved all manifestations of the disease significantly. The 2.9-fold increase in spleen weight in allografted animals is reduced to a 1.6-fold increase in the VX-497-treated mice. Serum IFN-gamma levels are increased 54-fold in the vehicle group while there is a 7.4-fold increase in VX-497-treated animals[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay [2]	The murine fibroblast L929 cell line is cultured in Eagle minimal essential medium supplemented with 10% fetal bovine serum, nonessential amino acids, 50 U of penicillin per mL, 50 μg of streptomycin per mL, and 2 mM l-glutamine. EMCV is infected at 500 PFU/107 L929 cells. Cells are left untreated or are treated with different concentrations of murine IFN-α alone, VX-497 alone, or combinations thereof. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Mol Immunol. 2019 Oct;114:226-232.
- Antiviral Res. 2018 Jan;149:34-40.

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REFERENCES

[1]. Jain J, et al. VX-497: a novel, selective IMPDH inhibitor and immunosuppressive agent. J Pharm Sci. 2001 May;90(5):625-37.

[2]. Markland W, et al. Broad-spectrum antiviral activity of the IMP dehydrogenase inhibitor VX-497: a comparison with ribavirin and demonstration of antiviral additivity with alpha interferon. Antimicrob Agents Chemother. 2000 Apr;44(4):859-66.

[3]. Decker CJ, et al. The novel IMPDH inhibitor VX-497 prolongs skin graft survival and improves graft versus host disease in mice. Drugs Exp Clin Res. 2001;27(3):89-95.

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