

Product Data Sheet

Product Name: Ledipasvir D-tartrate

Cat. No.: GC36437

Chemical Properties

Cas. No. 1502654-87-6

SMILES O=C(OC)N[C@H](C(N([C@H](C1=NC=C(C2=CC(C(F)(F)C3=C4C=CC(C5=CC=C6N=C([C@H]7N(C([C@@H](NC(OC)=O)C(C)C)=O)[C@]8([H])CC[C@@]7([H])C8)NC6=C5)=C3)=C4C=C2)N1)C9)CC%109CC%10)=O)C(C)C.O[C@@H]([C@@H](C(O)=O)O)C(O)=O

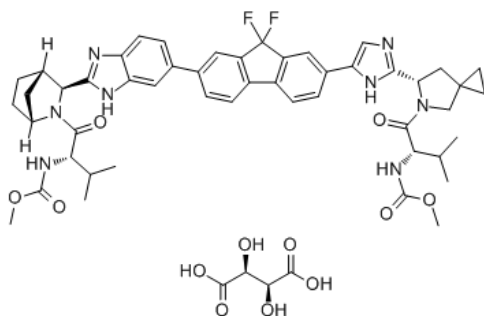
Formula $C_{53}H_{60}F_2N_8O_{12}$ M.Wt 1039.09

Solubility DMSO: ≥ 28 mg/mL (26.95 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

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

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Animal experiment: Rats, Dogs and Monkeys[1] Pharmacokinetic studies are performed in male naïve Sprague-Dawley(SD) rats, non-naïve beagle dogs, and cynomolgus monkeys (three animals per dosing route). Intravenous (IV) administration is dosed via infusion over 30 min in a vehicle containing 5% ethanol, 20% PEG400, and 75% water (pH adjusted to 3.0 with HCl). Oral dosing is administered by gavage in a vehicle containing 5% ethanol, 45% PEG 400, and 50% of 50 mM citrate buffer, pH 3. Blood samples are collected over a 24 h period postdose into Vacutainer tubes containing EDTA-K2. Plasma was isolated, and the concentration of the test compound in plasma was determined with LC/MS/MS after protein precipitation with acetonitrile.

References:

- [1]. Link JO, et al. Discovery of ledipasvir (GS-5885): a potent, once-daily oral NS5A inhibitor for the treatment of hepatitis C virus infection. J Med Chem. 2014 Mar 13;57(5):2033-46
- [2]. Hernandez D, et al. Natural prevalence of NS5A polymorphisms in subjects infected with hepatitis C virus genotype 3 and their effects on the antiviral activity of NS5A inhibitors. J Clin Virol. 2013 May;57(1):13-8.

Background

Ledipasvir D-tartrate is an inhibitor of the hepatitis C virus NS5A, with EC₅₀ values of 34 pM against GT1a and 4 pM against GT1b replicon. EC₅₀: 34 pM (GT1a), 4 pM (GT1b)[1]

Ledipasvir has GT1a and 1b EC₅₀ values of 31 and 4 pM, respectively, and protein-adjusted EC₅₀ values of 210 pM (GT1a) and 27 pM (GT1b) and the intrinsic EC₅₀ of 39 is 310 fM for GT1a and 40 fM for GT1b. Ledipasvir is highly protein-bound both in human serum and in the cell-culture medium (containing 10% BSA) of the replicon assay[1]. Ledipasvir exhibits an EC₅₀ value of 141 nM against the JFH/3a-NS5A replicon[2].

Ledipasvir is remarkable not only on the basis of its high replicon potency but also on the basis of its low clearance, good bioavailability, and long half-lives in rat, dog, and monkey and low predicted clearance in human. The pharmacokinetics of Ledipasvir is measured in rats and dogs. Ledipasvir

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shows good half-lives (rat 1.83 ± 0.22 hr, dog 2.63 ± 0.18 hr) in plasma, low systemic clearance (CL), and moderate volumes of distribution (Vss) that are greater than total body water volume[1].

[1]. Link JO, et al. Discovery of ledipasvir (GS-5885): a potent, once-daily oral NS5A inhibitor for the treatment of hepatitis C virus infection. J Med Chem. 2014 Mar 13;57(5):2033-46. [2]. Hernandez D, et al. Natural prevalence of NS5A polymorphisms in subjects infected with hepatitis C virus genotype 3 and their effects on the antiviral activity of NS5A inhibitors. J Clin Virol. 2013 May;57(1):13-8.

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