

Product Data Sheet

Product Name: Lumacaftor-d4

Cat. No.: GC70684

Chemical Properties

Cas. No. 2733561-44-7

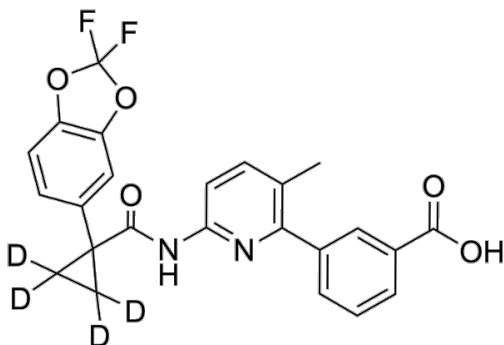
Formula $C_{24}H_{14}D_4F_2N_2O_5$ M.Wt 456.43

Solubility DMSO : 25 mg/mL (54.77 mM; ultrasonic and warming and heat to 60°C; Hygroscopic DMSO has a significant impact on the solubility of product, please use newly opened DMSO) Storage -20°C

General For obtaining a higher solubility , please warm the tube at 37 °C and shake it in the tips ultrasonic bath for a while. Stock solution can be stored below -20°C for several months.

Shipping Evaluation sample solution : ship with blue ice All other available size: ship with RT , or Condition blue ice upon request.

Structure



Background

Lumacaftor-d4 is the deuterium labeled Lumacaftor [1].

Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug

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

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molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs^[1].

In fischer rat thyroid (FRT) cells, Lumacaftor improves F508del-CFTR maturation by 7.1 ± 0.3 fold ($n=3$) compared with vehicle-treated cells (EC_{50} , 0.1 ± 0.1 μM ; $n=3$) and enhances F508del-CFTR-mediated chloride transport by approximately fivefold (EC_{50} , 0.5 ± 0.1 μM ; $n=3$). At Lumacaftor concentrations greater than 10 μM , the response is reduced, resulting in a bell-shaped dose-response relationship with an IC_{50} of approximately 100 μM . Lumacaftor is orally bioavailable in rats and achieved in vivo plasma levels significantly above concentrations required for in vitro efficacy^[2]. Lumacaftor produces a concentration-dependent increase in the HRP luminescence signal after incubation with cells at 37°C or 27°C in both cell lines, with a similar EC_{50} value of approximately 0.3 μM . In F508-HRP CFBE41o⁻ cells at 37°C, Lumacaftor increases the signal maximally to approximately 250 luminescence arbitrary units (a.u.) over the DMSO control baseline of approximately 60 a.u., representing an approximately 4-fold signal increase. Similarly, with the R1070W-HRP CFBE41o⁻ cells, Lumacaftor increases the signal maximally to approximately 220 a.u. over the DMSO control baseline of approximately 85 a.u., representing an approximately 2.5-fold signal increase. Therefore, both cell lines produced robust signals with a good dynamic range for high-throughput screening^[3].

Oral dosing of 1 mg/kg Lumacaftor in male Sprague-Dawley rats results in a C_{max} of 2.4 ± 1.3 μM with a $t_{1/2}$ of 7.7 ± 0.4 h (mean $\pm$ SD; $n=3$), indicating that that Lumacaftor is orally bioavailable and able to reach plasma levels that significantly exceeded EC_{50} s for F508del-CFTR correction^[2].

References:

[1]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-232.

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