

Product Data Sheet

Product Name: Zaurategrast

Cat. No.: GC37960

Chemical Properties

Cas. No. 455264-31-0

SMILES O=C1C(Br)=C(C12CCCCC2)N[C@H](C(O)=O)CC3=CC=C(NC4=NC=CC5=CC=NC=C45)C=C3

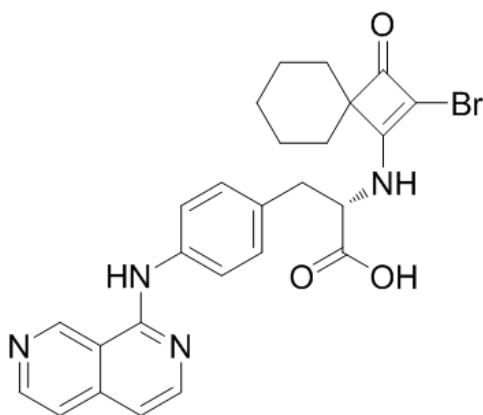
Formula $C_{26}H_{25}BrN_4O_3$ M.Wt 521.41

Solubility DMSO: 100 mg/mL (191.79 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: Mice[3] Male Wistar rats (250-320 g) and CD-1 mice (20-25 g), Non-naive male Beagle dogs weighing 10 kg, and non-naive male cynomolgus monkeys weighing 3 kg are used. For plasma pharmacokinetic studies, CT7758 is administered orally (5-10 mL/kg, 30 mg/kg) or intravenously (2 mL/kg, 3 mg/kg) as a solution in 10 mM phosphate buffer. CDP323 is administered orally as a 1% methylcellulose suspension containing 0.1% Tween 80 (same dosage volume as CT7758). Compounds are delivered to fasted animals with the food returned 4 hours postdose. Blood samples are collected at the designated time points. Plasma is prepared by centrifugation, collected, and stored at -20°C until analysis by liquid chromatography-tandem mass spectrometry (LC-MS/MS).

References:

- [1]. Wolf C, et al. Pharmacodynamic consequences of administration of VLA-4 antagonist CDP323 to multiple sclerosis subjects: a randomized, double-blind phase 1/2 study. PLoS One. 2013;8(3):e58438.
- [2]. Chanteux H, et al. In Vitro Hydrolysis and Transesterification of CDP323, an $\alpha 4 \beta 1 / \alpha 4 \beta 7$ Integrin Antagonist Ester Prodrug. Drug Metab Dispos. 2014 Jan;42(1):153-61.
- [3]. Chanteux H, et al. Cross-Species Differences in the Preclinical Pharmacokinetics of CT7758, an $\alpha 4 \beta 1 / \alpha 4 \beta 7$ Integrin Antagonist. Drug Metab Dispos. 2015 Sep;43(9):1381-91.

Background

Zaurategrast (CT7758) is a potent and oral-effective $\alpha 4$ -integrin inhibitor. $\alpha 4$ -integrin[1]

CDP323 is an ethyl ester prodrug of CT7758, a potent carboxylic acid antagonist of $\alpha 4 \beta 1$ (very late antigen-4, VLA-4) and, to a lesser extent, $\alpha 4 \beta 7$ integrins. CDP323 is developed as a VLA-4 antagonist prodrug for the treatment of multiple sclerosis[2].

CDP323 is a potent and effective $\alpha 4$ inhibitor that is well tolerated at oral doses up to 1000 mg twice daily (bid). Relative to placebo, all dosages of Zaurategrast (CDP-323) significantly decreased the capacity of lymphocytes to bind vascular adhesion molecule-1 (VCAM-1) and the expression of $\alpha 4$ -integrin on VCAM-1-binding cells. CDP323 at daily doses of 1000 or 2000 mg induced significant

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increases in total lymphocyte count and suppressed VCAM-1 binding by reducing unbound very late antigen-4 expression on lymphocytes[1]. After oral administration of CDP323, CT7758 is by far the most abundant circulating plasma component, peaking between 0.5 and 1.5 hours irrespective of the species. These data suggested that CDP323 is rapidly absorbed and efficiently hydrolyzed into CT7758. Plasma exposure of CT7758 showed a large species variability with dog>rat=mice>cynomolgus monkey. In the tested dose range of 25-50 mg/kg, the estimated oral bioavailability (i.e., based on intravenous administration of CT7758 and assuming linear PK) is 29, 27, 8, and 0.3% in mice, rat, dog, and cynomolgus monkey, respectively. CDP323 increased the absorption of CT7758 by 5- to 10-fold in rodents, whereas no significant increase is observed in dog and monkey[3].

[1]. Wolf C, et al. Pharmacodynamic consequences of administration of VLA-4 antagonist CDP323 to multiple sclerosis subjects: a randomized, double-blind phase 1/2 study. PLoS One. 2013;8(3):e58438. [2]. Chanteux H, et al. In Vitro Hydrolysis and Transesterification of CDP323, an $\alpha 4 \beta 1 / \alpha 4 \beta 7$ Integrin Antagonist Ester Prodrug. Drug Metab Dispos. 2014 Jan;42(1):153-61. [3].

Chanteux H, et al. Cross-Species Differences in the Preclinical Pharmacokinetics of CT7758, an $\alpha 4 \beta 1 / \alpha 4 \beta 7$ Integrin Antagonist. Drug Metab Dispos. 2015 Sep;43(9):1381-91.

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