

Product Data Sheet

Product Name: Setipiprant

Cat. No.: GC19327

Chemical Properties

Cas. No. 866460-33-5

SMILES O=C(O)CN1C2=C(CN(C(C3=C4C=CC=CC4=CC=C3)=O)CC2)C5=C1C=CC(F)=C5

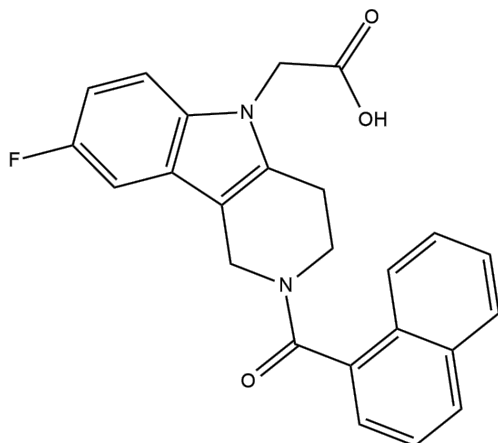
Formula $C_{24}H_{19}FN_2O_3$ M.Wt 402.42

Solubility DMSO : ≥ 36 mg/mL (89.46 mM) Storage Store at RT

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

Cell experiment [1]:

Cell lines hESC

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

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Whole blood was collected from healthy volunteers. Polymorphonuclear leukocytes (PMNs) were isolated by Polymorphprep density gradient centrifugation (500g, 30min). After hypotonic lysis to remove red blood cells, a cell suspension containing eosinophils was obtained. Resuspend PMNs in PBS buffer containing $\text{Ca}^{2+}/\text{Mg}^{2+}$ (supplemented with 0.1%BSA, 10mM Hepes, 10mM glucose, pH7.4), adjust the concentration to 1×10^6 cells/mL, and tag eosinophils with CD49d-APC antibody Incubation at room temperature for 1 hour. Mix 45 μL of human plasma, 10 μL of detection buffer with 30 μL of PMNs (1.3×10^7 cells/mL), add different concentrations of Setipiprant and pre-incubate for 10 minutes, then add 15nMPGD₂ to activate the cells and incubate at 37°C for 5 minutes. The FACS Aria flow cytometer was used to gate eosinophils by CD49d-APC fluorescence signal and lateral scattering (SSC), and to detect the changes in forward scattering (FSC)-an increase in FSC reflects changes in cell shape (such as degranulation, polarization).

Preparation Method

Reaction Conditions 1-10 μM ; 10 min

Applications Setipiprant inhibits eosinophil activation and shape changes induced by PGD₂.

Animal experiment [1]:

Animal models Male Wistar rats

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Preparation Method	Plasma samples of rats were collected at different time points after administration. The efficacy was evaluated by measuring the pharmacokinetic parameters in plasma, including AUC_{0-last} (area under the drug-time curve), CL (plasma clearance rate), $T_{1/2}$ (half-life), and F (oral bioavailability), etc. These parameters were obtained by analyzing plasma samples collected at different time points after administration in rats, and ultimately the pharmacokinetic characteristics of Setipiprant in rats were determined. Among them, the oral bioavailability was 44%, and the plasma exposure (AUC_{0-last}) was 58,500ng·h/mL. The plasma clearance rate was $1.3\text{mL}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$, and the half-life was 6 hours.
Dosage form	2mg/kg
Applications	Setipiprant can effectively inhibit aldose reductase in the lens and kidneys of rats.

References:

[1] Fretz H, Valdenaire A, Pothier J, et al. Identification of 2-(2-(1-Naphthoyl)-8-fluoro-3,4-dihydro-1H-pyrido[4,3-b]indol-5(2H)-yl)acetic Acid (Setipiprant/ACT-129968), a Potent, Selective, and Orally Bioavailable Chemoattractant Receptor-Homologous Molecule Expressed on Th2 Cells (CRTH2) Antagonist. *Journal of Medicinal Chemistry* 2013, 56(12):4899-4911.

Background

Setipiprant is a selective and orally available prostaglandin D2 receptor 2 (DP2, also known as CRTH2) antagonist, which is a γ -carboline derivative with an IC_{50} of 6nM^[1]. As a G protein-coupled receptor, the DP2 receptor is mainly expressed on the surface of immune cells such as eosinophils and Th2 cells, and is involved in regulating allergic inflammatory responses, immune cell migration, and cytokine release^[2]. By specifically blocking the DP2 receptor, Setipiprant has shown significant anti-inflammatory effects in models of inflammatory diseases such as allergic asthma and atopic dermatitis^[3].

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In vitro, when hESC cells are treated with Setipiprant (1-10 μ M) for 10 minutes, the compound inhibits PGD₂-induced eosinophil activation and shape change by blocking the CRTH2 receptor^[1].

In vivo, after intravenous injection of Setipiprant (2mg/kg) in rats and dogs, relevant bioavailability data indicate that the compound exhibits good oral bioavailability and excellent pharmacokinetic properties in both animal species^[1]. In addition, Setipiprant (1%) can effectively inhibit the activities of rat lens aldose reductase and kidney aldose reductase^[4].

References:

- [1] Fretz H, Valdenaire A, Pothier J, et al. Identification of 2-(2-(1-Naphthoyl)-8-fluoro-3,4-dihydro-1H-pyrido[4,3-b]indol-5(2H)-yl)acetic Acid (Setipiprant/ACT-129968), a Potent, Selective, and Orally Bioavailable Chemoattractant Receptor-Homologous Molecule Expressed on Th2 Cells (CRTH2) Antagonist. *Journal of Medicinal Chemistry* 2013, 56(12):4899-4911.
- [2] Kupczyk M, Kuna P Targeting the PGD₂/CRTH2/DP1 Signaling Pathway in Asthma and Allergic Disease: Current Status and Future Perspectives. *Drugs* 2017, 77(12):1281-1294.
- [3] Strasser DS, Farine H, Holdener M, et al. Development of a decision-making biomarker for CRTH2 antagonism in clinical studies. *New Horizons in Translational Medicine* 2015, 2(4):118-125.
- [4] Ballekova J, Soltesova-Prnova M, Majekova M, et al. Does inhibition of aldose reductase contribute to the anti-inflammatory action of setipiprant? *Physiol Res* 2017, 66(4):687-693.

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