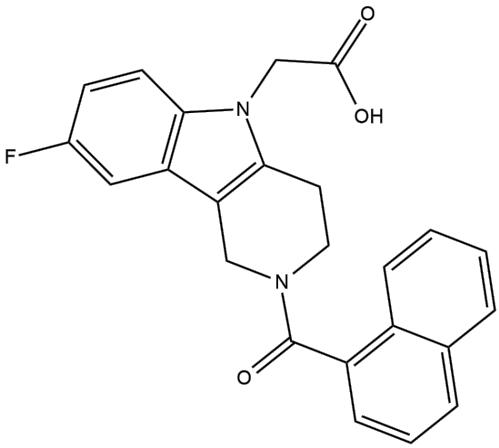
Product Data Sheet

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

Product Data Sheet

Preparation Method	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 Ca^{2+}/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 1hour. Mix 45μL of human plasma, 10μL of detection buffer with 30μL of PMNs (1.3×10^7cells/mL), add different concentrations of Setipiprant and pre-incubate for 10 minutes, then add 15nMPGD_2 to activate the cells and incubate at 37°C for 5 minutes. The FACSAria 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).
Reaction Conditions	1-10μM; 10 min
Applications	Setipiprant inhibits eosinophil activation and shape changes induced by PGD_2.

Animal experiment [1]:

Animal models	Male Wistar rats

Product Data Sheet

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 $AUC_{0\text{-}last}$ (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 ($AUC_{0\text{-}last}$) was 58,500ng·h/mL. The plasma clearance rate was 1.3mL·min^{-1}·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].

Product Data Sheet

In vitro, when hESC cells are treated with Setipiprant (1-10μM) for 10 minutes, the compound inhibits PGD_2-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.

Caution: Product has not been fully validated for medical applications. For research use only.
Tel: (909) 407-4943 Fax: (626) 353-8530 E-mail: tech@glpbio.com
Address: 10292 Central Ave. #205, Montclair, CA, USA