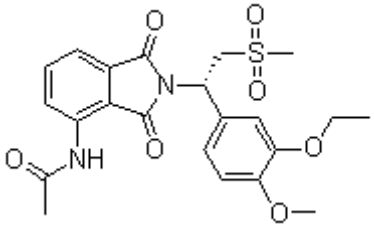
Product Introduction

Apremilast (CC-10004)

Apremilast (CC-10004) is a potent and orally active **PDE4** and **TNF-α** inhibitor with **IC50** of 74 nM and 77 nM, respectively.

Technical Data:

Molecular Weight (MW):	460.5	
Formula:	$C_{22}H_{24}N_2O_7S$	
Solubility (25 ℃) * <1 mg/ml means slightly soluble or insoluble:	DMSO 92 mg/mL	
	Water <1 mg/mL	
	Ethanol <1 mg/mL	
Purity:	>98%	
Storage:	3 years -20℃ Powder	
	6 months-80℃ in DMSO	
CAS No.:	608141-41-9	

Biological Activity

Apremilast is more potent for inhibition of PDE4 compared with cAMP or cGMP hydrolysing enzymes from other PDE families. Apremilast displays a broad pattern of anti-inflammatory activity in a variety of cell types, inhibits TNF-α, IL-12 and IL-23 production, as well as NK and keratinocyte responses. Apremilast is found to inhibit the zymosan-induced PMN production of IL-8 with IC50 of 94 nM. Apremilast inhibits fMLF-induced PMN CD18 and CD11b expression with IC50 of 390 nM and 74 nM, respectively, and inhibits fMLF-induced adhesion of PMN to HUVECs with IC50 of 150 nM. Apremilast inhibits keratinocyte TNF-αproduction, with no effect on keratinocyte cell viability as measured by intracellular ATP levels. [3] [4].

Apremilast is stable in the presence of human microsomes (t1/2 > 60 min). It is 90% protein bound in human plasma. Oral and intravenous administration of it in female rats showed that it have good pharmacokinetics with low clearance, a moderate volume of distribution, and a 64% oral bioavailability. In a LPS-induced TNF-αinhibition model in rats, examined the TNF-α inhibitory ability of Apremilast in vivo, and the ED50 is determined to be 0.03 mg/kg. In another LPS-induced neutrophilia model in rats, Apremilast exhibited an ED50 range from 0.3 mg/kg to 0.9 mg/kg.[1]

References

[1] Man HW, et al. J Med Chem, 2009,52(6), 1522-1524.

[2] Muller GW, et al. Bioorg Med Chem Lett, 1998,8(19), 2669-2674.

[3] PH Schafer, et al. Br J Pharmacol, 2010, 159(4), 842–855.

[4] Fiona E McCann,et al. Arthritis Res Ther, 2010, 12(3), R107.