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产品名称: **RVT-501**
产品别名: **Lotamilast; E6005**

生物活性:							
Description		Lotamilast (RVT-501; E6005) is a selective phosphodiesterase 4 (PDE4) inhibitor with an IC50 of 2.8 nM.					
IC50 & Target		IC50: 2.8 nM (human PDE4)[1]					
In Vitro		Lotamilast potently and selectively inhibits human PDE4 activity with an IC50 of 2.8 nM and suppresses the production of various cytokines from human lymphocytes and monocytes with IC50 values ranging from 0.49 to 3.1 nM[1].					
In Vivo		Lotamilast is currently in phase 2 development for patients with mild-to-moderate atopic dermatitis. In mice models, the topical application of Lotamilast produces an immediate antipruritic effect as well as an anti-inflammatory effect with reduced expression of cytokines/adhesion molecules. On the basis of these observed effects, topical RVT-501 ameliorates the appearance of atopic dermatitis-like skin lesions in two types of AD models, hapten- and mite-elicited models, exhibiting inhibitory effects comparable to that of tacrolimus[1]. A single topical application of Lotamilast significantly inhibits spontaneous scratching during 1–2 h after application in mice with chronic dermatitis; the inhibition is partial and similar between 0.01% and 0.03%. Topical application of 0.03% Lotamilast to the rostral back significantly inhibits the increased activity of the cutaneous nerve in mice with chronic dermatitis. The cutaneous concentration of cAMP is significantly decreased in mice with chronic dermatitis, and this decrease is reversed by topical Lotamilast application[2].					
Solvent&Solubility		In Vitro: DMSO : ≥ 100 mg/mL (211.64 mM) * "≥" means soluble, but saturation unknown.					
		Preparing	Solvent	Mass	1 mg	5 mg	10 mg
			Concentration				
			1 mM	2.1164 mL			
		Stock Solutions	5 mM	0.4233 mL	2.1164 mL	4.2329 mL	
10 mM	0.2116 mL		1.0582 mL	2.1164 mL			
*请根据产品在不同溶剂中的溶解度选择合适的溶剂配制储备液，一旦配成溶液，请分装保存，避免反复冻融造成的产品失效。 储备液的保存方式和期限: -80℃, 6 months; -20℃, 1 month。 -80℃ 储存时，请在 6 个月内使用， -20℃ 储存时，请在 1 个月内使用。							
References		[1]. Ishii N, et al. Antipruritic effect of the topical phosphodiesterase 4 inhibitor E6005 ameliorates skin lesions in a mouse atopic dermatitis model. J Pharmacol Exp Ther. 2013 Jul;346(1):105-12. [2]. Andoh T, et al. Topical E6005, a novel phosphodiesterase 4 inhibitor, attenuates spontaneous itch-related responses in mice with chronic atopy-like dermatitis. Exp Dermatol. 2014 May;23(5):359-61.					
实验参考:							
Animal Administration		Mice: Lotamilast is applied to the hair-clipped rostral back. Observation of hind-paw scratching and electrophysiological recording of the cutaneous nerve branch are conducted. The effects of topical application of E6005 are evaluated 1 h after application, because topical application of the vehicle					



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	elicited hind-paw scratching for 40 min. The cutaneous concentration of cAMP is measured by enzyme immunoassay[2].
Kinase Assay	PDE isoenzyme activities are quantified by measuring the formation of [³ H]5'-AMP or [³ H]5'-GMP from [³ H]cAMP or [³ H]cGMP using an enzyme isolated from bovine brain (for PDE1), differentiated U-937 cells (for PDE2), human platelets (for PDE3 and PDE5), and U-937 cells (for PDE4). The test compounds (RVT-501), reference compounds, or vehicle (water) is added to a reaction buffer. The reaction is initialized by addition of the enzyme, and the mixture is incubated for 60 minutes at 22°C. After incubation, the reaction is stopped by heating the plate to 60°C for 3 minutes, after which time scintillation proximity assay beads are added. After 20 minutes of shaking at 22°C, the amount of [³ H]5'-AMP or [³ H]5'-GMP is quantified with a scintillation counters[1].
References	[1]. Ishii N, et al. Antipruritic effect of the topical phosphodiesterase 4 inhibitor E6005 ameliorates skin lesions in a mouse atopic dermatitis model. J Pharmacol Exp Ther. 2013 Jul;346(1):105-12. [2]. Andoh T, et al. Topical E6005, a novel phosphodiesterase 4 inhibitor, attenuates spontaneous itch-related responses in mice with chronic atopy-like dermatitis. Exp Dermatol. 2014 May;23(5):359-61.

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