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产品名称: **Tirasemtiv**
 产品别名: **CK-2017357**

生物活性:																				
Description	Tirasemtiv is an activator of the fast skeletal muscle troponin complex.																			
IC₅₀ & Target	Troponin[1]																			
In Vitro	Tirasemtiv is a fast skeletal troponin activator that sensitizes the sarcomere to calcium; this mechanism of action amplifies the response of muscle to neuromuscular input producing greater force when nerve input is reduced. Tirasemtiv selectively sensitizes fast skeletal muscle troponin to calcium (Ca ²⁺), and slows the rate of Ca ²⁺ release from the regulatory troponin complex of fast skeletal muscle[1].																			
In Vivo	A single dose of Tirasemtiv significantly increases submaximal isometric force, forelimb grip strength, grid hang time, and rotarod performance in a female transgenic mouse model (B6SJL-SOD1 ^{G93A}) of ALS with functional deficits. Additionally, diaphragm force and tidal volume are significantly higher in Tirasemtiv-treated female B6SJL-SOD1 ^{G93A} mice. At the 25% deficit milestone, vehicle-treated B6SJL-SOD1 ^{G93A} mice demonstrated forelimb grip strength of 49.6±4.6 g. Tirasemtiv increases grip strength by 38% to 68.6±8.1g (p<0.05, single tailed t-test). Tirasemtiv doses of 2, 2, 2, and 4 mg/kg given at approximately 20 min intervals to achieve a cumulative dose of 10 mg/kg. Regression analysis of the log dose vs. response relationship indicated that Tirasemtiv significantly increased muscle force in WT and mid-stage B6SJL-SOD1 ^{G93A} mice (WT p<0.0001; mid-stage p=0.0028). At later stages of disease, the mice exhibited a trend for increased muscle function in response to Tirasemtiv compared to baseline (p=0.064) ^[1] .																			
Solvent&Solubility	<p>In Vitro: DMSO : ≥ 52 mg/mL (225.82 mM) * "≥" means soluble, but saturation unknown.</p>																			
	<table border="1"> <thead> <tr> <th rowspan="2">Preparing</th> <th>Solvent Mass</th> <th rowspan="2">1 mg</th> <th rowspan="2">5 mg</th> <th rowspan="2">10 mg</th> </tr> <tr> <th>Concentration</th> </tr> </thead> <tbody> <tr> <td rowspan="3">Stock Solutions</td> <td>1 mM</td> <td>4.3427 mL</td> <td>21.7136 mL</td> <td>43.4273 mL</td> </tr> <tr> <td>5 mM</td> <td>0.8685 mL</td> <td>4.3427 mL</td> <td>8.6855 mL</td> </tr> <tr> <td>10 mM</td> <td>0.4343 mL</td> <td>2.1714 mL</td> <td>4.3427 mL</td> </tr> </tbody> </table>	Preparing	Solvent Mass	1 mg	5 mg	10 mg	Concentration	Stock Solutions	1 mM	4.3427 mL	21.7136 mL	43.4273 mL	5 mM	0.8685 mL	4.3427 mL	8.6855 mL	10 mM	0.4343 mL	2.1714 mL	4.3427 mL
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<p>*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°C, 6 months; -20°C, 1 month。-80°C 储存时, 请在 6 个月内使用, -20°C 储存时, 请在 1 个月内使用。</p>																				
References	[1]. Hwee DT, et al. Fast skeletal muscle troponin activator tirasemtiv increases muscle function and performance in the B6SJL-SOD1 ^{G93A} ALS mouse model. PLoS One. 2014 May 7;9(5):e96921.																			
实验参考:																				
	<p>Mice^[1] Wild-type background strain B6SJL/J mice and B6SJL-SOD1^{G93A} mice over-expressing the human SOD-1 gene with mutation G93A are group-housed in a 12-hour light cycle and fed standard chow and water ad libitum. Tirasemtiv is administered in solution (50% PEG300/10% EtOH/40% Cavitron cyclodextrin formulation) as a single slow bolus over a 2 minute period via a catheter in the</p>																			



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Animal Administration	contralateral femoral artery placed above the aortic bifurcation. Tirasemtiv bolus injections (2, 2, 2, and 4 mg/kg) are given at approximately 20 min intervals to achieve a cumulative dose of 10 mg/kg in order to assess the dose response, with a maximal dosage volume of 5 mL/kg. At the end of each experiment, a single terminal blood sample is drawn via cardiac puncture for compound concentration analysis.
References	[1]. Hwee DT, et al. Fast skeletal muscle troponin activator tirasemtiv increases muscle function and performance in the B6SJL-SOD1G93A ALS mouse model. PLoS One. 2014 May 7;9(5):e96921.



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