

MEN11467

Catalog No: tcsc7328



Available Sizes

Size: 1mg

Size: 5mg

Size: 10mg

Size: 20mg



Specifications

CAS No:

214487-46-4

Formula:

$C_{38}H_{40}N_4O_3$

Pathway:

Neuronal Signaling;GPCR/G Protein

Target:

Neurokinin Receptor;Neurokinin Receptor

Purity / Grade:

>98%

Solubility:

10 mM in DMSO

Observed Molecular Weight:

600.75

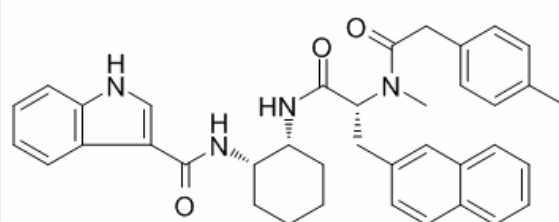
Product Description

MEN11467 is a selective and orally- effective peptidomimetic **tachykinin NK₁ receptor** antagonist.

IC50 & Target: Tachykinin NK₁ receptor^[1]

In Vitro: MEN11467 potently inhibits the binding of [³H] substance P (SP) to tachykinin NK₁ receptors in the IM9 limphoblastoid cell line (pK_i=9.4±0.1). MEN11467 is highly specific for the human tachykinin NK₁ receptors, since it has negligible effects (pK_i2 or NK₃ receptors and to a panel of 30 receptors ion channels unrelated to tachykinin receptors. The antagonism exerted by MEN11467 at tachykinin NK₁ receptors is insurmountable in saturation binding experiments, both K_D and B_{max} of SP are significantly reduced by MEN11467 (0.3-10 nM). In the guinea-pig isolated ileum, MEN11467 (0.03-1 nM) produces a nonparallel rightward shift of the concentration-response curve to SP methylester with a concomitant reduction of the E_{max} to the agonist (pK_B=10.7±0.1). Moreover the antagonist activity of MEN11467 is hardly reversible despite prolonged washout^[1]. The pseudopeptide tachykinin NK₁ receptor antagonist, MEN11467 is used to study tachykininergic involvement in antigen-induced mucus secretion in ferret trachea in vitro. MEN11467 (1 nM-10 μM) inhibits [Sar⁹]SP-induced ³⁵SO₄ output in a concentration-dependent manner with an approximate IC₅₀ of 0.3 μM^[2].

In Vivo: MEN11467 produces a long lasting (>2-3 h) dose-dependent antagonism of bronchoconstriction induced by the selective tachykinin NK₁ receptor agonist, [Sar⁹, Met(O₂)¹¹]SP in anaesthetized guinea-pigs (ID₅₀s=29±5, 31±12 and 670±270 μg/kg, after intravenous, intranasal and intraduodenal administration, respectively), without affecting bronchoconstriction induced by methacholine. After oral administration MEN11467 produces a dose-dependent inhibition of plasma protein extravasation induced in guinea-pig bronchi by [Sar⁹, Met(O₂)¹¹] (ID₅₀= 6.7±2 mg/kg) or by antigen challenge in sensitized animals (ID₅₀=1.3 mg/kg). After i.v. administration MEN11467 weakly inhibits the GR 73632-induced foot tapping behaviour in gerbil (ED₅₀=2.96±2 mg/kg), indicating a poor ability to block central tachykinin NK₁ receptors^[1]. Treatment with MEN11467 (1 mmol/kg twice weekly for 2 weeks) results in a temporary growth arrest of the U373 MG xenograft that last for about 10 days until the last MEN11467 administration (TVI%=56). Thereafter, the tumor start to regrow. MEN11467 anti-tumor activity is partially reverted by the simultaneous administration of an equimolar dose of exogenous substance P (SP), suggesting the specificity of tachykinin NK₁ receptor activation in glioma growth. Prolonged s.c. treatment with a higher MEN11467 dose (1.7 mmol/kg at five times a week for 6 weeks) completely inhibits the growth of U373 MG tumor for the entire length of the experiment, even following administration of a low exogenous SP dose. After 6 weeks, the tumor mass is not increased compared to the untreated control with TVI%=96%^[3].



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