

Alvelestat

Catalog No: tcsc1684



Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg



Specifications

CAS No:

848141-11-7

Formula:

$C_{25}H_{22}F_3N_5O_4S$

Pathway:

Metabolic Enzyme/Protease

Target:

Elastase

Purity / Grade:

>98%

Solubility:

DMSO : ≥ 33 mg/mL (60.49 mM)

Alternative Names:

AZD9668

Observed Molecular Weight:

545.53

Product Description

Alvelestat (AZD9668) is a novel, oral inhibitor of neutrophil elastase (NE) with the pIC₅₀ of 7.9 for Human NE.

IC₅₀ Value: 7.9 ± 0.12 (pIC₅₀, Human NE); 4.9 nM (K_i value, Human NE) [1]

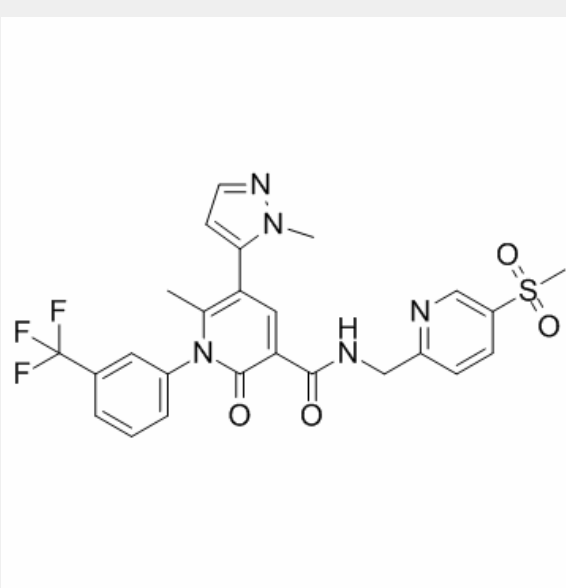
Target: Neutrophil elastase

in vitro: AZD9668 had a high binding affinity for human NE (K_D = 9.5 nM) and potently inhibited NE activity. The calculated pIC₅₀ (IC₅₀) and K_i values for AZD9668 for human NE were 7.9 (12 nM) and 4.9 nM, respectively. In contrast to earlier NE inhibitors, the interaction between AZD9668 and NE was rapidly reversible. AZD9668 was also highly selective for NE over other neutrophil-derived serine proteases. In cell-based assays, AZD9668 inhibited plasma NE activity in zymosan-stimulated whole blood. In isolated human polymorphonuclear cells, AZD9668 inhibited NE activity on the surface of stimulated cells and in the supernatant of primed, stimulated cells. AZD9668 showed good crossover potency to NE from other species [1].

in vivo: Six hundred and fifteen patients were randomised: placebo (302), AZD9668 60 mg bid (313). AZD9668 showed no effect on lung function: change in mean pre-bronchodilator FEV₁ versus placebo was 0.01L (95% confidence interval: -0.03, 0.05; p=0.533). AZD9668 did not significantly improve respiratory signs and symptoms, SGRQ-C score or time to first exacerbation. Adverse events were similar for AZD9668 and placebo [2]. AZD9668 was well tolerated at single doses up to 150 mg and multiple doses up to 70 mg twice daily. PK were dose linear; median time to peak plasma concentration was reached at 0.5 - 1.5 hours and the short elimination half-life was consistent with twice daily dosing. Steady state was reached by Day 2 of twice daily dosing with negligible accumulation. Approximately 40% of AZD9668 was eliminated renally as unchanged compound. Ex vivo zymosan-stimulated inhibition of NE activity was dose-dependent, with maximal inhibition achieved at 60 mg [4].

Toxicity: A total of 838 patients were randomised to AZD9668 5 mg bid (212 patients), 20 mg bid (206 patients), 60 mg bid (202 patients) or placebo (218 patients). AZD9668 showed no effect on lung function, respiratory signs and symptoms, QoL or biomarkers [3].

Clinical trial: Phase II study of a neutrophil elastase inhibitor (AZD9668) in patients with bronchiectasis.



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