Web: www.taiclone.com
Tel: +886-2-2735-9682
Email: order@taiclone.com

BMS-378806

Catalog No: tcsc0525

Available Sizes

Size: 5mg

Size: 10mg

Size: 50mg

Size: 100mg

Specifications

CAS No:
357263-13-9

Formula:
$C_{22}H_{22}N_4O_4$

Pathway:
Anti-infection

Target:
HIV

Purity / Grade:
>98%

Solubility:
10 mM in DMSO

Alternative Names:
BMS-806

Observed Molecular Weight:
406.43

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Product Description

BMS-378806 is a potent **HIV-1** attachment inhibitor that interferes with CD4-gp120 interactions. BMS-378806 selectively inhibits the binding of HIV-1 gp120 to the CD4 receptor with **EC_{50}** of 0.85-26.5 nM in virus.

IC50 & Target: HIV[1]

In Vitro: In a series of biochemical assays, BMS-378806 is not an effective inhibitor of HIV integrase, protease, or reverse transcriptase, but did compete with soluble CD4 binding to a monomeric form of gp120 in an ELISA assay with IC_{50}=100 nM. The specificity of BMS-378806 toward inhibition of HIV-1 is confirmed by evaluation against HIV-2, SIV, MuLV, RSV, HCMV, BVDV, VSV, and influenza virus, with no significant inhibitory activity observed at concentrations ranging from 10 to 30 μM and no overt cytotoxicity toward the host cells, CC_{50}>225 μM. BMS-378806 is not a potent inhibitor of any of the five major human CYP isoforms, evaluated as recombinant preparations, with IC_{50} values of >100 μM for CYP1A2 and CYP2C9, 23 μM for CYP2C19, 20 μM for CYP2D6, and 39 to 81 μM for CYP3A4. Moreover, since BMS-378806 is metabolized by CYP450 1A2, 2D6, and 3A4, it is unlikely to lead to severe drug−drug interactions in a clinical setting[1]. BMS-378806 inhibits viral replication by interfering with the binding interactions of gp120 with the cellular CD4 receptor. The IC_{50}s determined for the gp120s from HIV LAI, BAL, NA420LN40, SF162, NL4-3, NA420B33, YU2, AD8, JRCSF, and 92US15.6 are 0.1, 0.1, 0.3, 0.5, 0.6, 0.7, 0.9, 1.0, 1.1, and 1.6 μM, respectively. A similar observation is also made for BMS-378806 (IC_{50}s range from 0.2 to 9.6 μM)[2]. BMS-378806 binds directly to gp120 at a stoichiometry of approximately 1:1, with a binding affinity similar to that of soluble CD4. The potential BMS-378806 target site is localized to a specific region within the CD4 binding pocket of gp120 by using HIV-1 gp120 variants carrying either compound-selected resistant substitutions or gp120-CD4 contact site mutations[3].

In Vivo: In toxicology studies, BMS-378806 is well tolerated in rats at doses of 100 mg/kg/day for 2 weeks and in dogs at doses of 90 mg/kg for 10 days. The dose-proportional increases in the AUC and C_{max} are observed between doses of 5 and 25 mpk, when BMS-378806 is administered either in the solution or suspension formulation. In all three species, plasma levels of drug exceeded the concentrations required to half-maximally inhibit virus replication in vitro. The volume of distribution of BMS-378806 ranges from 0.4 to 0.6 L/kg, indicative of partitioning beyond plasma; however, examination of brain levels in the rat reveals minimal CNS penetration [1].

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