Pirmitegravir

Cat. No.: HY-130000

CAS No.: 2245231-10-9

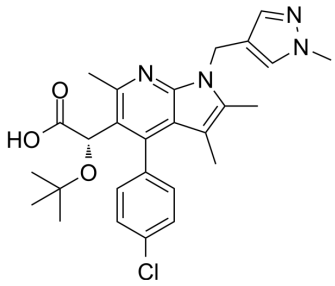
Molecular Formula: $C_{27}H_{31}ClN_4O_3$

Molecular Weight: 495.01

Target: HIV Integrase; HIV

Pathway: Metabolic Enzyme/Protease; Anti-infection

Storage: Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description

Pirmitegravir is a potent and first-in-class inhibitor of allosteric integrase (ALLINI) that targets LEDGF/p75 binding site. Pirmitegravir displays picomolar IC_{50} in human PBMCs with a >24,000 therapeutic index against HIV-1. Pirmitegravir harbors outstanding anti-virus and safety properties[1].

IC_{50} & Target

allosteric integrase (ALLINI)[1]

In Vitro

Pirmitegravir (Compound STP0404) inhibits dual tropic HIV-189.6 at 1.4 nM IC_{50} in CEMx174 cells[1].
Pirmitegravir (Compound STP0404) is a highly potent ALLINI with picomolar to single-digit nanomolar IC_{50} values that inhibits both wild type and Ral-resistant HIV-1 strains[1].
Pirmitegravir (Compound STP0404) displays IC_{50} of 0.41 nM against HIV-1NL4-3 without observable cytotoxicity in human PBMCs at 10 μM (TC_{50} >10μM)[1].
MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Pirmitegravir (Compound STP0404) displays appropriate PK profiles for once daily administration[1].
Pirmitegravir (Compound STP0404) lacks micronucleus-inducing and bone marrow cell proliferation inhibitory potentials in rats (500, 1000 and 2000 mg/kg/day), supporting that STP0404 is not genotoxic[1].
Assessment of Pharmacokinetics (PK) profile of Pirmitegravir (Compound STP0404) in rat and dog[1].

PK Values	Rat		Dog	
	10 mg/kg (p.o)	5 mg/kg (i.v)	2 mg/kg (p.o)	2 mg/kg (i.v)
$T_{1/2}$ (hr)	4.56	3.83	6.90	6.11
AUC (hr.nM)	78074	42676	4683	9260
C_{max} (nM)	21380	-	3983	-
F_t (%)	92.8	-	50.6	-

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Model:	SD rats and beagle dogs[1]
Dosage:	1, 2, 5, and 10 mg/kg
Administration:	i.v.; p.o.
Result:	The half-life (T1/2) was 3–7 h, and oral bioavailability (Ft) was 50–93% in these two animal species. Systemic exposure, which was determined by area under the curve and maximum concentration of STP0404 in plasma (AUC and C_{max}), increased dose-dependently from 2 to 10 mg/kg.

REFERENCES

[1]. Maehigashi T, et al. A highly potent and safe pyrrolopyridine-based allosteric HIV-1 integrase inhibitor targeting host LEDGF/p75-integrase interaction site. PLoS Pathog. 2021;17(7):e1009671.

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