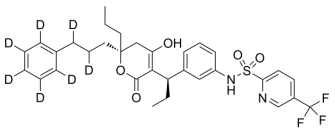
Tipranavir-d_7

Cat. No.:	HY-15148S1
Molecular Formula:	$C_{32}H_{28}D_7F_3N_2O_5S$
Molecular Weight:	623.73
Target:	HIV Protease; HIV; SARS-CoV; Isotope-Labeled Compounds
Pathway:	Anti-infection; Metabolic Enzyme/Protease; Others
Storage:	Please store the product under the recommended conditions in the Certificate of Analysis.



BIOLOGICAL ACTIVITY

Description	Tipranavir-d_7 is deuterated labeled Tipranavir (HY-15148). Tipranavir (PNU-140690) inhibits the enzymatic activity and dimerization of HIV-1 protease, exerts potent activity against multi-protease inhibitor (PI)-resistant HIV-1 isolates with IC_{50}s of 66-410 nM[1][2]. Tipranavir inhibits SARS-CoV-2 $3CL^{pro}$ activity[3].
In Vitro	Stable heavy isotopes of hydrogen, carbon, and other elements have been incorporated into drug molecules, largely as tracers for quantitation during the drug development process. Deuteration has gained attention because of its potential to affect the pharmacokinetic and metabolic profiles of drugs[1]. Tipranavir (PNU-140690) inhibits the enzymatic activity of HIV-1 protease, blocks the dimerization of protease subunits, and exerts potent activity against a wide spectrum of wild-type and multi-PI-resistant HIV-1 variants. When a mixture of 11 multi-PI-resistant (but TPV-sensitive) clinical isolates (HIV_{11MIX}), which include HIV_B and HIV_C, is selected against Tipranavir, HIV_{11MIX} rapidly (by 10 passages [HIV_{11MIX}^{P10}]) acquires high-level Tipranavir (PNU-140690) resistance and replicates at high concentrations of Tipranavir (PNU-140690). $cHIV_B^{I54V}$ and $cHIV_B^{I54V/V82T}$ are significantly resistant to Tipranavir (PNU-140690), with IC_{50}s of 2.9 and 3.2 μM, respectively, which are 11- and 12-fold increases in comparison to the IC_{50} against $cHIV_B$, respectively[2]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Tipranavir (PNU-140690) is administered orally twice daily and must be given in combination with low-dose ritonavir (RTV) to boost Tipranavir bioavailability. In Tipranavir/r-cotreated mice, the Tipranavir (PNU-140690) abundance in the liver, spleen, and eyes is significantly higher than that in mice treated with Tipranavir alone. Tipranavir (PNU-140690) metabolites accounts for 31 and 38% in the serum and liver in the Tipranavir-alone group. In Tipranavir (PNU-140690) and Tipranavir (TPV/r)-cotreated mice, only 1 and 2% of metabolites are detected in the serum and liver. Sprague-Dawley rats are administered a single dose of [^{14}C]Tipranavir (PNU-140690) with coadministration of RTV. The most abundant metabolite in feces is an oxidation metabolite. In urine, no single metabolite is found to be significantly present[3]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

REFERENCES

[1]. Qi Sun, et al. Bardoxolone and bardoxolone methyl, two Nrf2 activators in clinical trials, inhibit SARS-CoV-2 replication and its 3C-like protease. Signal Transduct Target Ther. 2021 May 29;6(1):212.

[2]. Li F, et al. Metabolism-mediated drug interactions associated with ritonavir-boosted tipranavir in mice. Drug Metab Dispos. 2010 May;38(5):871-8.

[3]. Aoki M, et al. Loss of the protease dimerization inhibition activity of tipranavir (TPV) and its association with the acquisition of resistance to TPV by HIV-1. J Virol. 2012

Dec;86(24):13384-96.

[4]. Russak EM, et al. Impact of Deuterium Substitution on the Pharmacokinetics of Pharmaceuticals. Ann Pharmacother. 2019 Feb;53(2):211-216.

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