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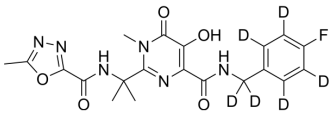
Raltegravir-d_6

Cat. No.:	HY-10353S1
CAS No.:	1100750-98-8
Molecular Formula:	$C_{20}H_{15}D_6FN_6O_5$
Molecular Weight:	450.45
Target:	HIV; HIV Integrase; 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	Raltegravir-d6 is a deuterated labeled Raltegravir[1]. Raltegravir is a potent integrase (IN) inhibitor, used to treat HIV infection.
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]. PFV IN carrying the S217H substitution is 10-fold less susceptible to Raltegravir with IC_{50} of 900 nM. PFV IN displays 10% of WT activity and is inhibited by Raltegravir with an IC_{50} of 200 nM, indicating a appr twofold decrease in susceptibility to the IN strand transfer inhibitor (INSTI) compared with WT IN. S217Q PFV IN is as sensitive to Raltegravir as the WT enzyme[2]. Raltegravir is metabolized by glucuronidation, not hepatically. Raltegravir has potent in vitro activity against HIV-1, with a 95% inhibitory concentration of 31±20 nM, in human T lymphoid cell cultures. Raltegravir is also active against HIV-2 when Raltegravir is tested in CEMx174 cells, with an $IC_{95}$of 6 nM. Raltegravir metabolism occurs primarily through glucuronidation. Drugs that are strong inducers of the glucuronidation enzyme, UGT1A1, significantly reduce Raltegravir concentrations and should not be used. Raltegravir exhibits weak inhibitory effects on hepatic cytochrome P450 activity. Raltegravir does not induce CYP3A4 RNA expression or CYP3A4-dependent testosterone 6-β-hydroxylase activity[3]. Raltegravir cellular permeativity is reduced in the presence of magnesium and calcium[4]. Raltegravir and related HIV-1 integrase (IN) strand transfer inhibitors (INSTIs efficiently block viral replication[5]. In acutely infected human lymphoid $CD4^+$ T-cell lines MT-4 and CEMx174, SIVmac251 replication is efficiently inhibited by Raltegravir, which shows an EC_{90} in the low nanomolar range[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.
In Vivo	Raltegravir induces viro-immunological improvement of nonhuman primates with progressing SIVmac251 infection. One non-human primate shows an undetectable viral load following Raltegravir monotherapy[6]. MCE has not independently confirmed the accuracy of these methods. They are for reference only.

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[4]. Hicks C, et al. Raltegravir: the first HIV type 1 integrase inhibitor. Clin Infect Dis. 2009 Apr 1;48(7):931-9

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