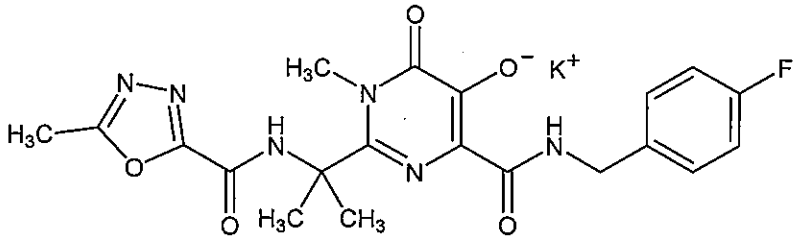
Raltegravir (USAN adopted name), also known as MK-0518, is a potent, HIV integrase strand transfer inhibitor active against the Human Immunodeficiency Virus (HIV-1) and represents the first in class HIV integrase inhibitor for the treatment of patients infected with the HIV. The chemical name for raltegravir potassium is *N*-[(4-Fluorophenyl)methyl]-1,6-dihydro-5-hydroxy-1-methyl-2-[1-methyl-1-[[(5-methyl-1,3,4-oxadiazol-2-yl)carbonyl]amino]ethyl]-6-oxo-4-pyrimidinecarboxamide monopotassium salt. Raltegravir is a white to off-white powder; it is soluble in water, slightly soluble in methanol, very slightly soluble in ethanol and acetonitrile and insoluble in isopropanol. The empirical formula is $C_{20}H_{20}FKN_6O_5$ and the molecular weight is 482.51. The structural formula is:



Raltegravir inhibits the catalytic activity of HIV integrase, an HIV-encoded enzyme that is required for viral replication. Inhibition of integrase prevents the covalent insertion, or integration, of the HIV genome into the host cell genome during the early phase of infection. HIV genomes that fail to integrate cannot direct the production of new infectious viral particles, so inhibiting integration prevents propagation of the viral infection. Raltegravir did not significantly inhibit human phosphoryltransferases including DNA polymerases α, β, and γ.

Raltegravir has been extensively evaluated in both in vitro and in vivo toxicity studies, including a standard battery of genetic toxicity studies (bacterial mutagenicity, chromosome aberration, and mouse micronucleus assays), to support clinical investigations and registration of this compound for use in combination with other anti-retroviral agents for the treatment of HIV–1 infection in treatment-experienced patients with evidence of HIV–1 replication despite ongoing antiretroviral therapy. This nonclinical evaluation has demonstrated the inhibition of the target enzyme within the HIV and is well-tolerated with no evidence of pharmacologically mediated toxicity in any species tested.

MRL has completed a comprehensive clinical pharmacology and clinical development program to support the use of raltegravir administered, in a combination regimen with other antiretroviral agents, at an oral dose of 400 mg twice daily without regard to food in patients with HIV infection. Extensive drug-drug interation studies have been completed, and two phase IIb and two phase III placebo-controlled clinical trials support the safety and efficacy of raltegravir in the treatment of the proposed patient population. Taken together, data from these clinical studies demonstrate a significant benefit for raltegravir in combination therapy with other ARTs for the treatment of HIV–1 infection in treatment-experienced patients with evidence of HIV–1 replication despite ongoing antiretroviral therapy. Taking into account the observed safety profile, the benefit-risk of raltegravir for the proposed indication is considered positive.