Raltegravir

Brand Name: Isentress
Drug Class: Integrase Inhibitors

Drug Description

Raltegravir, also known as MK-0518, is a first-in-its-class oral integrase inhibitor. Inhibition of integrase prevents insertion of HIV DNA into the human DNA genome, thus blocking the ability of HIV to replicate. [1]

HIV/AIDS-Related Uses

Raltegravir was approved by the FDA on October 12, 2007, for use with other antiretroviral agents in the treatment of HIV infection. It is the first integrase inhibitor approved by the FDA. This drug received accelerated approval for use in treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to multiple antiretroviral regimens. The FDA's decision was based on a 24-week clinical trial analysis, in which raltegravir with optimized background therapy (OBT) in treatment-experienced HIV infected patients led to significant reductions in HIV viral load and increases in CD4 counts.[2] [3] Raltegravir has also been investigated in Phase II trials for the treatment of HIV in patients who are treatment-naive.[4] [5] [6]

Two Phase III trials are ongoing to further investigate raltegravir in patients who have multidrug-resistant HIV strains.[7] On August 17, 2006, Merck opened a worldwide expanded access program (EAP) for HIV patients with limited or no treatment options. Patients and health care professionals can call 1-888-577-8839 or visit http://www.earmrk.com for more information. The EAP for raltegravir is a noncomparative, multicenter, open-label, voluntary treatment use study. The study will continue for a short time after FDA approval and the start of commercial marketing. Enrolled patients will receive twice-daily 400-mg raltegravir in addition to OBT; safety and tolerability will be monitored.[8]

On January 29, 2009, the FDA granted traditional approval for raltegravir, for use with other antiretroviral agents in the treatment of HIV infection in treatment-experienced adults.[9]

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Raltegravir inhibits the catalytic activity of HIV-1 integrase, an HIV-1-encoded enzyme required for viral replication. Inhibition of integrase prevents covalent insertion of unintegrated, linear HIV-1 DNA into the host cell genome, therefore preventing the formation of HIV-1 provirus. In preliminary studies, raltegravir did not significantly inhibit human phosphoryltransferases, including DNA polymerases alpha, beta, and gamma.[10] Raltegravir is associated with high performance against HIV in treatment-naïve and limited-treatment option patients, potentially because of its binding interaction with the HIV preintegration complex. When raltegravir binds to the complex, it dissociates at a rate slower than the half-life of the complex itself, which makes its binding essentially irreversible. Thus, efficacy of raltegravir may be dependent on intracellular binding levels of raltegravir to the preintegration complex, rather than on the serum levels of raltegravir.[11]

Raltegravir may be administered with or without food. Raltegravir was administered without regard to food in the pivotal safety and efficacy studies in HIV-infected patients. The effect of consumption of low-, moderate- and high-fat meals on steady-state raltegravir pharmacokinetics was assessed in healthy volunteers. Administration of multiple doses of raltegravir following a moderate-fat meal (600 Kcal, 21 g fat) did not affect raltegravir AUC to a clinically meaningful degree with an increase of 13% relative to fasting. Raltegravir C12 hr was 66% higher and Cmax was 5% higher following a moderate-fat meal compared to fasting. Administration of raltegravir following a high-fat meal (825 Kcal, 52 g fat) increased AUC and Cmax by approximately 2-fold and increased C12 hr by 4.1-fold. Administration of raltegravir following a low-fat meal (300 Kcal, 2.5 g fat) decreased AUC and Cmax by 46% and 52%, respectively; C12 hr was essentially unchanged. Food appears to increase pharmacokinetic variability relative to fasting. [12]

The raltegravir AUC and Cmax increase dose proportionally over the dose range of 100 mg to 1,600 mg. With twice-daily dosing, PK steady state

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is achieved within approximately the first 2 days of dosing. Considerable variability was observed in the PK of raltegravir in clinical trials. In clinical trial participants receiving twice-daily raltegravir 400 mg, drug exposures were characterized by a geometric mean AUC within the first 12 hours of 14.3 mcM(hr) and a plasma concentration at 12 hours of 142 nM. The absolute bioavailablilty of raltegravir has not been established.[13]

Carcinogenicity studies of raltegravir in mice did not show any carcinogenic potential. At the highest dose levels, 400 mg/kg/day in females and 250 mg/kg/day in males, systemic exposure was 1.8-fold (females) or 1.2-fold (males) greater than the AUC (54 ?M hr) at the 400-mg twice daily human dose. Treatment-related squamous cell carcinoma of nose/nasopharynx was observed in female rats dosed with 600 mg/kg/day raltegravir for 104 weeks. These tumors were possibly the result of local irritation and inflammation due to local deposition and/or aspiration of drug in the mucosa of the nose/nasopharynx during dosing. No tumors of the nose/nasopharynx were observed in rats dosed with 150 mg/kg/day(males) and 50 mg/kg/day (females) and the systemic exposure in rats was 1.7-fold (males) to 1.4-fold (females) greater than the AUC (54 ?M hr) at the 400-mg twice daily human dose.[14]

Raltegravir is in FDA Pregnancy Category C. No adequate or well-controlled studies of raltegravir have been done in pregnant women; also, no PK studies have been conducted to date in pregnant women. In animal studies, no treatment-related effects on embryonic/fetal survival or fetal weights were observed in rabbits (up to 1,000 mg/kg/day) and rats (up to 600 mg/kg/day) receiving up to three- to four-fold the exposure at the recommended human dose of raltegravir. No treatment-related external, visceral, or skeletal changes were observed in rabbits. However, treatment-related increases compared with controls in the incidence of supernumerary ribs were seen in rats at dosages of 600 mg/kg/day (exposures threefold the exposure at the recommended human dose of raltegravir). Plasma transfer of raltegravir was demonstrated in both rabbits and rats. At a maternal dosage of 600 mg/kg/day in rats, mean raltegravir concentrations in fetal plasma were approximately 1.5- and 2.5-fold greater than in maternal plasma at 1 hour and 24 hours postdose, respectively. Mean raltegravir concentrations in fetal plasma were approximately 2% of the mean maternal concentration at both 1 and 24 hours post-dose at a maternal dosage of 1,000 mg/kg/day in rabbits.[15]

Raltegravir should be used during pregnancy only if clearly needed. To monitor maternal-fetal outcomes of pregnant women exposed to raltegravir and other antiretroviral agents, an Antiretroviral Pregnancy Registry has been established. Physicians may register patients online at http://www.APRegistry.com or by calling 1-800-258-4263. It is not known whether raltegravir or its metabolites are distributed into human milk; however, raltegravir is secreted into the milk of lactating rats. Mean raltegravir concentrations in milk were approximately threefold greater than those in maternal plasma at a maternal dosage of 600 mg/kg/day in rats. Because of both the potential for HIV transmission and serious adverse reactions in nursing infants, HIV-infected mothers should be instructed not to breastfeed their infants if they are receiving raltegravir.[16]

Raltegravir is approximately 83% bound to human plasma protein over the concentration range of 2 to 10 mcM. The apparent terminal half-life of raltegravir is approximately 9 hours, with a shorter alpha-phase half-life (about 1 hour) accounting for much of the AUC. Following administration of an oral dose of radiolabeled raltegravir, approximately 51% and 32% of the dose was excreted in feces and urine, respectively. In feces, only raltegravir was present, most of which is likely derived from hydrolysis of raltegravir-glucuronide secreted in bile as observed in preclinical trials in animals. Two components, raltegravir and raltegravir-glucuronide, were detected in urine and accounted for approximately 9% and 23% of the dose, respectively. The major circulating compound was raltegravir, which represented 70% of the radioactivity; the remaining radioactivity in plasma was accounted for by raltegravir-glucuronide. Studies using isoform-selective chemical inhibitors and cDNA-expressed uridine diphosphate glucuronosyltransferases (UGTs) show that

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UGT1A1 is the main enzyme responsible for formation of raltegravir-glucuronide; thus, the data indicate the major mechanism of clearance of raltegravir in humans is UGT1A1-mediated glucuronidation.[17]

A two-part, Phase II, dose-ranging trial in treatment-naive patients compared 10-day raltegravir monotherapy in 28 patients with placebo in 7 patients. At least 50% of patients in each raltegravir dose group achieved a viral load of at least 400 copies/ml by Day 10.[18] After 16 weeks of therapy, dosages of raltegravir 100, 200, 400, or 600 mg twice daily achieved greater than 50-fold viral load level reductions. In 50% to 57% of patients taking raltegravir, viral load levels decreased to less than 400 copies/ml and to less than 50 copies/ml in 13% to 29% of patients.[19] All dose groups had superior, statistically significant antiretroviral activity compared with placebo.[20] In the second part of the study, 198 treatment-naive patients were randomly assigned to receive either the same dosages of raltegravir twice daily or efavirenz 600 mg once daily, both in combination with tenofovir disoproxil fumarate and lamivudine. At Week 24 of therapy, 85% to 95% of patients on raltegravir-based regimens achieved viral load levels less than 50 copies/ml across all dosages. In the efavirenz-based regimen, 92% of patients achieved viral load levels less than 50 copies/ml. By Week 48, these viral reductions had been maintained by 85% to 98% of raltegravir-receiving patients and by 83% to 88% of efavirenz-receiving patients.[21] Viral loads became undetectable more rapidly in patients who received raltegravir at any dose than in those who received efavirenz. CD4 cell responses were similar among treatment arms. Virologic failure occurred in 3% of patients in each group; of the 5 raltegravir recipients who experienced virologic failure before Week 48, 2 had viruses with the N155H amino acid substitution, a mutation known from in vitro experiments to be selected by raltegravir.[22] Viral load reduction was achieved more quickly with the raltegravir regimen compared with the efavirenz regimen; however, the overall potent and durable antiretroviral activity of raltegravir was otherwise similar to efavirenz at Weeks 24 and 48.[23]

A second Phase II, randomized, double-blind, placebo-controlled trial compared 200, 400, and 600 mg twice-daily dosages of raltegravir with placebo; all patients received optimized background therapy (OBT). All 179 patients enrolled had viral loads of greater than 5,000 copies/ml, were failing highly active antiretroviral therapy (HAART), and had resistance to at least one drug in each anti-HIV drug class. At Week 24 analysis, mean viral load decreases from baseline observed in all the raltegravir-receiving groups and the placebo group were 99% and 50%, respectively. Four patients discontinued the study because of adverse events: 3 (2%) across all raltegravir-treated groups and 1 (2%) in the placebo group. Forty-one study participants (14 [11%] across all raltegravir-treated groups and 27% [60%] in the placebo group) discontinued because of lack of efficacy of their treatment assignments. Raltegravir at all doses studied provided better viral suppression than placebo when added to OBT.[24]

In a Phase III, double-blind study that involved 563 treatment-naïve patients with no antiretroviral resistance, raltegravir plus tenofovir/emtricitabine was compared with efavirenz plus tenofovir/emtricitabine after 48 weeks of treatment. Virologic suppression was achieved in 86% of raltegravir-treated patients compared with 82% of efavirenz-treated patients, and patients in the raltegravir arm experienced significantly shorter times to suppression. Patients treated with raltegravir also experienced a mean CD4 T-cell increase of 189 cells/mm3 compared with a mean increase of 163 cells/mm3 in the efavirenz-treated group.[25]

Two ongoing Phase III, randomized, double-blind, placebo-controlled trials in participants failing HAART on OBT are evaluating the efficacy, safety, and tolerability of raltegravir.[26] [27] These trials, BNCHMRK-1 and -2, are triple-blind, randomized studies that compare oral raltegravir 400 mg twice daily with placebo in addition to OBT in HIV-infected participants. All participants were failing existing HAART regimens and were resistant to three classes of oral anti-HIV drug therapy. Each trial includes more than 200 participants in the treatment arms and more than 100 in the placebo arms. Primary endpoints for both studies are CD4 count increases from baseline,

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percentage of participants with viral load reduction to less than 400 copies/ml, and percentage of participants with viral load reduction to less than 50 copies/ml. Raltegravir demonstrated superior efficacy compared with placebo in all endpoints at Week 16, Week 24, and Week 48 interim analyses. In BNCHMRK-1's Week 16 analysis, viral load decreased to less than 400 copies/ml in 77% of treatment arm participants and in 41% of placebo arm participants. Viral load decreased to less than 50 copies/ml in 61% and 33% of treatment arm and placebo arm participants, respectively. CD4 counts increased from baseline on average by 83 cells/mm3 and by 31 cells/mm3 in treatment and placebo arms, respectively. At 48 Weeks, the percentage of participants with viral load levels less than 50 copies/ml was statistically significantly greater in the treatment arm compared with the placebo arm, with a difference of 22% to 43% ($p < 0.001$). A total of 74% of patients in the treatment arm (compared with 75% at Week 24) had viral load levels less than 400 copies/ml; 65% of treatment-arm patients (compared with 60% at Week 24) has viral load levels less than 50 copies/ml.[28] In BNCHMRK-2's Week 16 analysis, 77% of treatment arm participants and 43% of placebo-arm participants displayed viral load levels less than 400 copies/ml. The analysis also showed that 62% of the treatment-arm participants and 36% of the placebo arm participants displayed levels less than 50 copies/ml. CD4 counts increased from baseline by 86 cells/mm3 in treatment-arm participants and by 40 cells/mm3 in placebo-arm participants. Endpoint differences were statistically significant in favor of raltegravir efficacy in both trials.[29] [30] In analysis of BNCHMRK-2 at Week 48, viral load levels reached less than 400 copies/ml in 71% of treatment-arm patients and less than 50 copies/ml in 60%. The difference of 14% to 35% between treatment and placebo arms at achieving viral load levels less than 50 copies/ml was statistically significant in favor of raltegravir as well ($p < 0.001$).[31]

Raltegravir 400 mg twice daily was substituted for enfuvirtide in multi-drug regimens of 29 patients with multi-drug-resistant HIV who had viral load levels less than 50 copies/ml. Viral load levels remained consistent and suppressed, and the change appeared safe and effective at all time points (1, 2, 3, and 4 months).[32]

Raltegravir at concentrations of 6 to 50 nM resulted in 95% inhibition (EC95) of viral spread in mitogen-activated human peripheral blood mononuclear cells (PBMCs) infected with diverse, primary clinical isolates of HIV-1, including isolates resistant to reverse transcriptase inhibitors and protease inhibitors (PIs). Raltegravir also inhibited replication of an HIV-2 isolate when tested in CEMx174 cells (EC95 value = 6 nM). Additive to synergistic antiretroviral activity was observed when human T cells infected with the H9IIIB variant of HIV-1 were incubated with raltegravir in combination with non-nucleoside reverse transcriptase inhibitors (delavirdine, efavirenz, and nevirapine), nucleoside analog reverse transcriptase inhibitors (abacavir, didanosine, lamivudine, stavudine, tenofovir, zalcitabine, and zidovudine), PIs (amprenavir, atazanavir, indinavir, lopinavir, nelfinavir, ritonavir, and saquinavir), or the entry inhibitor enfuvirtide.[33]

Mutations observed in the HIV-1 coding sequence that contributed to raltegravir resistance (evolved from either in cell culture or in clinical trial participants who receive raltegravir) generally included an amino acid substitution at either Q148 (changed to H, K, or R) or N155 (changed to H) plus one or more substitutions (e.g., L74M/R, E92Q, T97A, E138A/K, G140/S, V151I, G163R, H183P, Y226C/D/F/H, S230R, D232N). Amino acid substitution at Y143C/H/R is another pathway to raltegravir resistance. By Week 48 in the BENCHMRK trials, at least one of the 3 primary raltegravirresistance-associated substitutions, Y143C/H/R, Q148H/K/R, and N155H, was observed in 63 (64.3%) of the 98 virologic failure subjects with evaluable genotypic data from paired baseline and raltegravir treatment-failure isolates. Some (n=18) of those HIV isolates harboring one or more of the 3 primary raltegravir resistance-associated substitutions were evaluated for raltegravir susceptibility yielding a median decrease of 47.3-fold (mean 73.1 ± 60.8-fold decrease, ranging from 0.9- to 200-fold) compared to baseline isolates.[34]

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In ongoing analyses of the Phase III BENCHMRK studies in treatment-experienced, antiretroviral-resistant, HIV-infected patients, genotypes from 64 patients were evaluated after new resistance mutations developed during virologic failure. Mutants N155, Q148, and Y143 occurred in most of these patients, and Q148H was the dominant resistance mutation. Resistance mutations were replaced with others on follow-up genotypes; although 27% of genotypes had more than two resistance mutations at first evaluation, 47% had more than two mutations on a second evaluation. Secondary mutations to Q148 increased resistance several hundredfold compared with secondary N155H mutations. Mutations to Q148 and N155 affect the dissociation rate of raltegravir, rather than the binding of raltegravir, to the preintegration complex.[35]

In a resistance study of another investigational integrase inhibitor, GS-9137, site-directed mutant viruses carrying the T66I mutation remained susceptible to raltegravir. However, mutant viruses with the E92Q mutation experienced resistance to GS-9137 and cross resistance to raltegravir.[36] No cross resistance to approved antiretrovirals has been observed with raltegravir.[37]

Adverse Events/Toxicity

In Phase II studies, the most commonly reported treatment-related adverse effects were diarrhea, nausea, fatigue, headache, and itching. Other reported adverse effects included constipation, flatulence, and sweating. Overall, raltegravir was well tolerated, and its adverse effects were comparable to those in the placebo group.[38] [39] In the second part of one Phase II study, the most common adverse effects occurring after 24 weeks of treatment were headache, dizziness, and nausea. Eight serious, nondrug-related adverse effects occurred overall (7/160 in the raltegravir arm and 1/38 in the efavirenz arm); one patient taking twice-daily raltegravir 600 mg discontinued treatment because of elevated liver function tests. Drug-related clinical adverse events were less common with raltegravir than with efavirenz.[40]

Raltegravir has been generally well tolerated in ongoing Phase III studies (BENCHMRK-1 and -2) as well. The most common adverse effects of all intensities, regardless of causality, reported in treatment-experienced adult study participants so far include diarrhea, nausea, headache, and pyrexia.[41] [42] Additionally, Grade 2 to 4 creatine kinase laboratory abnormalities were observed in clinical trial participants treated with raltegravir.[43] The manufacturer notes that because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be compared directly to rates in the clinical trials of another drug and may not reflect rates observed in practice.[44]

In a Phase III, double-blind study in treatment-naïve HIV-infected patients, those in the raltegravir arm experienced lower rates of drug-related adverse effects compared with those in the efavirenz arm (44% vs. 77%, respectively). Central nervous system toxicity occurred in 10% of raltegravir-treated patients compared with 18% of efavirenz-treated patients.[45]

Immune reconstitution syndrome has been reported in patients treated with combination antiretroviral therapy; this may include raltegravir-containing regimens. During the initial phase of combination antiretroviral treatment, a patient whose immune system improves may develop an inflammatory response to indolent or residual opportunistic infections, (e.g., Mycobacterium avium infection, cytomegalovirus infections, Pneumocystis jirovecii pneumonia, tuberculosis, or reactivation of varicella zoster virus), which may necessitate further evaluation and treatment.[46]

In the clinical studies, P018 and P019, participants with chronic (but not acute) active hepatitis B and/or hepatitis C virus co-infection were permitted to enroll provided that baseline liver function tests did not exceed 5 times the upper limit of normal (ULN). The rates of AST and ALT abnormalities were higher in the subgroup of participants with hepatitis B and/or hepatitis C virus co-infection for both treatment groups. In general the safety profile of raltegravir in subjects with hepatitis B and/or hepatitis C virus co-infection was similar to subjects without hepatitis B and/or hepatitis C virus co-infection. Grade 2 or higher laboratory abnormalities that represent a worsening Grade

Adverse Events/Toxicity (cont.)

from baseline of AST, ALT or total bilirubin occurred in 25%, 31% and 12%, respectively, of co-infected subjects treated with raltegravir as compared to 8%, 7% and 8% of all other subjects treated with raltegravir.[47]

The following adverse reactions have been identified during postapproval use of raltegravir. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Skin and Subcutaneous Tissue Disorders: rash, Stevens-Johnson syndrome; Psychiatric Disorders: depression (particularly in patients with a pre-existing history of psychiatric illness), including suicidal ideation and behaviors.[48]

Carcinogenicity studies of raltegravir in mice did not show any carcinogenic potential. At the highest dose levels, 400 mg/kg/day in females and 250 mg/kg/day in males, systemic exposure was 1.8-fold (females) or 1.2-fold (males) greater than the AUC (54 µM?hr) at the 400-mg twice daily human dose. Treatment related squamous cell carcinoma of nose/nasopharynx was observed in female rats dosed with 600 mg/kg/day raltegravir for 104 weeks. These tumors were possibly the result of local irritation and inflammation due to local deposition and/or aspiration of drug in the mucosa of the nose/nasopharynx during dosing. No tumors of the nose/nasopharynx were observed in rats dosed with 150 mg/kg/day (males) and 50 mg/kg/day (females) and the systemic exposure in rats was 1.7-fold (males) to 1.4-fold (females) greater than the AUC (54 µM hr) at the 400-mg twice daily human dose.[49]

Drug and Food Interactions

Based on the results of drug interaction studies and clinical trials data, no dose adjustment of raltegravir is required when raltegravir is coadministered with antiretroviral agents.[50] The addition of enfuvirtide to a raltegravir-containing regimen appears to increase virologic response. At Week 24 analysis of one dose-ranging study conducted in treatment-experienced, HIV infected participants, viral load decreased to less than 400 copies/ml in 60% of participants receiving raltegravir monotherapy and in 90% of patients receiving combined raltegravir and enfuvirtide.[51]

Raltegravir should be used with caution when administered with strong inducers of uridine diphosphate glucuronosyltransferase (UGT1A1), including rifampin. These inducers of UGT1A1 may reduce plasma concentrations of raltegravir.[52] Similar to rifampin, ritonavir-boosted tipranavir reduces plasma concentrations of raltegravir. However, in clinical trials, comparable efficacy of raltegravir was observed in this treatment group when compared with study participants not receiving ritonavir-boosted tipranavir.[53]

Drugs that inhibit UGT1A1 may increase plasma levels of raltegravir. Clinical trial data suggested that concomitant use of raltegravir and atazanavir (a strong inhibitor of UGT1A1) boosted with ritonavir caused increased plasma concentrations of raltegravir. However, this increase was not significant enough to warrant dose adjustment when coadministering raltegravir and atazanavir.[54]

Raltegravir may be taken with or without food.[55] Raltegravir was administered without regard to food in the pivotal safety and efficacy studies in HIV-infected patients. The effect of consumption of low-, moderate- and high-fat meals on steady-state raltegravir pharmacokinetics was assessed in healthy volunteers. Administration of multiple doses of raltegravir following a moderate-fat meal (600 Kcal, 21 g fat) did not affect raltegravir AUC to a clinically meaningful degree with an increase of 13% relative to fasting. Raltegravir C12 hr was 66% higher and Cmax was 5% higher following a moderate-fat meal compared to fasting. Administration of raltegravir following a high-fat meal (825 Kcal, 52 g fat) increased AUC and Cmax by approximately 2-fold and increased C12 hr by 4.1-fold. Administration of raltegravir following a low-fat meal (300 Kcal, 2.5 g fat) decreased AUC and Cmax by 46% and 52%, respectively; C12 hr was essentially unchanged. Food appears to increase pharmacokinetic variability relative to fasting.[56]

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Contraindications

Caution is recommended when coadministering raltegravir with other strong UGT1A1 inducers due to reduced raltegravir plasma concentrations.[57]

In drug interaction studies, raltegravir did not have a clinically meaningful effect on the pharmacokinetics of the following: hormonal contraceptives, lamivudine, tenofovir, etravirine.[58]

Clinical Trials

For information on clinical trials that involve Raltegravir, visit the ClinicalTrials.gov web site at http://www.clinicaltrials.gov. In the Search box, enter: Raltegravir AND HIV Infections.

Dosing Information

Mode of Delivery: Oral.[59]

Dosage Form: Tablets containing raltegravir 400 mg.[60]

The recommended dose of raltegravir in treatment-experienced HIV-infected adults is one 400-mg tablet twice daily.[61] No dosage adjustment is necessary in patients with mild to moderate hepatic or severe renal impairment.[62] For patients undergoing coadministration with rifampin, the recommended dose of raltegravir has been increased to 800 mg twice daily.[63]

Raltegravir 100, 200, 400, or 600 mg taken every 12 hours and given for up to 48 weeks was previously studied in a Phase II trial.[64]

Storage: Store tablets at a controlled room temperature of 20 C to 25 C (68 F to 77 F); excursions are permitted to 15 C to 30 C (59 F to 86 F).[65]

Chemistry

CAS Name: 4-Pyrimidinecarboxamide, 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- monopotassium salt[66]

CAS Number: 518048-05-0[67]

Molecular formula: C20-H20-F-K-N6-O5 (monopotassium salt)[68]

Molecular weight: 482.51[69]

Physical Description: White to off-white powder (as a potassium salt).[70]

Solubility: Soluble in water, slightly soluble in methanol, very slightly soluble in ethanol and acetonitrile, and insoluble in isopropanol.[71]

Other Names

MK0158[72]

MK-0518[73]

RAL[74]

Further Reading

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Manufacturer Information

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One Merck Dr
P.O. Box 100
Whitehouse Station, NJ 08889-0100
(800) 609-4618

Raltegravir
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(800) 609-4618

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

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