

Raltegravir (*Isentress*)

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Drug Summary

Raltegravir was the first integrase inhibitor approved by the United States Food and Drug Administration. Raltegravir is an excellent antiretroviral therapy option because it has relatively good tolerability, no food requirements, few drug interactions, and limited metabolic adverse effects. For years, raltegravir has been widely used in initial antiretroviral therapy, in treatment-experienced patients who do not have HIV integrase resistance, and for postexposure prophylaxis. Until recently, raltegravir has been approved only for twice daily dosing (400 mg twice daily dosing), but, in May 2017, the U.S. Food and Drug Administration approved once daily dosing with 1200 mg (two 600 mg tablets). Failure of a regimen containing raltegravir often results in drug resistance mutations that confer resistance to both raltegravir and elvitegravir; cross-resistance to dolutegravir also may be present with more extensive raltegravir resistance.

Key Clinical Trials

In antiretroviral therapy-naïve individuals with wild-type virus, raltegravir plus two NRTIs was shown to be noninferior to efavirenz [[STARTMRK](#)], noninferior to dolutegravir [[SPRING-2](#)], and superior to ritonavir-boosted darunavir or ritonavir-boosted atazanavir based on a combined endpoint of virologic efficacy and tolerability [[ARDENT \(ACTG 5257\)](#)]. In patients with drug-resistant HIV but no previous treatment with integrase inhibitors, raltegravir plus an optimized background regimen resulted in significantly higher rates of HIV suppression than placebo plus optimized regimen [[BENCHMRK 1 and 2](#)], but lower rates of HIV suppression as compared with dolutegravir plus optimized regimen [[SAILING](#)]. A phase 3 trial is in progress evaluating once daily 1200 mg raltegravir (2 x 600 mg tablets) versus standard dose raltegravir 400 mg twice daily, both given with tenofovir DF-emtricitabine [[ONCEMRK \[unpublished\]](#)]. Results from this study at week 48 showed viral suppression in 88% of the participants in the once daily raltegravir arm versus 89% of those individuals taking twice daily raltegravir.

Adverse Effects

Raltegravir is generally well-tolerated; adverse effects to raltegravir are uncommon and usually mild. Headaches, muscle aches, rash, and hypersensitivity reaction have infrequently been reported. The rare hypersensitivity reactions have included Drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome.

Use In Pregnancy

In the HHS Perinatal Guidelines section Recommendations for Use of Antiretroviral Drugs During Pregnancy (last updated October 19, 2017), **raltegravir** plus a Two-NRTI Backbone is designated as the Preferred Integrase Inhibitor Regimen in the category Preferred Initial Regimens in Pregnancy.

- For additional information regarding the safety and toxicity of raltegravir in pregnancy see the HHS Perinatal Guidelines summary on [Raltegravir](#).
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Resistance

For a listing of the most common clinically significant mutations associated with raltegravir (RAL) resistance, see the [INSTI Resistance Notes on the Stanford University HIV Drug Resistance Database](#).

Key Drug Interactions

The HIV Insite Database of Antiretroviral Drug Interactions for [Raltegravir \(Isentress\)](#). For complete information on raltegravir-related drug interactions, see the [Drug Interactions section in the Raltegravir \(Isentress\) Prescribing Information](#).
