Rilpivirine (*Edurant*)

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**Drug Summary**

Rilpivirine, a non-nucleoside reverse transcriptase inhibitor (NNRTI), offers several advantages, but also several drawbacks as compared to other anchor antiretroviral agents. Rilpivirine is generally well tolerated and has less effect on serum lipid markers as compared to older NNRTIs. For initial therapy, rilpivirine is not recommended for individuals with an HIV RNA level above 100,000 copies/mL or a CD4 count less than 200 cells/mm$^3$ due to inferior virologic response rates in those groups. In addition, it must be taken with a meal and it is contraindicated for individuals who are taking a proton pump inhibitor. Rilpivirine has a relatively low barrier to resistance, and the emergence of resistance-associated mutations while taking rilpivirine frequently results in cross-resistance to other NNRTIs. Several recent trials have investigated the use of rilpivirine (in standard tablet formulation and as a long-acting nanosuspension injectable formulation) in combination with one other antiretroviral agent as part of a two-drug combination maintenance strategy.

**Key Clinical Trials**

Rilpivirine was compared head-to-head with efavirenz in two major phase 3 trials—one compared the fixed-dose combinations rilpivirine-tenofovir DF-emtricitabine with efavirenz-tenofovir DF-emtricitabine [*ECHO (C209)*] and the other compared rilpivirine and efavirenz both given with two NRTIs [*THRIVE (C215)*]. These trials demonstrated similar virologic efficacy between rilpivirine and efavirenz, except more virologic failures occurred in the rilpivirine arm among the subset of participants with a baseline HIV RNA greater than 100,000 copies/mL or CD4 count less than 200 cells/mm$^3$. Virologic failure on the rilpivirine-containing regimens led to higher rates of NNRTI resistance and cross-resistance when compared with virologic failure on efavirenz. Several studies evaluated switching to the rilpivirine-tenofovir DF-emtricitabine single-tablet regimen from other antiretroviral regimens, including two NRTIs plus a boosted protease inhibitor [*SPIRIT (GS-264-0106)*] and from efavirenz-tenofovir DF-emtricitabine [*GS-264-0111*]. In both of these studies, participants had good maintenance of virologic suppression following the switch, but these studies had strict inclusion criteria and included only carefully selected patients.
**Adverse Effects**

Rilpivirine is generally well tolerated, but adverse effects can include headache, insomnia, depression, rash, or elevated hepatic aminotransferase levels. Supratherapeutic doses of rilpivirine can cause QT prolongation; therefore, caution should be used when coadministering rilpivirine-containing therapy with other QT prolonging agents, and QT should be monitored in this setting.

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**Resistance**

For a listing of the most common clinically significant mutations associated with rilpivirine (RPV) resistance, see the [NNRTI Resistance Notes on the Stanford University HIV Drug Resistance Database](https://www.hiv.uw.edu/page/treatment/drugs/rilpivirine).

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**Key Drug Interactions**

For complete information on rilpivirine-related drug interactions, see the [Drug Interactions section in the Rilpivirine (Edurant) Prescribing Information](https://www.hiv.uw.edu/page/treatment/drugs/rilpivirine).