Etravirine (*Intelence*)

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**Drug Summary**

Etravirine is a later generation non-nucleoside reverse transcriptase inhibitor (NNRTI) that usually retains some activity in the setting of common NNRTI resistance-associated mutations. It is typically used as part of salvage therapy and not as a component of initial antiretroviral treatment. Etravirine is generally well tolerated, but the recommended dosing requires twice daily administration after a meal. In addition, etravirine has important drug interactions with some other antiretroviral medications, notably with dolutegravir and with ritonavir-boosted atazanavir. The effectiveness of etravirine as a second-line NNRT can be compromised by high-level resistance to etravirine in patients who have virologic failure with an earlier generation NNRTI. The degree of resistance to etravirine depends on the number and specific mutations that develop; several specific scoring systems can be used to predict the antiviral activity of etravirine in patients with NNRTI resistance. A unique feature of etravirine is that it dissolves in water and can be taken immediately after dispersion in water; this feature provides an antiretroviral medication option for patients who may have difficulty or an inability to swallow pills. Studies have shown that in certain circumstances etravirine can be effective if given once daily but it is only FDA approved for twice-daily dosing.

**Key Clinical Trials**

Data for etravirine as part of initial antiretroviral therapy are limited. A phase 2 randomized trial that compared once-daily etravirine to efavirenz, each with two nucleoside reverse transcriptase inhibitors (NRTIs), found non-inferior rates of virologic suppression at 48 weeks; etravirine caused fewer neuropsychiatric adverse events than efavirenz [SENSE]. In a single-arm, open-label study, once-daily etravirine given with tenofovir disoproxil fumarate (DF)-emtricitabine was only moderately successful, with 77% of patients achieving an HIV RNA less than 50 copies/mL [08-2070]. For treatment-experienced individuals, two trials that enrolled participants with detectable viremia and documented NNRTI resistance plus protease inhibitor resistance demonstrated improved virologic responses with use of twice-daily etravirine plus optimized background regimen as compared to placebo plus optimized background regimen; all participants in these trials received ritonavir-boosted darunavir and some received enfuvirtide [DUET 1 and DUET 2]. A noncomparative trial that included individuals with virologic failure and multiclass drug resistance (resistance mutations in the NRTI, NNRTI, and PI classes), found high rates of virologic suppression using a salvage regimen that included etravirine plus ritonavir-boosted darunavir plus raltegravir (for most, it also included an
optimized background regimen) [TRIO]. In two studies, patients on virologically suppressive regimens containing efavirenz [SSAT-029] or a protease inhibitor [ETRA-SWITCH] maintained undetectable HIV RNA after they switched to etravirine.

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**Adverse Effects**

Etravirine is generally well tolerated but can cause rash, nausea, diarrhea, and elevations in hepatic aminotransferase levels.

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**Resistance**

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

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**Key Drug Interactions**

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