

The Food and Drug Administration (FDA), on January 18, 2007, granted accelerated approval for etravirine 100 mg tablets, a non-nucleoside reverse transcriptase inhibitor (NNRTI), an antiviral drug that helps to block reverse transcriptase, an enzyme necessary for HIV virus replication. It is the first NNRTI to demonstrate antiviral activity in patients with NNRTI-resistant virus. Etravirine will be sold under the trade name Intelence.

Etravirine is indicated for use in combination with other antiretroviral agents for the treatment of human immunodeficiency virus type 1 (HIV -1) infection in antiretroviral treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to a non-nucleoside reverse transcriptase inhibitor (NNRTI) and other antiretroviral agents.

Accelerated approval is a regulatory mechanism that allows earlier approval of drugs used to treat serious or life-threatening conditions, based on surrogate endpoints that demonstrate meaningful therapeutic advantage over existing treatment. Accelerated approval is based on evidence of a drug's effect on a surrogate endpoint that reasonably suggests clinical benefit. Accelerated approval requires any necessary studies to establish and define the degree of clinical benefit to patients be completed before traditional approval can be granted.

FDA granted this accelerated approval based on 24 week viral load and CD4 data from 1,203 adults in two randomized, double-blind, placebo-controlled trials (DUET-1 and -2 studies) conducted in clinically advanced, antiretroviral treatment-experienced adults with evidence of resistance to NNRTI(s) and protease inhibitors (PIs). The studies compared 599 patients receiving etravirine 200 mg twice daily plus optimized background regimen with 604 patients receiving optimized

background regimen plus placebo. All patients received darunavir/rtv (DRV/rtv) as part of their optimized background regimen.

The 24 week pooled analysis of the DUET studies showed significantly more patients in the etravirine arm as compared to the placebo arm achieved undetectable viral load (less than 50 copies/mL); 59.8 percent vs. 40.2 percent ($p < 0.0001$), and significantly greater mean increase in CD4+ cell count from baseline of 81 vs. 64 cells/mm³ ($p < 0.0022$).

The most common adverse events reported were rash (16.9 percent) and nausea (13.9 percent).

In general, rash was mild to moderate, occurred primarily in the second week of therapy, and was infrequent after Week 4. Rash generally resolved within 1-2 weeks on continued therapy. Patients developing a rash while taking etravirine should contact their doctor.

Rare cases of serious skin reactions such as Stevens-Johnson syndrome and erythema multiforme have been reported. Treatment with etravirine should be discontinued if severe rash develops.

Elevations in total cholesterol and low density lipoprotein (LDL) and initiation of lipid lowering therapy were more common in etravirine-treated subjects compared with those in the placebo arm.

Etravirine should be used with caution in patients with severe hepatic impairment (Child-Pugh class C) as pharmacokinetics of etravirine have not been studied in these patients.

To avoid drug interactions, patients starting etravirine treatment should tell their doctors about all the medications

they take. Information about drug interactions is contained in the etravirine package insert.

The long-term effects of etravirine are not known, and its safety and effectiveness in children ages 16 years and younger has not been studied.

Etravirine also has not been studied in pregnant women. Women who are taking HIV medications when they get pregnant are advised to consult their physician or other health care professional about use of etravirine during pregnancy and about registering with the Antiviral Pregnancy Registry.

Etravirine is distributed by Tibotec Therapeutics, Bridgewater, N.J., a division of Ortho Biotech Products, L.P.

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