

# HIV CareLink

A Newsletter for HIV/AIDS  
Primary Care Providers

Volume 9 - Issue 3

SPECIAL BULLETIN

January 24, 2008

## Etravirine (INTELENCE™) Approved by FDA

Jeffrey Beal, MD

Clinical Director, Florida/Caribbean AIDS Education and Training Center

On January 18<sup>th</sup> the FDA announced the approval of a new NNRTI: etravirine/ETV (INTELENCE™) (TMC-125) from Tibotec Therapeutics. The drug is indicated for adult patients who have evidence of viral replication and HIV-1 strains resistant to an NNRTI and other ARVs. To view the full product information, please visit <http://www.intelence-info.com/intelence/full-prescribing-info.html>

### DOSAGE

200 mg (two 100 mg tablets) taken twice daily following a meal. Patients with trouble swallowing may disperse the tablet in a glass of water, stir well and drink immediately. Rinse the glass several times. Completely swallow each rinse.

### PRICING

The wholesale cost of a 30-day supply is \$654 (<http://www.stifel.wallst.com/research/company/companyNews.asp?symbol=unj&docKey=100-021x0211-1>)

### ADVERSE REACTIONS

Most common, occurring >10% vs placebo, were rash and nausea. Immune reconstitution inflammatory syndrome (IRIS) and Steven-Johnson syndrome (<1%) have occurred.

### DRUG INTERACTIONS

- Do not combine with the following ARVs:
  - Tipranavir/ritonavir, fosamprenavir/ritonavir, atazanavir/ritonavir
  - Any unboosted PI including full-dose RTV.
  - NNRTIs
- A substrate of CYP3A4, CYP2C9, and CYP2C19; drugs that induce or inhibit these enzymes may alter the therapeutic effect or adverse reaction profile of ETV
- An inducer of CYP3A4, and inhibitor of CYP2C9 and CYP2C19 and may alter effects of drugs metabolized by these enzymes
- Examples of effects on levels of ETV or other drugs when combined (See product label for more information):
  - ↓ certain antiarrhythmics
  - ↑ anticoagulants

- Some anticonvulsants (carbamazepine, phenobarbital, phenytoin) →↓ ETV
- Antifungals → ↑ ETV
  - ↔ fluconazole
  - ↓ itraconazole
  - ↓ ketoconazole
  - ↔ posaconazole
  - ↑ voriconazole
- ↓ clarithromycin (use azithromycin for MAC treatment)
- Rifampin and rifapentine →↓ ETV
- Rifabutin – if dosed without ritonavir-boosted PI dose at 300 mg/d. Do not use with boosted PI.
- ↑ diazepam
- Dexamethasone →↓ ETV
- St. John's Wort →↓ ETV
- HMG-CoA Reductase Inhibitors
  - ↓ atorvastatin
  - ↑ fluvastatin
  - ↔ pravastatin
  - ↔ rosuvastatin
- ↔ methadone
- ↓ sildenafil

### USE IN SPECIAL POPULATIONS

- Pregnancy: Category B
- Patients with hepatic or renal impairment: metabolized in liver; no dose adjustment in mild Child-Pugh Class A or B, not studied in Class C. No dose adjustment when used in patients with Hepatitis B or C. No dosage adjustments for renal impairment.

### VIROLOGIC RESPONSE TO ETV

- Presence of V179D/F or T, or Y181C or G190S was associated with decreased virologic response
- Presence of K103N did not affect response to ETV
- At baseline, the presence of ≥ 3 IAS-USA-defined NNRTI substitutions resulted in a decreased response to ETV

### EDITORS

Jeffrey Beal, M.D.  
(239) 839-4645  
aetbeal@embarqmail.com

Joanne Orrick, Pharm.D., B.C.P.S.  
(352) 273-7845  
orricjj@ufl.edu

### MANAGING EDITOR

Kimberly Alfonso, M.Acc.  
(813) 974-4430  
alfonso@fmhi.usf.edu

### ABOUT US

The Florida/Caribbean AIDS Education and Training Center provides HIV education, consultation, and resource materials to health care providers in Florida, Puerto Rico and the US Virgin Islands.

Major funding is provided by the US Public Health Service's Health Resources Services Administration (HRSA) DHHS-HAB Grant No. H4AHA00049 through the University of South Florida Center for HIV Education and Research, Michael Knox, Ph.D., Director





CLINICAL TRIALS DATA-Pooled Analysis of TMC125-C206 and TMC125-C216

Demographic and Baseline Disease Characteristics (Adapted from Table 10 of the Etravirine Package Insert)		
	Pooled TMC125-C206 and TMC125-C216 Trials	
	INTELENCE™ + BR N=599	Placebo + BR N=604
<b>Demographic Characteristics: Similar between arms with median age of approximately 45 years, 90% male, and 70% white patients.</b>		
<b>Baseline Disease Characteristics</b>		
Median Baseline Plasma HIV-1 RNA (range), log <sub>10</sub> copies/mL	4.8 (2.7-6.8)	4.8 (2.2-6.5)
Percentage of Subjects with Baseline Viral Load:		
< 30,000 copies/mL	27.5%	28.8%
≥ 30,000 copies/mL and < 100,000 copies/mL	34.4%	35.3%
≥ 100,000 copies/mL	38.1%	35.9%
Median Baseline CD4+ Cell Count (range), cells/mm <sup>3</sup>	99 (1-789)	109 (0-912)
Percentage of Subjects with Baseline CD4+ Cell Count:		
< 50 cells/mm <sup>3</sup>	35.6%	34.7%
≥ 50 cells/mm <sup>3</sup> and < 200 cells/mm <sup>3</sup>	34.8%	34.5%
≥ 200 cells/mm <sup>3</sup>	29.6%	30.8%
Median (range) Number of Primary PI Mutations	4 (0-7)	4 (0-7)
Percentage of Subjects with Previous Use of NNRTIs:		
0	8.2%	7.9%
1	46.9%	46.7%
>1	44.9%	45.4%
Percentage of Subjects with Previous Use of the following NNRTIs:		
Efavirenz	70.3%	72.5%
Nevirapine	57.1%	58.6%
Delavirdine	13.7%	12.7%
Median (range) Number of NNRTI Resistance-Associated Mutations	2 (0-5)	2 (0-4)

Efficacy at Week 24 for subjects in the INTELENCE™ and placebo arms for the pooled TMC125-C206 and TMC125-C216 study populations are shown in Table 11.

Table 11: Outcomes of Treatment at Week 24 of the TMC125-C206 and TMC125-C216 Trials (Pooled Analysis)		
	Pooled TMC125-C206 and TMC125-C216 Trials	
	INTELENCE™ + BR N=599	Placebo + BR N=604
Virologic Responders at Week 24 Viral Load < 50 HIV-1 RNA copies/mL	358 (59.8%)	243 (40.2%)
Virologic Failures (VF) at Week 24 Viral Load ≥ 50 HIV-1 RNA copies/mL	190 (31.7%)	320 (53.0%)
Death*	9 (1.5%)	16 (2.6%)
Discontinuations before Week 24 †:		
due to VF	2 (0.3%)	3 (0.5%)
due to Adverse Events	28 (4.7%)	11 (1.8%)
due to other reasons	12 (2.0%)	11 (1.8%)
* all deaths, including the follow-up period		
† all discontinuations up to and including day 154 of the treatment period		
BR=background regimen		

The complete collection of previous issues of HIV CareLink are available online.

To view past issues, please visit the archives at:

[www.FAETC.org/Newsletter](http://www.FAETC.org/Newsletter)