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**U.S. FOOD AND DRUG ADMINISTRATION (FDA) GRANTS TRADITIONAL
APPROVAL FOR INTELENCE[®] (ETRAVIRINE)**

[*Bridgewater, NJ, November 25, 2009*] – The FDA granted traditional approval for INTELENCE[®] (etravirine) tablets, a non-nucleoside reverse transcriptase inhibitor (NNRTI). INTELENCE is the only NNRTI specifically indicated for use in treatment-experienced adults who are experiencing virologic failure with HIV-1 strains resistant to an NNRTI and other antiretroviral (ARV) agents. The traditional approval is based on 48-week data from two Phase 3 studies known as DUET-1 and DUET-2. INTELENCE is currently marketed in the U.S. by Tibotec Therapeutics, a division of Centocor Ortho Biotech Products, L.P.

“With its efficacy and tolerability demonstrated in 48-week studies, etravirine (INTELENCE) has become an important option for many treatment-experienced patients with resistance to NNRTIs or other antiretrovirals,” said DUET clinical investigator Charles Hicks, MD, associate professor of medicine at Duke University’s Division of Infectious Diseases in Durham, North Carolina.

INTELENCE received accelerated approval by the FDA in January 2008 and has been approved in more than 50 countries since then. In January 2009, an application for traditional approval was submitted to the FDA, which included 48-week data from DUET-1 and DUET-2.

INTELENCE, in combination with other antiretroviral agents, is indicated 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 an NNRTI and other antiretroviral (ARV) agents. This indication is based on Week 48 analyses from two randomized, double-blind, placebo-controlled trials of INTELENCE. Both studies were conducted

in clinically advanced, three-class antiretroviral (NNRTI, N[t]RTI, PI) treatment-experienced adults.

The following points should be considered when initiating therapy with INTELENCE:

- Treatment history and, when available, resistance testing, should guide the use of INTELENCE.
- The use of other active antiretroviral agents with INTELENCE is associated with an increased likelihood of treatment response.
- In patients who have experienced virologic failure on an NNRTI-containing regimen, do not use INTELENCE in combination with only N[t]RTIs.
- The risks and benefits of INTELENCE have not been established in pediatric patients or in treatment-naïve adult patients.

The DUET studies, identical in design and conducted across the Americas, Australia, Canada, Europe and Thailand, examined the use of INTELENCE in combination with other antiretroviral agents in adult treatment-experienced HIV-1 patients with documented resistance to NNRTIs and protease inhibitors (PIs). Participants in the DUET studies were randomized to receive INTELENCE 200 mg twice daily or placebo, each given in addition to a background regimen. For all patients, the BR included darunavir/ritonavir, plus at least two investigator-selected antiretroviral drugs (N(t)RTIs with or without enfuvirtide).

At 48 weeks, significantly more study participants achieved an undetectable viral load (defined as less than 50 HIV-1 RNA copies/mL) with INTELENCE tablets plus a background regimen compared with placebo plus a background regimen. In the pooled 48-week analysis of DUET-1 and -2, 60 percent of INTELENCE-treated patients had a confirmed undetectable viral load at 48 weeks compared with 38 percent of placebo-treated patients. In each study, this difference was significant [$p < 0.0001$].

The most commonly reported adverse drug reactions of moderate to severe intensity (≥ 2 percent) which occurred at a higher rate than placebo were rash (10 percent vs. 3 percent) and peripheral neuropathy (4 percent vs. 2 percent).

The recommended oral dose of INTELENCE tablets is 200 mg (two 100 mg tablets) taken twice daily following a meal. Patients who are unable to swallow INTELENCE tablets whole may disperse the tablets in a glass of water.

Important Safety Information

INTELENCE does not cure HIV infection or AIDS, and does not prevent passing HIV to others.

Warnings & Precautions

- **Severe Skin and Hypersensitivity Reactions:**

- Severe, potentially life-threatening, and fatal skin reactions have been reported in patients taking INTELENCE. These include cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme
- Hypersensitivity reactions have also been reported and were characterized by rash, constitutional findings, and sometimes organ dysfunction, including hepatic failure

In the DUET studies, Grade 3 and 4 rashes were reported in 1.3% of patients receiving INTELENCE compared to 0.2% of patients in the placebo arm.

Discontinuation rate due to rash was 2.2% in patients taking INTELENCE.

Rash occurred most commonly during the first 6 weeks of therapy

Discontinue INTELENCE immediately if signs or symptoms of severe skin reactions or hypersensitivity reactions develop (including, but not limited to, severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, facial edema, hepatitis, eosinophilia, angioedema)

- Monitor clinical status including liver transaminases, and initiate appropriate therapy

- Delay in stopping INTELENCE treatment after the onset of severe rash may result in a life-threatening reaction
- **Fat Redistribution:** Redistribution and/or accumulation of body fat have been observed in patients receiving antiretroviral (ARV) therapy. The causal relationship, mechanism, and long-term consequences of these events have not been established
- **Immune Reconstitution Syndrome:** has been reported in patients treated with ARV therapy, including INTELENCE

Use in Specific Populations

- **Hepatic Impairment:** INTELENCE should be used with caution in patients with severe hepatic impairment (Child-Pugh Class C) as pharmacokinetics of INTELENCE have not been evaluated in these patients

Adverse Reactions

- The most common adverse drug reactions ($\geq 2\%$) of at least moderate intensity (\geq Grade 2) reported in patients taking INTELENCE and that occurred at a higher rate compared with placebo were rash (10% vs 3%) and peripheral neuropathy (4% vs 2%)

Drug Interactions

- INTELENCE should not be coadministered with the following ARVs: tipranavir/ritonavir, fosamprenavir/ritonavir, atazanavir/ritonavir, full-dose ritonavir (600 mg bid), protease inhibitors administered without low-dose ritonavir, and other NNRTIs
- INTELENCE should not be co-administered with carbamazepine, phenobarbital, phenytoin, rifampin, rifapentine, rifabutin (when part of a regimen containing protease inhibitor/ritonavir) or products containing St. John's wort (*Hypericum perforatum*)
- INTELENCE and lopinavir/ritonavir should be coadministered with caution
- Coadministration of INTELENCE with other agents such as substrates, inhibitors, or inducers of CYP3A, CYP2C9, CYP2C19, and/or P-glycoprotein may alter the therapeutic effect or adverse reaction profile of INTELENCE or the coadministered drug(s). **This is not a complete list of potential drug interactions**

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch, or call 1-800-FDA-1088

Please see full Prescribing Information for more details. Full prescribing information is also available at www.INTELENCE-info.com.

About Tibotec Therapeutics

Tibotec Therapeutics, a division of Centocor Ortho Biotech Products, L.P., headquartered in Bridgewater, N.J., is dedicated to delivering innovative virology therapeutics that help healthcare professionals address serious unmet needs in people living with HIV.

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