FDA Approves New Dosage Strength For INTELENCE(R)

The U.S. Food and Drug Administration(FDA) approved a label update to include a 200 mg formulation of INTELENCE® (etravirine), a non-nucleoside reverse transcriptase inhibitor (NNRTI) indicated for the treatment of human immunodeficiency virus (HIV-1) in treatment-experienced adults with resistance to an NNRTI and other antiretroviral (ARV) agents.

The recommended oral dose of INTELENCE tablets is 200 mg (one 200 mg tablet or two 100 mg tablets) taken twice daily following a meal. The new 200 mg product formulation is expected to launch in the U.S. later this month, and the 100 mg tablet will remain available. Patients who are unable to swallow INTELENCE tablets whole may disperse the tablets in a glass of water.

The FDA granted accelerated approval to INTELENCE in January 2008, and it has since been approved in more than 65 countries. INTELENCE received traditional FDA approval in November 2009, based on 48-week data from the DUET-1 and DUET-2 studies, and is currently marketed in the U.S. by Tibotec Therapeutics, a division of Centocor Ortho Biotech Products, L.P.

INTELENCE Indication

INTELENCE, in combination with other antiretroviral agents, is indicated for the treatment of HIV-1 infection in ARV treatment-experienced adult patients who have evidence of viral replication and HIV-1 strains resistant to an NNRTI and other 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 ARV (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 ARV 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.

About the DUET studies

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 ARV 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 (BR). For all patients, the BR included darunavir/ritonavir, plus at least two investigator-selected antiretroviral drugs (N(t)RTIs with or without enfuvirtide).

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

-- Pregnancy Category B: INTELENCE should be used during pregnancy only if the potential benefit justifies the potential risk. No adequate and well-controlled studies have been conducted in pregnant women

Adverse Reactions

-- The most common adverse drug reactions (> or = 2%) of at least moderate

intensity (> or = 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)

-- 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)

Source:
Tibotec Therapeutics