



FDA Approves Label Update for PREZISTA® to Include 192-Week Data in HIV-1-Infected Adult Patients Starting Treatment

TITUSVILLE, N.J., Oct. 21, 2011 /PRNewswire/ -- Janssen Therapeutics, Division of Janssen Products, LP, announced today that the U.S. Food and Drug Administration (FDA) has approved a label update for PREZISTA®(darunavir) tablets to include 192-week data from the ARTEMIS study. ARTEMIS evaluated the efficacy and safety of PREZISTA with ritonavir® vs. lopinavir/r in combination with other antiretrovirals (ARVs) for the treatment of human immunodeficiency virus (HIV-1) in treatment-naive patients.

"Since its launch in 2006, PREZISTA has become one of the most prescribed antiretroviral agents in the protease inhibitor class. Having data showing the efficacy, safety, and tolerability of PREZISTA over 192 weeks should give added confidence to healthcare providers who are considering PREZISTA as an option for their patients who are starting treatment for the first time," said Vanessa Broadhurst, President, Janssen Therapeutics.

PREZISTA was developed by Tibotec Pharmaceuticals and is marketed in the U.S. by Janssen Therapeutics. PREZISTA, co-administered with ritonavir (PREZISTA/ritonavir), and with other antiretroviral agents, is indicated for the treatment of human immunodeficiency virus (HIV-1) infection.

This indication is based on analyses of plasma HIV-1 RNA levels and CD4+ cell counts from two controlled Phase 3 trials of 48 weeks duration in antiretroviral treatment-naive and treatment experienced patients and two controlled Phase 2 trials of 96 weeks duration in clinically advanced, treatment-experienced adult patients.

In treatment-experienced adult patients, the following points should be considered when initiating therapy with PREZISTA/r:

- Treatment history and, when available, genotypic or phenotypic testing should guide the use of PREZISTA/r.
- The use of other active agents with PREZISTA/r is associated with a greater likelihood of treatment response.

ARTEMIS 192-Week Study Results

The ARTEMIS study compared the efficacy and safety of PREZISTA/r 800/100 mg once daily (n=343) versus lopinavir/r 800/200 mg total daily dose (n=346) in treatment-naive adults with HIV-1. All patients received a fixed-dose combination of tenofovir and emtricitabine once daily. At 192 weeks, PREZISTA/r was shown to be non-inferior to lopinavir/r. This 192 week analysis showed that:

-- 70% of patients in the PREZISTA/r arm reached an undetectable viral load (less than 50 copies/mL) vs. 61% of patients in the lopinavir/r arm. Virologic failure was 12% in the PREZISTA/r arm and 15% in the lopinavir/r arm. Statistical superiority of PREZISTA/r over the lopinavir/r regimen was demonstrated in both the intent-to-treat (ITT) and on-protocol (OP) analysis.

-- The most common treatment-related adverse reactions (greater or equal to 5 percent) of moderate intensity (greater or equal to grade 2) among patients in the PREZISTA/r arm vs. lopinavir/r arm were: diarrhea (9 percent vs. 16 percent); headache (7 percent vs. 6 percent); abdominal pain (6 percent vs. 6 percent); and rash (6 percent vs. 7 percent).

About the ARTEMIS Study

ARTEMIS (AntiRetroviral Therapy with TMC114 ExaMined In naive Subjects) is an international, randomized, controlled, open-label, non-inferiority, Phase 3 trial that compared the efficacy and safety of PREZISTA/r versus lopinavir/r in treatment-naive HIV-1-infected adult patients with viral load greater than 5,000 copies/mL.

The main objective of the study was to demonstrate non-inferiority of PREZISTA/r versus lopinavir/r in the proportion of patients achieving virologic response, defined as confirmed HIV RNA less than 50 copies/mL. Non-inferiority of PREZISTA/r vs. lopinavir/r was defined as a maximum allowable difference of 12 percent for virologic response, with a one-sided significance level of alpha equal to 0.025.

Important Safety Information

PREZISTA does not cure HIV-1 infection or AIDS, and does not prevent passing HIV-1 to others.

Drug Interactions

- Coadministration of PREZISTA/ritonavir is contraindicated with drugs that are highly dependent on CYP3A for clearance and for which elevated plasma concentrations are associated with serious and/or life-threatening events (e.g., alfuzosin, dihydroergotamine, ergonovine, ergotamine, methylergonovine, cisapride, pimozide, oral midazolam, triazolam, lovastatin, or simvastatin)
- Coadministration of PREZISTA/ritonavir is also contraindicated with rifampin and products containing St. John's wort (*Hypericum perforatum*) because this may cause significant decrease in plasma concentration of darunavir, resulting in loss of therapeutic effect and development of resistance
- Coadministration is not recommended with indinavir, lopinavir/ritonavir, saquinavir, and pravastatin
- Caution should be used when prescribing agents such as sildenafil, vardenafil, tadalafil, or other substrates, inhibitors, or inducers of CYP3A in patients receiving PREZISTA/ritonavir.

This list of potential drug interactions is not complete.

Warnings & Precautions

- PREZISTA must be coadministered with ritonavir and food to achieve the desired antiviral effect. Failure to administer PREZISTA with ritonavir and food may result in a loss of efficacy of darunavir. Please refer to ritonavir prescribing information for additional information on precautionary measures
- **Drug-induced hepatitis** (e.g., acute hepatitis, cytolytic hepatitis) has been reported with PREZISTA/ritonavir. During the clinical development program (N=3063), hepatitis has been reported in 0.5% of patients receiving combination therapy with PREZISTA/ritonavir. Patients with preexisting liver dysfunction, including chronic active hepatitis B or C, have an increased risk for liver function abnormalities, including severe hepatic adverse events

Post-marketing cases of liver injury, including some fatalities, have been reported. A causal relationship with PREZISTA/ritonavir therapy has not been established

Appropriate laboratory testing should be conducted prior to initiating therapy with PREZISTA/ritonavir and patients should be monitored during treatment. Increased AST/ALT monitoring should be considered in patients with underlying chronic hepatitis, cirrhosis, or in patients who have pretreatment elevations of transaminases, especially during the first several months of PREZISTA/ritonavir treatment. Evidence of new or worsening liver dysfunction (including clinically significant elevation of liver enzymes and/or symptoms such as fatigue, anorexia, nausea, jaundice, dark urine, liver tenderness, hepatomegaly) in patients on PREZISTA/ritonavir should prompt consideration of interruption or discontinuation of treatment

- **Severe Skin Reactions:** Severe skin reactions (0.4%), accompanied by fever and/or elevations of transaminases in some cases, Stevens-Johnson Syndrome (<0.1%), and toxic epidermal necrolysis (post-marketing experience) have been reported in patients receiving PREZISTA/ritonavir. Discontinue PREZISTA/ritonavir immediately if signs or symptoms of severe skin reactions develop (including, but not limited to, severe rash or rash accompanied with fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, hepatitis and/or eosinophilia).

In clinical trials (N=3063), rash (all grades, generally mild to moderate, regardless of causality) occurred in 10.3% of patients receiving PREZISTA/ritonavir. Discontinuation due to rash was 0.5%

- **Sulfa Allergy:** PREZISTA should be used with caution in patients with known sulfonamide allergy
- **Diabetes Mellitus/Hyperglycemia and Hemophilia:** New-onset or exacerbations of preexisting diabetes mellitus, hyperglycemia, and increased bleeding in hemophiliacs have been reported in patients receiving protease inhibitors. Initiation or dose adjustments of insulin or oral hypoglycemic agents may be required. A causal relationship between protease inhibitors and these events has not been established
- **Fat Redistribution:** Redistribution and/or accumulation of body fat have been observed in patients receiving 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

- **Resistance/Cross Resistance:** The potential for HIV-1 cross-resistance among protease inhibitors has not been fully explored in PREZISTA/ritonavir-treated patients

Use in Specific Populations

- **Hepatic Impairment:** PREZISTA/ritonavir is not recommended for use in patients with severe hepatic impairment. There are no pharmacokinetic or safety data available in patients with severe hepatic impairment
- **Pregnancy:** PREZISTA 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

- **In treatment-naive adult patients,** the most common adverse drug reactions (greater than or equal to 5%) reported of at least moderate intensity (greater than or equal to Grade 2) in the PREZISTA/ritonavir arm through 192 weeks were diarrhea (9%), headache (7%), abdominal pain (6%), and rash (6%)
- **In treatment-experienced adult patients,** the most common adverse drug reactions (greater than or equal to 5%) reported of at least moderate intensity (greater than or equal to Grade 2) in the PREZISTA/ritonavir arm through 96 weeks were diarrhea (14%), nausea (7%), rash (7%), abdominal pain (6%), and vomiting (5%)

This is not a complete list of all adverse drug reactions reported with the use of PREZISTA/ritonavir.

Please see accompanying full Prescribing Information for more details. Full prescribing information is also available at

http://prezista.com/sites/default/files/pdf/us_package_insert.pdf

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.

About Janssen Therapeutics

At Janssen, we are dedicated to addressing and solving some of the most important unmet medical needs of our time in HIV and other infectious diseases. Driven by our commitment to patients, we develop innovative products, services and healthcare solutions to help people throughout the world. Headquartered in Titusville, New Jersey, Janssen Therapeutics, Division of Janssen Products, LP, is one of the Janssen Pharmaceutical Companies. Please visit JanssenTherapeutics.com for more information.