U.S. Food and Drug Administration Approves New Formulations of Viread® for Use by Children Living With HIV

January 18, 2012 7:16 PM ET

-- Viread Now Available in an Oral Powder and Three Lower-Strength Tablets --

FOSTER CITY, Calif.--(BUSINESS WIRE)--Jan. 18, 2012-- Gilead Sciences, Inc. (Nasdaq:GILD) announced today that the U.S. Food and Drug Administration (FDA) has approved Viread® (tenofovir disoproxil fumarate) in combination with other antiretroviral agents for the treatment of HIV-1 infection in pediatric patients ages 2-12. The FDA approved a supplemental New Drug Application (sNDA) for three lower-strength once-daily tablets of Viread in doses of 150 mg, 200 mg and 250 mg for children ages 6-12. The agency also approved a New Drug Application (NDA) for an oral powder formulation of Viread for children ages 2-5. The active ingredient in Viread, tenofovir disoproxil fumarate, is currently the most-prescribed molecule for adults receiving HIV therapy in the United States.

Viread was originally approved by the FDA in 2001 as a once-daily 300 mg tablet for individuals ages 18 and over for the treatment of HIV-1 infection in combination with other antiretrovirals. In March 2010, the 300 mg dose was approved for use in the United States among adolescents ages 12-17. In pediatric patients, the use of either the lower-strength tablets or the oral powder formulation of Viread is based on the patient's age and weight. The safety and efficacy of Viread has not been established in children less than two years of age. In HIV-infected adult patients, the dose is one 300 mg Viread tablet once daily taken orally, without regard to food. For adults unable to swallow Viread tablets, the oral powder formulation equal to 300 mg may be used.

The pediatric regulatory applications for Viread were supported by clinical data from a Phase 3 safety and efficacy study of a Viread-containing antiretroviral regimen compared to an antiretroviral regimen containing zidovudine or stavudine in HIV-infected treatment-experienced children ages 2-12. The safety profile observed in the study was consistent with that observed in clinical trials in adults. The applications were submitted to the FDA on July 18, 2011.

"Prenatal HIV testing and antiretroviral interventions during pregnancy have contributed to a dramatic decline in the number of children born with HIV in the United States. However, there remains an unmet need for heat-stable, taste-neutral pediatric formulations that do not require cold storage, particularly in resource-limited settings, where mother-to-child transmission remains a significant challenge," said Norbert Bischofberger, PhD, Executive Vice President, Research and Development and Chief Scientific Officer, Gilead Sciences. "We are very pleased to provide an important new therapeutic option for younger HIV patients, and will work to make the pediatric formulations of Viread available as quickly as possible."

According to the World Health Organization, there are approximately 2.5 million children under the age of 15 living with HIV worldwide, and more than 90 percent live in sub-Saharan Africa. In an effort to accelerate the availability of pediatric formulations in low-income countries, in July 2011, Gilead announced new incentives to encourage its Indian generic manufacturing partners to develop pediatric formulations of its HIV medicines.

Important Safety Product Information About Viread, Including Boxed Warnings

Indication and Usage

Viread is indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults and pediatric patients 2 years of age and older.

The following point should be considered when initiating therapy with Viread for the treatment of HIV-1 infection:

- Viread should not be used in combination with Atripla® (efavirenz/emtricitabine/tenofovir disoproxil fumarate), Complera® (emtricitabine/rilpivirine/tenofovir disoproxil fumarate), or Truvada® (emtricitabine/tenofovir disoproxil fumarate).

WARNINGS: LACTIC ACIDOSIS/SEVERE HEPATOMEGALY WITH STEATOSIS and POST TREATMENT EXACERBATION OF HEPATITIS

Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of

nucleoside analogs, including Viread, in combination with other antiretrovirals. Severe acute exacerbations of hepatitis have been reported in HBV-infected patients who have discontinued anti-hepatitis B therapy, including Viread. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue anti-hepatitis B therapy, including Viread. If appropriate, resumption of anti-hepatitis B therapy may be warranted.

Warnings and Precautions

- **New onset or worsening renal impairment:** New onset or worsening renal impairment, including cases of acute renal failure and Fanconi syndrome (renal tubular injury with severe hypophosphatemia), have been reported with the use of Viread. Assess creatinine clearance (CrCl) before initiating treatment with Viread. Monitor CrCl and serum phosphorus in patients at risk, including those who have previously experienced renal events while receiving Hepsera® (adefovir dipivoxil). Avoid administering Viread with concurrent or recent use of nephrotoxic drugs. Dosing interval adjustment of Viread and close monitoring of renal function are recommended in all patients with CrCl <50 mL/min.
- **Coadministration with Other Products:**
  - Do not use with other tenofovir-containing products (eg, Atripla, Complera, or Truvada)
  - Do not administer in combination with Hepsera.
- **Patients coinfected with HIV-1 and HBV:** Due to the risk of development of HIV-1 resistance, Viread should only be used in HIV-1 and HBV co-infected patients as part of an appropriate antiretroviral combination regimen. Testing for the presence of chronic hepatitis B should be offered to all patients with HIV-1 before initiating treatment with Viread.
- **Decreases in bone mineral density:** Decreases in bone mineral density (BMD) have been observed in HIV-infected patients. Consider monitoring BMD in patients with a history of pathologic fracture or who are at risk for osteopenia. Cases of osteomalacia (associated with proximal renal tubulopathy and which may contribute to fractures) have been reported in association with the use of Viread.
- **Fat Redistribution:** In HIV-infected patients redistribution/accumulation of body fat has been observed in patients receiving combination antiretroviral therapy.
- **Immune Reconstitution Syndrome:** Immune reconstitution syndrome has been reported in HIV-infected patients treated with combination antiretroviral therapy.
- **Early Virologic Failure:** HIV treatment regimens that only contain three nucleoside reverse transcriptase inhibitors (NRTI) are generally less effective than triple drug regimens containing two NRTIs used with a non-nucleoside reverse transcriptase inhibitor or HIV-1 protease inhibitor. Triple nucleoside regimens should be used with caution and patients should be carefully monitored and considered for treatment modification.

Adverse Reactions

- **Clinical Trials in Adults Patients with HIV-1 Infection:** In HIV-infected subjects the most common adverse reactions (incidence greater than or equal to 10%, Grades 2 - 4) are rash, diarrhea, headache, pain, depression, asthenia, and nausea.
- **Clinical Trials in Pediatric Subjects 2 Years of Age and Older with HIV-1 Infection:** In a clinical trial of 89 pediatric subjects treated with Viread (48 who were initially randomized to Viread and 41 who were initially randomized to continue stavudine or zidovudine and then received Viread in the extension phase) for a median exposure of 104 weeks, four subjects discontinued due to adverse reactions consistent with proximal renal tubulopathy.

Drug Interactions

- **Didanosine:** Coadministration increases didanosine concentrations. Use with caution and monitor for evidence of didanosine toxicity (eg, pancreatitis, neuropathy). Didanosine should be discontinued in patients who develop didanosine-associated adverse reactions. In adults weighing >60 kg, the didanosine dose should be reduced to 250 mg when it is coadministered with Viread. Data are not available to recommend a dose adjustment of didanosine for patients weighing <60 kg.
- **Atazanavir:** Coadministration decreases atazanavir concentrations and increases tenofovir concentrations. Use atazanavir with Viread only with additional ritonavir; monitor for evidence of tenofovir toxicity.
- **Lopinavir/ritonavir:** Coadministration increases tenofovir concentrations. Monitor for evidence of tenofovir toxicity.

Dosage and Administration

- Recommended dose of Viread for the treatment of HIV-1 in:
  - adult patients is 300 mg once daily without regard to food
  - pediatric patients is 8 mg of tenofovir disoproxil fumarate per kilogram of body weight (maximum of 300 mg) once daily.

Dose Adjustment for Patients with Altered Creatinine Clearance

- The dosing interval of Viread should be adjusted (using recommendations in the table below) and renal function closely monitored in patients with creatinine clearance <50 mL/min.

Dosage Adjustment for Patients with Altered Creatinine Clearance

	Creatinine clearance (mL/min)[a]			**Hemodialysis patients**
	≥50	**30-49**	**10-29**	
Recommended dosing interval	Every 24 hours	Every 48 hours	Every 72 to 96 hours	Every 7 days or after a total of approximately 12 hours of dialysis[b]

[a] Calculated using ideal (lean) body weight.

[b] Generally once weekly assuming three hemodialysis sessions a week of approximately 4 hours duration. Viread should be administered following completion of dialysis.

- The pharmacokinetics of tenofovir have not been evaluated in non-hemodialysis patients with creatinine clearance <10 mL/min; therefore, no dosing recommendation is available for these patients.
- No dose adjustment is necessary for patients with mild renal impairment (creatinine clearance 50-80 mL/min). Routine monitoring of calculated creatinine clearance and serum phosphorus should be performed in these patients.
- No data are available for dosing recommendations in pediatric patients with renal impairment.

Please see full Prescribing Information for Viread (including BOXED WARNINGS).

About Gilead Sciences

Gilead Sciences is a biopharmaceutical company that discovers, develops and commercializes innovative therapeutics in areas of unmet medical need. The company's mission is to advance the care of patients suffering from life-threatening diseases worldwide. Headquartered in Foster City, California, Gilead has operations in North America, Europe and Asia Pacific.

Forward-Looking Statement

This press release includes forward-looking statements, within the meaning of the Private Securities Litigation Reform Act of 1995, that are subject to risks, uncertainties and other factors, including the risk that physicians may not see advantages of Viread for the treatment of HIV infection over other therapies for children, and may therefore be reluctant to prescribe the product, and payers may be reluctant to approve or provide reimbursement for the product. These risks, uncertainties and other factors could cause actual results to differ materially from those referred to in the forward-looking statements. The reader is cautioned not to rely on these forward-looking statements. These and other risks are described in detail in Gilead's Quarterly Report on Form 10-Q for the quarter ended September 30, 2011, as filed with the U.S. Securities and Exchange Commission. All forward-looking statements are based on information currently available to Gilead, and Gilead assumes no obligation to update any such forward-looking statements.

U.S. full prescribing information for Viread is available at www.Viread.com.

Viread is a registered trademark of Gilead Sciences, Inc.

For more information on Gilead Sciences, please visit the company's website at www.gilead.com or call Gilead Public Affairs at 1-800-GILEAD-5 or 1-650-574-3000.

Source: Gilead Sciences, Inc.

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