
SPECIALTY PHARMACY NEWS

Rising Number of Patients, Drug Costs for HIV Boost Interest in Managing Therapies

An estimated 1.2 million people in the U.S. are living with HIV, and anywhere from 40,000 to 50,000 new cases are diagnosed each year. This has generated a pharmaceutical marketplace estimated at \$8 billion and growing as patients live longer due to improved medications and better disease management.

But this also means increasing costs for payers and patients alike. Payers face higher rates of antiretroviral (ARV) use and higher drug costs. Medco Health Solutions, Inc. in its *2009 Drug Trend Report* calculated an antiviral drug trend of 16% driven by 8.7% utilization growth and a 6.7% rise in unit cost. Keith Bradbury, Medco's executive director for drug information, tells *SPN* that over the next three years "we expect an annual trend increase of about 12% to 14% in the HIV category." This, he says, will be driven "about one-third by new users and about two-thirds by increases in price."

Stephen Cichy, executive vice president of managed care sales, marketing and product development for BioScrip Inc., tells *SPN* that the average ARV medication patient spends up to \$24,000 annually, although this can go as high as \$30,000 if additional supportive pharmaceuticals are needed. He says that on the payer and specialty pharmacy side, there is increased interest in managing treatment given the chronic nature of the disease and the growing availability of novel agents to treat more advanced HIV. He notes that payers are beginning to apply more formulary management strategies to ensure proper utilization, including prior authorizations and diagnostic requirements. Some payers, he says, are carving out HIV as a specialty benefit and using exclusive providers or closed-network distribution channels.

Bradbury notes that typical plan costs for ARV therapy are still a very small part, "likely less than 5% of total plan drug costs," since the number of patients affected by HIV is relatively low for most plans. But the cost of treating HIV infection is growing at about the same rate as the cost of drugs to treat cancer, although cancer drugs represent a larger part of total plan drug costs, about twice as much, when compared to ARV drugs. He also says that the cost of HIV therapies is growing slightly faster than the cost of drugs for treating multiple sclerosis, "and MS is not as preventable as HIV."

The HIV drug market is dynamic and evolving, pharmacy specialists interviewed by *SPN* say. Factors shaping

this market include revised CDC estimates of HIV incidence rates, changing patient demographics, the aging of HIV patients, new treatment practices, an active drug pipeline with some especially promising agents and better management strategies for improving compliance. These factors create unique challenges for specialty pharmacy companies, patients, providers and payers.

Aging HIV Population Creates Challenges

In August 2008, the CDC published its first national HIV incidence estimates using a new technology and methodology that more directly measured new infection rates. The analysis showed that in 2006 (the latest year for which data were available), an estimated 56,300 new infections occurred. This number was substantially higher than the previous estimates of 40,000 annual new infections. While that did not signal an actual increase in the number of HIV infections, the CDC says it provides a far more accurate picture of the extent of the infected population.

The CDC's estimates also illustrated the trend shift in new infections into the Hispanic/Latino and Black/African American populations. By 2006, the CDC reported that almost 60% of new HIV infections were among Hispanic/Latino and Black/African American men, with 67% of new infections occurring among Hispanic/Latina and Black/African American women.

Of special concern, observers say, is the aging of the HIV patient population. "Before antiretroviral therapy, the time between infection and death was estimated to range between eight and 13 years," Cichy says. "Today, patients with HIV are living upwards of 35 to 40 or more years after infection." But as they live longer, patients may begin to experience drug resistance and increased risk of developing conditions characteristic of aging that can complicate a patient's treatment. These conditions include cirrhosis, cardiovascular disease, renal disease, diabetes and cancer. Patients on ARV therapy for an extended period of time, says Cichy, may experience adverse effects that can compound comorbid conditions. He notes that patients on protease inhibitors may experience hyperlipidemia and/or diabetes, which are more common in the aging population.

The HIV drug pipeline, meanwhile, is pushing toward new combination agents that make a once-a-day pill the most likely scenario for the future.

Bradbury expects new ARV treatments coming down the line over the next three years to be similar to existing treatments, such as new protease inhibitors, new non-nucleoside reverse transcriptase inhibitors (NNRTIs) and nucleoside reverse transcriptase inhibitors (NRTIs). These drugs, he says, will be targeted toward the treatment-resistant HIV viruses, and will contribute to the 12% to 14% drug trend in the category, "since they are likely to be more costly than existing treatments." The HIV virus is expected to develop resistance to current and future ARVs, so new safer and more effective ARVs will be coming to market to address these resistant strains.

Gilead Has Multiple Drugs in Development

Most eyes are on Gilead Sciences, Inc., a company that has been focusing heavily on agents for the HIV treatment-naive population.

In 2006, Gilead launched Atripla, a three-in-one once-a-day agent, now being taken by about one-third of U.S. HIV patients. Atripla combines Truvada — which is Emtriva (emtricitabine) and Viread (tenofovir disoproxil fumarate) — with Bristol-Myers Squibb Co.'s Sustiva (efavirenz). Atripla was the first once-a-day HIV drug to hit the market.

Earlier this year, Gilead announced the development of Quad, a complete regimen in a once-a-day pill. Quad combines elvitegravir, GS-9350, emtricitabine and tenofovir in a fixed-dose, full-regimen pill for treatment-naive patients. Analysts say that it will directly compete with Merck's Isentress (raltegravir), and that it eventually could replace Atripla. It may also be an alternative for people who are intolerant of the side effects of Sustiva, as well as women who may have children.

On July 20, Gilead reported that the company is working on a new once-a-day combination of Truvada with Tibotec Pharmaceuticals Ltd.'s TMC278, a late-stage NNRTI. While Gilead says it's not yet sure how the regimen will be formulated, they hope to bring the product to market by 2011. If successful, it would directly compete with Atripla and, possibly, Quad.

Sylvia Eash, a Decision Resources analyst, tells SPN that with Quad, Gilead is putting four molecules, including its own booster, in one pill to compete with Merck's Isentress. Gilead is conducting trials against Atripla, its own drug, so it could be a successor to that drug. The goal is a drug regimen that's convenient for patients, well-tolerated and clinically effective. Gilead's Truvada/ TMC278 combination, Eash says, reflects a pre-emptive strike against revenues the company could lose when Sustiva goes off patent in 2013.

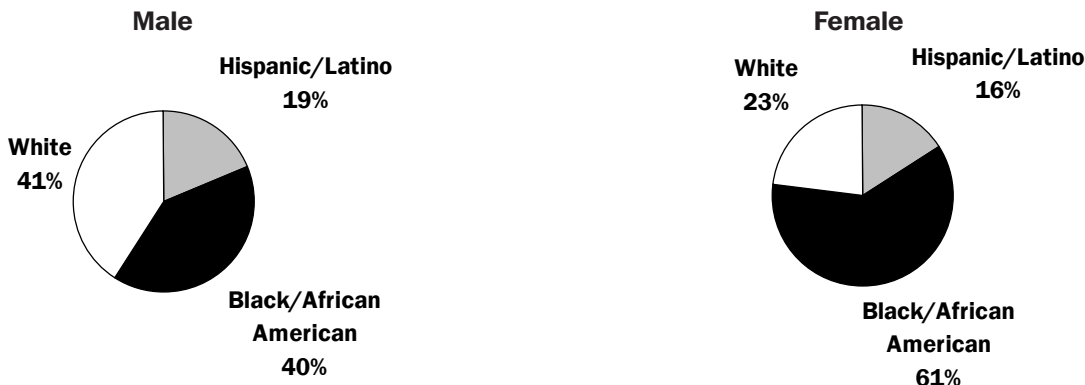
In a report on the HIV pharmaceutical market released last month, Decision Resources said that it expects Quad to make significant inroads in the HIV market, predicting that by 2018 it will become the highest-selling ARV in major markets as patients shift from lower-cost regimens to Quad because of its safety, convenience and effectiveness.

The company also says that Isentress, the first integrase inhibitor on the market (in 2007) (SPN 11/07, p. 1), is being well received by physicians and patients because of its efficacy, safety and simple dosing, and the drug should see substantial uptake over the next several years.

But Merck came under attack last month from the AIDS Healthcare Foundation because of Isentress' steep retail price — \$12,864 per patient per year, making it what critics say is the most expensive of any ARV recommended

Estimated Percentage of New HIV Infections by Sex and Race/Ethnicity — United States 2006

N = 54,230



Note: Data have been adjusted for reporting delay. Data presented on blacks/African Americans, Hispanics/latinos and whites only. The small number of new infections in Asians/Pacific Islanders and American Indians/Alaska Natives precludes further stratification

SOURCE: CDC

by the government as a first-line treatment for patients. Isentress received expanded FDA approval last month for this use (see drug approval briefs, p. 11).

But Decision Resources expects Quad to drive market growth in the treatment-naïve patient market and become the leading therapy. Decision Resources also has its eyes on GlaxoSmithKline/Shionogi's S/GSK1349572, a new integrase inhibitor that has shown potent activity in treatment-naïve patients. GlaxoSmithKline also says it is demonstrating a promising resistance profile.

Another factor driving the increasing use of ARV medications is new treatment guidelines stressing earlier treatment interventions for asymptomatic patients with CD4 counts below 350 cells/mm. This, Decision Resources says, will lead to a longer duration of lifelong HIV therapy, thereby increasing the use of ARVs.

Advances in HIV drug development, especially once-a-day regimens, are driving better patient adherence. But Sara Deno, Pharm.D., BioScrip's director of clinical studies, tells SPN that the average rate of adherence to ARV medications in community practice ranges anywhere from 53% to 70%. The concern, she says, is that drug resistance can occur quickly in patients who are noncompliant.

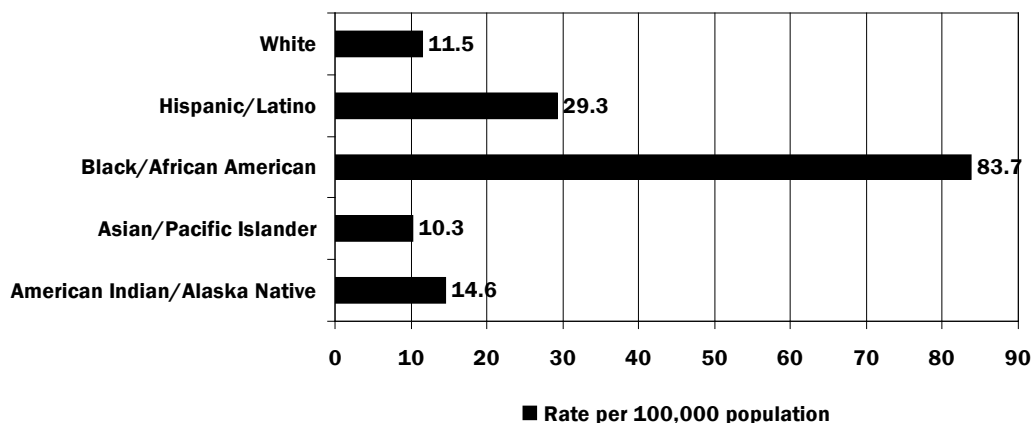
Noncompliance may be related to low literacy levels, age-related challenges (such as cognitive impairment or vision loss), stigma and treatment fatigue (SPN 4/08, p. 1). But Deno says that treatment-related side effects also are a major issue, and one that BioScrip has been addressing with some success through its community-based pharmacy model.

In 2007, for example, BioScrip began working to address the side effects associated with the drug Kaletra (lopinavir/ritonavir), primarily diarrhea during the first few months of therapy, and how they impacted patient adherence. Deno says that BioScrip created a targeted intervention program based at its community pharmacies involving both nurses and pharmacists for patients receiving Kaletra for the first time. Upon starting the regimen, patients received a brochure on side-effect management and adherence tips, along with counseling when they filled their first prescription. Patients also were contacted twice by a nurse during the first 14 days of their regimen. Patients who did not refill their prescriptions were contacted to discuss the reasons behind their decision.

BioScrip measured the impact of the intervention on the three-month attrition rate, and then compared attrition at three months with national baseline data for enrolled patients. According to Deno, the study found that the discontinuation rate due to the adverse events for patients enrolled in the program was decreased four times compared to national data. Deno says the results point to the effectiveness of BioScrip's community-based model, in which specially trained pharmacists work with drug companies, local providers and patients who are new to certain therapies to offer counseling and other interventions that can increase drug regimen adherence.

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Estimated Rate of New HIV Infections by Race/Ethnicity — United States, 2006



Note: Data have been adjusted for reporting delay.
SOURCE: CDC