The Future of Generic HIV Drugs in Rhode Island

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ABSTRACT

The number of HIV-infected persons in the United States continues to increase and most patients with HIV will be on antiretroviral therapy (ART) for many decades. The introduction of generic antiretroviral medications has the potential for significant cost savings which may then be accompanied by improved access. State AIDS Drug Assistance Programs will be made more effective by the switch to generic ARTs. Cost savings and barriers to the introduction of generic ART are discussed.

KEYWORDS: HIV/AIDS, generic drugs, antiretrovirals, Rhode Island

INTRODUCTION

Over the past three decades, HIV has emerged as an important health and policy issue on a number of levels – global, national, as well as local. Currently, more than 1.1 million people are living with HIV/AIDS in the United States alone, of which a CDC-databased modeling estimated 3,730 to 4,061 live in Rhode Island.[1] However, since the development of antiretroviral therapy (ART), HIV is no longer a uniformly fatal ailment; instead, through the effective use of ART, HIV/AIDS has become a treatable chronic disease.

Although the importance of ART is clear, many low-income people living with HIV/AIDS in the United States face difficulties with access. Without insurance or other forms of support, ART is prohibitively expensive in the United States. The cost of ART differs significantly among countries. In India, for example, where many generic antiretroviral medications are produced, the cost of the popular fixed-dose combination formulation of emtricitabine/tenofovir/efavirenz is approximately $1,200 per year. This, in fact, represents one of the most expensive, non-nucleoside reverse transcriptase inhibitor-based ART regimens in India.[2] Meanwhile, in the United States, where almost all antiretroviral agents remain patented, the full out-of-pocket cost of a year's worth of this same combination therapy (branded as Atripla®) has been quoted by a local Rhode Island CVS Pharmacy at $26,364 (oral communication, November 2012).

Even situated in the relative context of differing economic scales, the discrepancy between the cost of ART in India and the cost of ART in the United States is tremendous. The difference can be attributed in part to the dichotomy between patented and generic medications. Due to a number of international agreements and variations in drug patenting policy, generic antiretroviral medications already exist in many countries globally. When will such generic antiretroviral drugs be widely available in the United States, and in Rhode Island more specifically?

In fact, the more widespread introduction of generic antiretroviral drugs in the United States is not far in the future. Patents on some popular antiretroviral drugs have recently expired, and patents on many more are expected to expire in the near future. Of great relevance, the patent on efavirenz, a component of the previously mentioned drug regimen co-formulated as Atripla®, is expected to expire in late 2013. The expected patent expiry of the remaining two components of branded Atripla® are also just a few years away – emtricitabine in 2015 and tenofovir in 2017 (**Table 1**).[3] With

Table 1. Key HIV drugs with recent or imminent patent expiries, by drug class

Drug Class	Drug	Brand name	Manufacturer	Patent expiry
Nucleoside reverse transcriptase inhibitors	Lamivudine	Epivir	GlaxoSmithKline	2010
	Abacavir	Ziagen	GlaxoSmithKline	2012
	Emtricitabine	Emtriva	Gilead	2015
	Tenofovir	Viread	Gilead	2017
Non-nucleoside reverse transcriptase inhibitors	Efavirenz	Sustiva	Bristol-Myers Squibb	2013
	Delavirdine	Rescriptor	Pfizer	2013
Protease inhibitors	Darunavir	Prezista	Tibotec	2015
	Tipranavir	Aptivus	Boehringer Ingelheim	2015
	Ritonavir	Norvir	Abbott	2016

these key antiretroviral patent expirations expected in the near future, it becomes important to consider the implications of the introduction of generic ART in Rhode Island.

HIV/AIDS IN RHODE ISLAND

In Rhode Island, the state Department of Health has published reports based on modeling from nationwide CDC statistics that estimated the total number of people living with HIV/AIDS in Rhode Island in 2011 to be between 3,730 and 4,061. Some uncertainty regarding the actual prevalence of HIV/AIDS in the state, however, still remains. Between 2000 and 2011, the time period for which reliable data has been processed, 1,548 cases of newly diagnosed HIV among Rhode Island residents were reported to the state Department of Health. This is but a minimum estimate; the true incidence of new infections is almost certainly greater.[1]

The HIV/AIDS epidemic in Rhode Island reflects many nationwide trends in HIV/AIDS infection. For example, racial and ethnic minorities, particularly African Americans and Latinos, are vastly overrepresented in the epidemic.[4] These same groups also represent those more likely to lack health insurance in the United States.[5] Thus, overrepresentation in the HIV/AIDS epidemic, compounded with widespread lack of insurance coverage, likely makes access to ART especially difficult for minorities.

For low-income, under-insured or uninsured Rhode Island residents living with HIV/AIDS, the state AIDS Drug Assistance Program (ADAP) is key in facilitating access to costly but necessary HIV-associated medications. ADAP is a payer of last resort for patients who are otherwise unable to access life-sustaining ART. The RI ADAP requires a budget of nearly $10 million a year. Prescription drugs, particularly antiretroviral medications, account for the vast majority of program expenditures.[6] In 2010, the RI ADAP served a total of 846 drug-eligible clients, continuing the program's growth.[7] But as a result of sequestration, many state programs are facing cuts in the federal grants supporting ADAP.

Access to and cost-savings in ART are especially important now, given the increasing number of people living with HIV/AIDS due to longer life expectancies from improved treatment, and recent changes in national HIV/AIDS treatment guidelines recommending that all ART-naïve people initiate treatment regardless of immunologic status.[8] As a result, demand for ART will likely continue to increase; the introduction of cheaper generic antiretroviral drugs merits consideration.

Cost-savings

Generic antiretroviral drugs could significantly affect Rhode Island, and their widespread adoption is certain to bring welcome cost-savings to the state, as well as the state ADAP in particular.

Many of those living with HIV/AIDS in Rhode Island are already on ART. In the largest clinical population of people living with HIV/AIDS in Rhode Island, as cared for at the Immunology Clinic at the Miriam Hospital, an estimated 80% of the patients in care are on ART and are virally suppressed. Nearby Thundermist Health Center, which cares for an additional 73 patients, offers similar data (Dr. Brian Montague, DO, oral communication, March 2013). Overall, local infectious disease physicians estimate the current rate of ART use among all people living with HIV/AIDS in Rhode Island to be 60% (Dr. Timothy Flanigan, MD and Dr. Brian Montague, DO, oral communication, March 2013). The population of HIV-positive patients in care in Rhode Island can be conservatively estimated to be 2,000 individuals, as it has been published that the 1,500 HIV-positive patients cared for at The Miriam Hospital represent over 75% of the HIV care provided within Rhode Island.[4]

Given these numbers, a rough estimate of cost-savings in Rhode Island resulting from the future availability of generic antiretrovirals, as illustrated by the specific example of the commonly-used ART regimen Atripla® (emtricitabine/tenofovir/efavirenz), can be calculated with the following assumptions: 2,000 people living with HIV/AIDS are in care in Rhode Island, 80% of those in care are on ART, 50% would benefit from going on the generic regimen in question, and a 50% cost-savings would result from going generic (the full cost of Atripla® from a local CVS Pharmacy is $26,364 per year). This would result in approximately $10.5 million a year in savings on HIV drugs in Rhode Island alone.

In particular, cost-savings to the Rhode Island ADAP would especially benefit the state health care system. In recent years, ADAPs have lacked funding and have been forced to institute unfortunate cost-containment measures, such as waiting lists and limited drug formularies. Although no waiting list currently exists for the RI ADAP, the long-term sustainability of the program is questionable, especially given the increasing number of people living with HIV/AIDS and the new guidelines recommending universal ART. A rough estimate of cost-savings to the state ADAP resulting from the availability of the generic components of popular branded Atripla® can be reached. Given that the RI ADAP served 846 HIV-positive clients in 2010 and that the full cost of out-of-pocket Atripla® from a local CVS Pharmacy is $26,364 per year, and assuming that half of all patients would benefit from being on the generic regimen in question and that a 50% cost reduction would be experienced from going generic, the RI ADAP could potentially save as much as $5.6 million a year.[7]

Although, with the full implementation of health care reform in the near future, Medicaid expansion and subsidized private insurance may transition as many as 40% of the people currently dependent on ADAP to Medicaid, it will not change the significance of the cost-savings to the state resulting from adoption of generic ART. The health care system as a whole stands to benefit greatly, no matter the details of coverage.

Barriers to generics

Although generic antiretroviral drugs in the United States appear promising, a number of potential barriers to their widespread adoption exist.

Concerns about the efficacy of generic antiretrovirals, for example, exist despite numerous studies showing their efficacy in reducing morbidity and mortality, as well as in eliciting high levels of patient compliance and drug tolerance. Importantly, generic ART has been found to be just as effective as brand name ART in reducing viral load.[2, 9, 10] Quality-assured generic drugs and originator branded drugs, then, ought to be considered equally safe and efficacious. Additionally, in the United States, much of the doubt surrounding the clinical viability of generic-based ART stems not necessarily from the pharmacological efficacy of the generic medication itself, but rather from the expected lack of generic fixed-dose combination antiretroviral formulations. Typically, fixed-dose combination formulations allow for a simple one pill once per day dosing regimen. However, because generic antiretroviral agents will only be available separately, going generic in the United States would likely mean requiring patients to take multiple pills per day, thus increasing their pill burden. Higher pill burden has been suggested to cause lower adherence, which would affect the overall efficacy of the treatment regimen. However, studies have shown that it may not be the number of pills taken per dose, but rather the number of daily doses, that is key to determining patient adherence.[11,12] Nonetheless, a number of health care providers may be resistant to accept generics-based antiretroviral therapy, fearing that they may be making an unfavorable trade-off in choosing cost considerations over treatment integrity.

Furthermore, the practice of drug rebates among ADAPs, including the RI ADAP, may complicate the widespread adoption of generic antiretroviral drugs. The RI ADAP negotiates with pharmaceutical companies for discounts in its purchase of antiretroviral drugs; these discounts often take the form of drug rebates. Drug rebates require ADAPs to purchase drugs from companies at sans-rebate face value; only after drug purchase and distribution do pharmaceutical companies reimburse ADAPs with the negotiated rebate value. The specifics of the negotiation process and resulting rebates are not released to the public. Underfunded ADAPs often rely on drug rebates to supplement budgets, providing a welcome source of flex spending money. Nationally, drug rebates account for 33% of the overall national ADAP budget in fiscal year 2011. In Rhode Island, the state ADAP has been reported to have received drug rebates constituting approximately $1 million in fiscal year 2011, 10% of the overall yearly ADAP budget.[6] These drug rebates may be problematic, as they ultimately serve as a tool for pharmaceutical companies to hook ADAPs into maintaining artificially high antiretroviral drug prices. Because the provision of drug rebates incentivizes ADAPs to keep buying branded drugs from the parent pharmaceutical company and reduces the need to seek out cheap generic alternatives, drug rebates may represent a significant institutional barrier against the future widespread adoption of generic ARV agents in Rhode Island, as well as the United States more generally.

CONCLUSION

The introduction of generic antiretroviral medications has the potential to significantly benefit patients and the health care system alike. Generic antiretrovirals have been shown to be safe and efficacious, allowing for more patients to access affordable, life-saving ART. Furthermore, generic antiretrovirals will also lead to great cost-savings for the health care system generally, as well as the ADAP specifically. Although certain barriers may pose difficulties to their widespread adoption, generic drugs offer a promising path for the future of HIV care.

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