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Medicare Part D has big impact on HIV treatment interruptions

Decreased access to meds, six-fold increase in interruptions

Some of the concerns and predictions HIV/AIDS advocates made two years ago about the impact of Medicare Part D—the prescription drug benefit—on HIV antiretroviral treatment appear to be coming true.

The drug benefit's emphasis on consumer cost-sharing is associated with HIV-infected patients having decreased access to medications and six-time greater treatment interruptions, a new study finds.1

The study found that about 11% (14 of 125 participants) reported having their antiretroviral therapy interrupted for more 48 hours or longer, and 71.4% of those with interruptions were covered by Medicare Part D.

Most of the respondents who had treatment interruptions said they were due to new co-payments after they became enrolled in Medicare Part D. Even co-payments of $1 to $3 per drug are a significant cost burden for Medicare/Medicaid-eligible patients who have high numbers of prescriptions, the study notes.[1]

There are a number of reasons why HIV patients might interrupt their antiretroviral treatment, including forgetfulness, travel, stressful life events, substance abuse, and transportation problems, says **David Bangsberg**, MD, MPH, a senior scientist with the Massachusetts General Hospital in Boston, MA, and the Harvard Initiative for Global Health at the Harvard Medical School in Cambridge, MA.

But the new study shows a significant impact from the Medicare Part D coverage, as well, says Bangsberg, who is a co-author of the study.

"The study found that people living with HIV were more likely to have interruptions because of Medicare Part D," Bangsberg says.

The five-day window

There's a new theory in HIV medicine that clinicians have a five-day window in which to do something about a patient's medication inter-

ruption, Bangsberg notes.

"You've got five days to figure out how to get the patient back on antiretrovirals, and the clock is ticking," Bangsberg says. "If you know that someone is interrupted on day one or two, then you have enough time to do something about it."

So the key is to detect interruption problems in real time and have creative case managers work to solve the problem, Bangsberg says.

The latest medical consensus also appears to be that clinicians do not have to worry about the patients who miss 5 % of their antiretroviral doses, but patients who miss 20 to 30 % of their doses are entering a danger zone, he adds.

This is why HIV clinicians who work with populations impacted by Medicare Part D and treatment interruptions due to the drug program's failures are up in arms.

"Medicare Part D is driving regular doctors out in the field nuts," says **Moupali Das-Douglas**, MD, MPH, an assistant clinical professor at the University of California - San Francisco (UCSF) and director of research in HIV in San Francisco, CA. Das-Douglas is a lead author of the study.

Das-Douglas and her physician colleagues have witnessed how the Medicare Part D program policies have had an adverse impact on patients' health.

"In my clinic at Ward 86, San Francisco General, one of my colleagues' patients had a Medicare Part D problem, and he couldn't get his medication," Das-Douglas recalls. "He is a long-time survivor of AIDS and had been on the same regimen for 12 to 15 years, doing really well."

The man's viral load was suppressed and his CD4 cell count was high because he was very regimented about taking his antiretroviral drugs, she notes.

"Then because of Medicare Part D, he couldn't get medication for a month and a half, and he asked for to have his CD4 cell count and viral load tested," Das-Douglas says. "He wanted to prove that because of the policy problem his viral load had become unsuppressed, and indeed it had."

The new study also suggests that some HIV patients are using their personal priorities to triage their medications, often short-changing their ARTs, Das-Douglas notes.

"We asked participants detailed questions about their treatment interruptions," she says. "Some said they were filling other drugs over ARTs due to co-payments, or they might prioritize methadone or some psychiatric drug because they don't want to be in pain."

HIV clinics and providers are finding that dealing with Medicare Part D is time-consuming and at times overwhelming for staff.

"Our social worker staff spends so much time dealing with Medicare Part D that it's ridiculous," Das-Douglas says. "It's really unfortunate

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that this is such a poorly-designed policy because of the influence of pharmaceutical company lobbyists."

The main problem with Medicare Part D is that it cannot do what even the U.S. Veterans Affairs administration can do, which is to negotiate drug contracts as one large entity, Das-Douglas says.

It's only through such negotiations that an economy of scale can be achieved, and this is the only way to obtain fair prices, she adds.

"Medicare doesn't have that ability to negotiate, and it's specifically written into the law that they can't do it," Das-Douglas says.

The second mistake made with the bill is that it's designed in terms of forcing consumers to have price sensitivity, she notes.

"It's like thinking consumers are buying widgets," Das-Douglas says.

"They wanted consumers to have price sensitivity, as though someone on antiretroviral therapy (ART) would have a choice," she adds. "HIV patients either take their medication or they don't and then they get opportunistic infections (OIs), and they die."

Medicine not a 'cell phone plan'

All of the recent literature shows that HIV patients who stop taking their ARTs have an adverse health impact, especially if they were co-infected with hepatitis B, Das-Douglas says.

"They're trying to put price sensitivity into health care and it's ridiculous," Das-Douglas says. "They treat it like a cell phone plan where if you use up your minutes in a month, then you have to stop making cell phone calls."

Another problem is that while the AIDS Drug Assistance Program (ADAP) as a payer of last result worked well enough for many HIV patients, now people are supposed to sign up for Medicare Part D if they're eligible for Medicare, says **Christopher A. Douglas**, JD, staff attorney with the Legal Aid Society of San Mateo County in California.

"The way the rules are written, any person who signs up for the Medicare Part D plan has to follow its rules," Douglas explains. "And there are different formularies, different premium payments, and so right at the outset, there is the potential for things to go wrong."

It's so confusing and complex for even the typical Medicare recipient that Douglas spends some of his spare time helping his friends' parents understand their Part D coverage, he says. **(See story about the complexity of Medicare Part D, below.)**

When there are problems with Medicare Part D coverage among HIV patients who have poverty-level incomes, it's up to HIV doctors and their clinics to straighten out medication coverage problems, Douglas says.

This includes both patients having their standard medications not covered by Medicare Part D and patients having problems with deductibles, co-pays, and the doughnut hole.

"Clinicians need to be really proactive and call in or fax in an appeal," Douglas says. "The standard appeal takes five days."

An expedited appeal has to be answered in 48 hours, he adds.

While most doctors want to help patients with their medication reimbursement issues, the problem is they also have little time to deal with these adherence barriers, he adds.

"The most important thing for HIV clinicians is to work collaboratively as a team," Das-Douglas says. "The team needs a health care worker, a doctor, social worker, pharmacist, and, if necessary, a legal or policy advocate because each state and jurisdiction has different laws."

It takes local expertise and everyone working together as a team to treat HIV patients, who are the most vulnerable of populations, Das-Douglas says.

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Medicare Part D has many pitfalls for HIV/AIDS patients

Here are some common problems

As if HIV clinics and physicians didn't have enough government paperwork and bureaucracy to worry about, the nearly three-year-old Medicare Part D prescription drug coverage offers a labyrinth of obstacles, pitfalls, and other problems in keeping HIV patients adherent to

their antiretroviral treatment (ART).

For example, most Medicare recipients have to pay a co-pay that could be 20%, plus a monthly premium, and a deductible that changes each year, says Christopher A. Douglas, JD, staff attorney with the Legal Aid Society of San Mateo County in California.

Then there's the infamous doughnut hole: "Once you go into the doughnut hole you are responsible for 100% of the drug costs," Douglas says.

"So if the drug you were taking costs $500, then you have to pay $500 for it," he says.

A new analysis by the Kaiser Family Foundation in Washington, DC, has found that about 26 % of Medicare Part D prescription drug enrollees in 2007 reached the coverage gap or doughnut hole. This includes 22% who never got out of the hole for the rest of the year and 4 % who received catastrophic coverage.1

About one-fifth of the Part D enrollees who reached the coverage gap in 2007 stopped taking their medication in that drug class (about 15%), or reduced their medication use, or switched to a different medication in that class when they reached the gap.1

In addition, the analysis found that for some Medicare Part D enrollees, their monthly out-of-pocket spending nearly doubled during the coverage gap period. After a Medicare recipient pays roughly $3,500 in out-of-pocket medication costs while in the doughnut hole, then he or she enters the catastrophic coverage phase and Medicare Part D picks up more of the costs again.

"For a lot of people who are very sick, they'll get to the doughnut hole very quickly," Douglas says.

Often Medicare recipients will not realize they have reached the doughnut hole or even know that the doughnut hole exists until they show up at their pharmacy and are given a huge bill for their medications, Douglas says.

"The lack of understanding about Medicare Part D is so pervasive that in a good amount of the cases I see, people come in and think they've lost their coverage when they're in that doughnut hole," he explains. "They show up at the pharmacy, and the pharmacist says, 'You owe us $1,100,' and they don't know what's going on."

For many HIV-infected patients, there is more financial assistance under Medicare Part D, if they are Medicaid eligible, but they still might be faring worse than they were before Part D was enacted in 2006.

Two years ago, many of these same Medicare Part D patients might have received their ARTs uninterrupted from funding through the AIDS Drug Assistance Program (ADAP).

But now they have to be enrolled in Medicare Part D, and when they reach the doughnut hole, ADAP can begin paying for their medications, but only if all of the paperwork has been completed correctly.

For many low-income HIV patients this has not worked very well, says **Moupali Das-Douglas**, MD, MPH, an assistant clinical professor at the University of California - San Francisco (UCSF) and director of research in HIV in San Francisco, CA.

"In some states, ADAP is kicking in for the doughnut hole, but you have to have a really good social worker or legal advocate who can help patients do this, so a lot of people go without their drugs," Das-Douglas explains.

For many low-income HIV patients even the smallest of co-pays are unaffordable, Das-Douglas says.

"Economists and insurance people talk about it and say that a $5 co-pay for medications is great," Das-Douglas says.

"But for our patients, if they're paying $5 per medication, and they're on 10 medications per month, then a $50 co-pay is a big deal," she explains. "It's the difference between eating for a couple of days per week or paying for their medications."

Also, for these people, the other problem is that some of the antiretroviral drugs they were taking under ADAP might not be on the Medicare Part D formulary, and there have been no solutions offered to HIV patients when this occurs, Douglas says.

"The program I work in provides health access," Douglas says. "We help individual beneficiaries having problems navigate the system and get their needed medications."

The best solution for HIV providers and HIV patients would be if Medicare Part D would go away and a new and simpler plan with the ability to negotiate drug prices would be enacted, Douglas says.

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Starpharma optimistic new microbicide will beat odds

VivaGel uses condom coating dosing

Jackie Fairley, BVSc, BSc, MBA, chief executive officer of Starpharma of Victoria, Australia, recently fielded some questions from *AIDS Alert* about the company's investigational microbicide, VivaGel.®

AIDS Alert: Where is the investigational microbicide VivaGel in the clinical research pipeline?

Fairley: The stand-alone VivaGel product is undergoing clinical studies in increasing numbers of sexually active women in order to expand on the safety profile of the product prior to phase 3 efficacy trials. This phase of testing is equivalent to typical phase 2 for a more traditional pharmaceutical product.

AIDS Alert: Why are you confident that VivaGel will not turn into a disappointment for the HIV/AIDS community, as have other vaginal microbicides to date?

Fairley: Starpharma has established a large body of data on the product. These data so far indicate that VivaGel has excellent activity against a wide range of HIV strains in cell-based assays and in very demanding animal studies. Nonclinical and clinical data also demonstrate a favorable safety profile of the product in the studies conducted.

AIDS Alert: Using VivaGel as a condom coating is an interesting dosing strategy. But how will that help women in developing nations gain more power over their own HIV protection?

Fairley: Successful development of a VivaGel coated condom would be good news for women, as it would confirm what we already believe, i.e. that microbicides make sense from a commercial point of view and provide benefits to the community. We believe this success would in turn generate further interest in the microbicide field from commercial parties. Starpharma's own development program for the stand-alone VivaGel product, which more directly gives women control of their own protection, would be significantly boosted and advanced by the successful development of the condom coating product.

AIDS Alert: Would you please describe how your short study will serve as an adequate surrogate for antiviral efficacy of VivaGel in humans? And if there are problems with the microbicide, will this trial adequately highlight the problems before phase III trials begin?

Fairley: As announced recently, the clinical study referred to will measure the level of antiviral (HIV and HSV-2) activity retained by VivaGel® after vaginal administration. This assessment of antiviral activity, which will be by laboratory assay of vaginal samples collected up to 24 hours after VivaGel application, is important as it takes into account the effect of direct exposure of drug to the vaginal environment.

There are no validated surrogates for antiviral activity (or lack thereof) of microbicides in humans. However, until a product is proved effective, Starpharma's trial provides a potential surrogate for antiviral efficacy of VivaGel in humans ahead of Phase 3 studies, as it will determine if SPL7013 is active against virus after contact of the drug with the vaginal mucosa and vaginal secretions.

AIDS Alert: Why are you and others in the HIV/AIDS research world working so intently on finding a vaginal microbicide despite the problems this area of study has had so far?

Fairley: It is important to note that there may never be a vaccine for HIV, although researchers continue to renew efforts towards this goal. Microbicides such as VivaGel are the only other key technology under research and development for prevention. With thousands of people being infected with HIV or dying from AIDS each day, it is self-evident why this is such an incredibly important pursuit. Commercially, a microbicide market in the developed world has been estimated at $1-3.5 billion. Research problems and the resolution or understanding of these problems serve to inform and improve research methods over time. Starpharma is continually applying gold-standard and newly evolved research and development practices in the development of VivaGel in an attempt t ensure a successful outcome.

AIDS Alert: Is there anything else about VivaGel that you'd like to say?

Fairley: VivaGel is being developed as a vaginal microbicide for the prevention of HIV and HSV-2. Other applications of VivaGel are also under assessment, including prevention of human papillomavirus (HPV), and treatment of bacterial vaginosis (BV). All these conditions can lead to increased risk of HIV transmission and acquisition, so are important targets for VivaGel and present excellent commercial opportunities for Starpharma. ■

Research shows protective effect of male circumcision

Drops acquisition risk for at least 3.5 years

Just-presented research at the XVII International AIDS Conference in Mexico City indicates that adult male circumcision continues to reduce the risk of acquiring HIV through heterosexual intercourse for at least 3.5 years.[1]

This finding emerged from an analysis of long-term follow-up data on Kenyan men who have participated in a large clinical trial assessing the protective value of adult male circumcision against HIV infection.[2] The new finding gives further weight to the 2007 World Health Organization recommendation that male circumcision be recognized as an additional important intervention to reduce the risk of heterosexually acquired HIV infection in men.[3]

Three trials examining adult male circumcision — the one in Kisumu, Kenya, another in Rakai, Uganda, and an earlier one in Orange Farm, South Africa — were halted when interim review of data showed medically performed circumcision significantly lowers a man's risk of acquiring HIV through heterosexual intercourse.[4,5]

One of the concerns that has been expressed about the evidence for male circumcision's protective effect against HIV acquisition has been that all three randomized controlled trials of circumcision were stopped before their planned completion, and the studies extended only 18-24 months, observes **Robert Bailey**, PhD, MPH, professor of epidemiology at the School of Public Health at University of Illinois at Chicago and lead author of the recently presented Kenya study. Skeptics have said that the protective effect of circumcision would be eroded after periods of longer than 24 months, he notes.

The paper presented at the 2008 AIDS conference reported a continuation of the Kenyan study, following circumcised and uncircumcised men for 42 months, Bailey points out. The results show that the 60% protective effect of circumcision against HIV acquisition in Kenyan heterosexual men that researchers found after 24 months of follow-up is sustained for at least 42 months, he says. The results show it possibly is strengthened to 65%, Bailey adds.

"These results lend further support to the addition of male circumcision to our currently limited armamentarium of HIV prevention interventions and reinforce the need to introduce safe, affordable, voluntary male circumcision in high HIV-prevalent populations as rapidly as possible," he says.

Review the results

As of May 2008, 1,545 of 1,739 men (89%) had consented to extended follow-up, with 767 in the circumcision group and 778 in the control group. A total of 1,491 remain on study. Of the 1,393 in the control group, 525 (38%) became circumcised. Age and number of sexual partners at baseline were the same in controls who did and did not circumcise. Median follow-up was 30 months.

There were 27 HIV seroconversions in circumcised men and 62 in uncircumcised men, researchers report. The 42-month cumulative seroincidence was 2.6% [95% confidence interval (CI) 1.4, 3.9] among men randomized to immediate circumcision and 7.4% (5.2, 9.5) among controls ($p = 0.0002$). Rates for 24- to 30-, 30- to 36-, and 36- to 42-month follow-up intervals were 0.3%, 0.2%, and 0.7%, respectively, in the circumcision group vs. 1%, 1.3%, and 1.6% for controls. The relative risk of HIV infection in circumcised men was 0.36 (0.23, 0.57), corresponding to a 64% (43, 77) protective effect. Those results support expeditious provision of safe, affordable circumcision services as part of comprehensive HIV prevention strategies, researchers conclude.[1]

How many men in the United States are circumcised? About 80%, according to national probability samples of adults surveyed during 1999–2004 through the National Health and Nutrition Examination Surveys. This figure includes 88% of non-Hispanic white men, 73% of non-Hispanic black men, 42% of Mexican-American men, and 50% of men of other races/ethnicities.[6]

Data on circumcision and risk for HIV infection in the United States are limited, according a review of research by the Centers for Disease Control and Prevention (CDC).[7] In one cross- sectional survey of men who have sex with men (MSM), lack of circumcision was associated with a twofold increase in the odds of prevalent HIV infection.8 Results from a prospective study of MSM indicate that lack of circumcision was associated with a twofold increase in risk for HIV seroconversion.[9] In both studies, the results were statistically significant, and the data have been controlled statistically for other possible risk fac-

tors, the CDC review states.

Other studies have not followed suit. In a prospective cohort study of MSM, there was no association between circumcision status and incident HIV infection, even among men who reported no unprotected anal receptive intercourse.[10]

AAP reviews policy

According to the National Hospital Discharge Survey, 65% of U.S. newborns were circumcised in 1999, with the overall proportion of newborns circumcised stable from 1979 through 1999.[11]

In 1999, the American Academy of Pediatrics (AAP) revised its neutral stance on circumcision to a position that the data then available were insufficient to recommend routine neonatal male circumcision. In the 1999 position paper, the organization stated, "It is legitimate for the parents to take into account cultural, religious, and ethnic traditions, in addition to medical factors, when making this choice."[12] The organization reaffirmed its position in 2005.[7]

The original 1999 AAP policy on circumcision still is current, says **Debbie Linchesky**, an AAP spokeswoman. A new task force is updating the policy; however, it has not been released as of press time, she says. No projected release date has been issued, she states. *(Editor's note: CTU will cover the updated policy as soon as it is released.)*

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FDA Notifications

Generic didanosine approved by FDA

On Sept. 24, 2008, FDA approved a generic formulation of Didanosine (ddI) Delayed Release Capsules, 125 mg, 200 mg, 250 mg, and 400 mg, manufactured by Aurobindo Pharma Limited, Hyberdad, India. Didanosine is a Nucleoside Reverse Transcriptase Inhibitors (NRTI), which helps keep HIV, the virus that causes AIDS, from reproducing, and is intended to be used with other anti-retroviral agents for the treatment of HIV-1 infection.

The application was reviewed under the expedited review provisions of the President's

Emergency Plan for AIDS Relief (PEPFAR). Approval of the generic formulation means that there are no existing patents and/or exclusivities preventing marketing of this product in the United States, and qualifies it for purchase under the PEPFAR program outside the U.S.

This is a generic version of Videx EC, made by Bristol Myers Squibb Co.

As with all FDA-approved generics, this product must meet all of FDA's manufacturing quality, and clinical safety and effectiveness standards for U.S. marketing.

A list of approved and tentatively approved antiretrovirals associated with PEPFAR can be found at http://www.fda.gov/oia/pepfar.htm.

A list of approved generic drugs used in the treatment of HIV infection will be found at http://www.fda.gov/oashi/aids/viralsgeneric.html. ■

FDA approved pediatric efficacy supplement for Retrovir syrup

On Sept. 19, 2008, FDA approved a pediatric efficacy supplement for zidovudine (Retrovir) syrup, capsules and tablets allowing for a twice daily dosing regimen in children six weeks to 18 years of age. It also provides for dosing by weight in addition to dosing by body surface area.

Previously, zidovudine dosing recommendations for the treatment of HIV in children included three times daily dosing with dose calculated using body surface area. The new label has recommendations for twice daily or three times daily dosing by weight or by body surface area. The new recommendations should allow for more convenient dosing (twice daily) of zidovudine in children. The main changes include revisions to the Dosage and Administration section to include twice daily dosing in children as follows.

Pediatric Patients (6 weeks to <18 years of age): Healthcare professionals should pay special attention to accurate calculation of the dose of zidovudine, transcription of the medication order, dispensing information, and dosing instructions to minimize risk for medication dosing errors.

Prescribers should calculate the appropriate dose of zidovudine for each child based on body weight (kg) and should not exceed the recommended adult dose.

Before prescribing zidovudine capsules or tablets, children should be assessed for the ability to swallow capsules or tablets. If a child is unable to reliably swallow a zidovudine capsule or tablet, the zidovudine syrup should be prescribed.

Retrovir Syrup should be used to provide accurate dosage when whole tablets or capsules are not appropriate.

Alternatively, dosing for zidovudine can be based on body surface area (BSA) for each child. The recommended oral dose of zidovudine is 480 mg/m2/day in divided doses (240 mg/m2 twice daily or 160 mg/m2 three times daily). In some cases the dose calculated by mg/kg will not be the same as that calculated by BSA.

Additionally, the label was converted to Physician Labeling Rule (PLR) format to make product labeling more informative and accessible. The pregnancy related sections were modified with the conversion to PLR format to make the data more accessible to clinicians but content was not revised.

The complete revised label will be available soon at Drugs@FDA. Retrovir is a product of GlaxoSmithKline. ■

Abacavir tablet approved for pediatric patients

On Sept. 12, 2008, FDA granted tentative approval for abacavir sulfate 60 mg scored tablet for use in pediatric patients. Abacavir sulfate 60 mg scored tablets are manufactured by Aurobindo Pharma Limited, Hyberdad, India. Abacavir sulfate is an antiviral agent in the Nucleoside Reverse Transcriptase Inhibitor (NRTI) class.

"Tentative approval" means that FDA has concluded that a drug product meets all required quality, safety and efficacy standards, but is not eligible for marketing in the U.S. because of existing patents and/or exclusivity rights. Tentative approval, however, does make the product eligible for consideration for purchase outside the United States under the President's Emergency Plan for AIDS Relief (PEPFAR).

The application was reviewed under expedited review provisions developed for the PEPFAR program.

As with all generic applications, FDA conducts an on-site inspection of each manufacturing facility, and of the facilities performing the bioequivalence studies, to evaluate the ability of the manufacturer to produce a quality product and to assess the quality of the bioequivalence data supporting the application prior to granting approval or tentative approval to these applications.

A list of all Approved and Tentatively Approved Antiretrovirals in Association with the President's Emergency Plan is available on the FDA website. ■

FDA approves pediatric efficacy supplement for didanosine capsules

On Sept. 29, 2008, the FDA approved a pediatric efficacy supplement for didanosine (Videx) EC Delayed-Release Capsules, expanding the indication to include children weighing at least 20 kg.

The main changes include revisions to the Dosage and Administration section as follows: The recommended total daily dose to be administered once daily to pediatric patients weighing at least 20 kg who can swallow capsules is based on body weight (kg), consistent with the recommended adult dosing guidelines

Please consult the complete prescribing information for Videx Pediatric Powder for Oral Solution for dosage and administration of pediatric patients weighing less than 20 kg or who can not swallow capsules.

Section 8.4 Pediatric Use was updated to state the following: Use of didanosine in pediatric patients from 2 weeks of age through adolescence is supported by evidence from adequate and well-controlled studies of didanosine in adult and pediatric patients [see Dosage and Administration (2), Adverse Reactions (6.1), Clinical Pharmacology (12.3) and Clinical Studies (14). Additional pharmacokinetic studies in pediatric patients support use of the Videx EC in pediatric patients who weigh at least 20 kg.

Section 12.3 was added to describe the population pharmacokinetic analysis for children: A population pharmacokinetic analysis was conducted on pooled didanosine plasma concentration data from 9 clinical trials in 106 pediatric (neonate to 18 years of age) and 45 adult patients (greater than 18 years of age). Results showed that body weight is the primary factor associated with oral clearance. Based on the data analyzed, dosing schedule (once versus twice daily) and formulation (powder for oral solution, tablet and delayed-release capsule) did not have an effect on oral clearance. Didanosine exposure similar to that at recommended adult doses can be achieved in pediatric patients with a weight-based dosing scheme.

The results and conclusion from the hepatic impairment study were included in Section 12.3.

Hepatic Impairment: The pharmacokinetics of didanosine have been studied in 12 non-HIV infected subjects with moderate (n=8) to severe (n=4) hepatic impairment (Child-Pugh Class B or C). Mean AUC and Cmax values following a single 400 mg dose of didanosine were approximately 13% and 19% higher, respectively, in patients with hepatic impairment compared to matched healthy subjects. No dose adjustment is needed, because a similar range and distribution of AUC and Cmax values was observed for subjects with hepatic impairment and matched controls.

The following new language for disposal of unused medicines was incorporated in Section 17.

Dispose of unused medicines through community take-back disposal programs when available or place didanosine EC in an unrecognizable closed container in the household trash.

Additionally, the label was converted to Physician Labeling Rule (PLR) format to make product labeling more informative and accessible.

The revised label will be available soon at Drugs@FDA. Videx EC is a product of Bristol-Myers Squibb. ■

Alternative dosing regimen for atazanavir is approved

On Sept. 30, 2008, the FDA approved an alternative dosing regimen for atazanavir (Reyataz) for HIV-1 infected treatment-naïve patients who can take ritonavir. The recommended dosage is Reyataz 300 mg with ritonavir 100 mg once daily for treatment-naïve patients. The following revisions with respect to the new dosing regimen in treatment-naïve patients were

added to the package insert. Other minor revisions were made throughout the label.

Section 2.1 – Recommended Adult Dosage; Dose Recommendations for Therapy-Naive Patients: For treatment-naive patients, the recommended dosage is atazanavir 300 mg with ritonavir 100 mg once daily (all as a single dose with food);

• Or for treatment-naive patients who are unable to tolerate ritonavir, the recommended dosage is atazanavir 400 mg (without ritonavir) once daily taken with food.

The warnings and precautions rash subsection 5.3 was revised to update information from the atazanavir/ritonavir study in treatment-naïve patients as follows.

In controlled clinical trials, rash (all grades, regardless of causality) occurred in approximately 20% of patients treated with atazanavir. The median time to onset of rash was 7 weeks after initiation of atazanavir and the median duration of rash was 1.3 weeks. Rashes were generally mild-to-moderate maculopapular skin eruptions. Treatment-emergent adverse reactions of moderate or severe rash (occurring at a rate of equal to or greater than 2%) are presented for the individual clinical studies [see Adverse Reactions (6.1)]. Dosing with atazanavir was often continued without interruption in patients who developed rash. The discontinuation rate for rash in clinical trials was less than 1%. Atazanavir should be discontinued if severe rash develops. Cases of Stevens-Johnson syndrome, erythema multiforme, and toxic skin eruptions have been reported in patients receiving atazanavir. [See Contraindications (4).]

Section 6.0 adverse reactions was updated to include results from the treatment-naïve study as follows:

6.1 Clinical Trial Experience in Adults; Treatment-Emergent Adverse Reactions in Treatment-Naive Patients: The safety profile of atazanavir in treatment-naive adults is based on 1625 HIV-1 infected patients in clinical trials. 536 patients received atazanavir 300 mg with ritonavir 100 mg and 1089 patients received atazanavir 400 mg or higher (without ritonavir).

The most common adverse reactions are nausea, jaundice/scleral icterus, and rash.

6.3 Patients Co-infected With Hepatitis B and/or Hepatitis C Virus: Liver function tests should be monitored in patients with a history of hepatitis B or C.

In study AI424-138, 60 patients treated with atazanavir/ritonavir 300 mg/100 mg once daily, and 51 patients treated with lopinavir/ritonavir 400 mg/100 mg twice daily, each with fixed dose tenofovir-emtricitabine, were seropositive for hepatitis B and/or C at study entry. ALT levels greater than 5 times ULN developed in 8% (5/60) of the atazanavir/ritonavir-treated patients and 6% (3/50) of the lopinavir/ritonavir-treated patients. AST levels greater than 5 times ULN developed in 8% (5/60) of the atazanavir/ritonavir-treated patients and none (0/50) of the lopinavir/ritonavir-treated patients.

Section 12.3 Microbiology was updated to include resistance information form the treatment-naïve study as follows: Clinical Studies of Treatment-Naive Patients: Comparison of Ritonavir-Boosted atazanavir vs. Unboosted atazanavir: Study AI424-089 compared atazanavir 300 mg once daily with ritonavir 100 mg vs. atazanavir 400 mg once daily when administered with lamivudine and extended-release stavudine in HIV-infected treatment-naive patients.

Additionally the clinical trials section was updated to include the efficacy results from the treatment-naïve study as follows:

14.1 Adult Patients Without Prior Antiretroviral Therapy; Study AI424-138: a 96-week study comparing the antiviral efficacy and safety of atazanavir/ritonavir with lopinavir/ritonavir, each in combination with fixed-dose tenofovir-emtricitabine in HIV-1 infected treatment naive subjects. Study AI424-138 is a 96-week open-label, randomized, multicenter study, comparing atazanavir (300 mg once daily) with ritonavir (100 mg once daily) to lopinavir with ritonavir (400/100 mg twice daily), each in combination with fixed-dose tenofovir with emtricitabine (300/200 mg once daily), in 878 antiretroviral treatment-naive treated patients. Patients had a mean age of 36 years (range: 19–72), 49% were Caucasian, 18% Black, 9% Asian, 23% Hispanic/Mestizo/mixed race, and 68% were male. The median baseline plasma CD4+ cell count was 204 cells/mm3 (range: 2 to 810 cells/mm3) and the mean baseline plasma HIV-1 RNA level was 4.94 log10 copies/mL (range: 2.60 to 5.88 log10 copies/mL).

The complete revised label will be available soon at Drugs@FDA, http://www.fda.gov/cder/drugsatfda/datafiles/. Enter "Reyataz" in the search window, and follow links for "Label Information." ■

CDC underscores HIV threat to Latinos

Challenges: limited health care, language barriers

HIV remains a significant threat to the health of Latino communities in the United States, the Centers for Disease Control and Prevention warns.

Latinos are becoming infected with HIV at a rate three times greater than whites. While Latinos represent just 15% of the U.S. population, they make up 18% of those living with HIV /AIDS. Among Latinos, men who have sex with men are the most heavily affected by HIV, accounting for more than half of all new HIV infections among this population group in 2006.

Challenges include health care access, language barriers, migration, discrimination, socioeconomic status, and stigma surrounding homosexuality and HIV. ■

CE/CME *questions*

1. According to HIV and legal experts, which of the following is a major problem with how the Medicare Part D prescription drug benefit works for HIV patients?
   A. Its co-pays cost many HIV patients, who often are on 10 or more medications, more money than they can afford
   B. HIV patients typically will be impacted by the benefit's "doughnut hole" and might interrupt their treatment when forced to pay the entire cost themselves
   C. The drugs patients had been using under the AIDS Drug Assistance Program (ADAP) might not be the same permitted under Medicare Part D
   D. All of the above

2. True or False: The way Medicare Part D is supposed to save money is by giving the federal government authority to negotiate with pharmaceutical companies for the lowest drug prices.
   A. True
   B. False

3. Starpharma's VivaGel® antimicrobial is in phase 2 testing and so far has had which of the following findings?
   A. The data so far indicate that the microbicide has a favorable safety profile and excellent activity against a wide variety of HIV strains in cell-based assays and in very demanding animal studies
   B. The data so far indicate the microbicide is well-tolerated by women with only the adverse event of vaginal lining irritation
   C. The data so far show that the microbicide can prevent HIV infection among about half of the women who use it
   D. None of the above

Answers: 1. D; 2. B; 3. A.

COMING IN FUTURE MONTHS

- HIV/AIDS origins now traced back a century
- Rapid HIV testing is not catching on as expected
- Will national election results change anything in HIV funding world?
- As HIV infection rates rise among MSM, one clinic has prevention answer

United States Postal Service

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CE/CME objectives

The CE/CME objectives for *AIDS Alert*, are to help physicians and nurses be able to:

- Identify the particular clinical, legal, or scientific issues related to AIDS patient care;
- Describe how those issues affect nurses, physicians, hospitals, and clinics;
- Cite practical solutions to the problems associated with those issues.

Physicians and nurses participate in this medical education program by reading the issue, using the provided references for further research, and studying the questions at the end of the issue. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge.

To clarify confusion surrounding any question answered incorrectly, please consult the source material. After competing this activity at the end of each semester, you must complete the evaluation form provided and return it in the reply envelope provided to receive a letter of credit. When your evaluation is received, a letter of credit will be mailed to you.