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# Pharmacy finds way to improve quality through improved student program

*Pilot test showed improved quality, decreased costs*

Hospital pharmacists increasingly are pressed for time, and the trick for pharmacy managers is to find ways to improve quality and safety while improving staff efficiency.

The pharmacy department at Tampa General Hospital in Tampa, FL, has developed a new program for pharmacy students, called the student clinical service program, that has accomplished those goals.[1]

"We started this project with an interest in figuring out how to use our resources to accomplish better ways of doing things," says **Minh-Tri Duong**, PharmD, a post-graduate year 1 residency program director in the department of pharmacy at Tampa General Hospital.

The pharmacy department typically had pharmacy students work with preceptors to learn a variety of daily tasks assigned to pharmacists.

"They had various responsibilities as a pharmacist in training, but there was no consistent service delegated to students," Duong says.

As the demands on staff pharmacists increased, Duong looked at the student program as a possible way to improve quality and staff efficiency.

After meeting with pharmacists and preceptors, the department decided to start a pilot project in which pharmacy students would focus on two areas of responsibility throughout the course of their traditional training.

The two tasks selected were to have the students provide admission assessments and management of the IV to PO formulary switch program — the evaluation of patients on IV medications to see if they met criteria to be switched over to oral drugs, Duong says.

"We were lucky because there was an IV to PO policy, and my role then was to really design how the students would carry it out and how we'd teach them to do it," says **Lindsay Bock**, PharmD, clinical pharmacist at Tampa General Hospital.

The outcomes from the pilot project were impressive: Prior to having students handle the IV to PO switch program, the service was not consistently done because no one was able to get to those patients in time,

says **Linda Linderbeck**, BSPharm, BCOP, clinical pharmacist.

"Once we utilized the students, we were able to ensure that every patient who met criteria for switch was converted to PO meds," Linderbeck says.

This resulted in a cost savings for the department and ensured that patients were not on IV medications when they didn't need to be, Duong says.

"It decreased the number of days the patient needs to be on IV therapy by an average of five days," Duong says.

Also, the admission referrals' completion increased by 60% within a month of implementing the program, Bock says.

The students gave impressively positive feedback on the program, Linderbeck notes.

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"They enjoyed doing these activities, and they felt it enhanced their time here," she says. "They learned a bunch of things they might not have."

For example, students learned about different drug therapies during the process of assessing patients, Linderbeck says.

"It gave them a lot more opportunity to have face-to-face interactions with patients," she adds. "Even though there are pharmacists in the hospital, a lot of times patients don't get to meet the pharmacist during their stay, so this meant there was more interaction between patients and the pharmacy department, and the students appreciated this."

The students also said they liked the feeling of responsibility and ownership of the tasks they were assigned, Bock says.

Final evidence of the program's success was that more preceptors were receptive to having their students involved after the pilot project, Bock says.

And the program has evolved with hospital changes and market forces.

"Our pharmacy now is responsible for medication reconciliation and no longer has the admission assessment referral," Bock explains.

This transition, which takes place this spring, will mean a number of changes, Duong says.

"It's a huge responsibility for the department, and we'll revise the student clinical service to incorporate students in doing medication reconciliation and IV to PO switch and, potentially, other clinical services as well," Duong says.

The key for hospital pharmacies is to create a student clinical service program that remains flexible. Duong, Bock, and Linderbeck offer these suggestions for how it can be done:

- **Brainstorm to decide which areas to target:** Before starting the student clinical service program, Duong and Bock met with some of the preceptors and administrators to discuss the different roles and responsibilities of a pharmacist.

"Then we tried to narrow down these roles and responsibilities to the ones we felt would be most appropriate to delegate to a student," Duong says. "We looked at the defined criteria, and we set guidelines for students to follow."

Through this process, they decided that the admission assessment and the IV to PO switch program would be the best to assign to students because these had clear cut criteria and could be delegated entirely to students, Duong explains.

- **Create a manual:** Bock then created the 8.5-inch by 11-inch, soft-cover manual. It has 50 pages, which cover both the admission assessment and

IV to PO switch.

"I created a manual for both jobs and included examples of how the students would do the work, step by step," Bock says.

"We have a print shop in our hospital," she says.

Bock followed the IV to PO switch policy and criteria, writing the manual's point-by-point descriptions in a way that would be clear to students.

"It says, 'Here's what you need to do to complete this,'" she says.

The first page is a table of contents, and each section starts with why they will be doing the process in this way, Bock explains.

"We tested the manual on students and revised it throughout the whole process," she says. "Before we started collecting data on it, we had a couple of students try it out."

Once the manual was complete, Bock had 5-10 printed for distribution to new students.

"On the first day of the student's rotation in our facility, they're provided with this manual, and they're told to read it that night because training on it will start the next day," Bock adds.

• **Pilot test it for department buy-in**: Duong found volunteers among the preceptors for pilot testing the student clinical service program.

"We have about 10 preceptors, and three of the 10 participated in this project," Duong says.

"Some of the other preceptors were concerned that students who were providing the service would have their time taken away from their focused training," Duong notes. The student rotations range from four to eight weeks, but can also go longer, she notes.

Once the pilot test results were in, they found that the program enhanced the students' learning experience because students could provide the clinical service activities as part of their rotation, Linderbeck says.

"Students were still able to do the admission referrals and the IV to PO switch without it negatively impacting their focused training," Linderbeck adds. "So it gave students a little better understanding of the things all the pharmacists were doing throughout the day."

• **Show hospital pharmacists and administrators the pilot test results:** Once Bock presented the results of the study, the pharmacists were impressed, Duong says.

"Now many of the pharmacists are very much on board with developing a clinical student service program," Duong adds.

"Having the students do these tasks frees us up to get other things done, increases our clinical activity, and it clearly enhances the student program all around," she adds.

What the pilot test showed was that a student clinical service program could fulfill both clinical quality goals and hospital efficiency goals, Duong says.

"The main driver for this project was our looking at and understanding that the resources are scarce and demands for pharmacist time continue to increase," Duong says. "And we need to look and think outside of the box to finding other resources we can tap into for providing better patient care."

### *Reference*

1. Bock LM, Duong MT, Williams JS. Case study: Enhancing clinical services by using pharmacy students during advanced experiential rotations. *Am J Health Syst Pharm* 2008;65:566-569. ■

# Hospital improves pediatric emergency training

*Exam shows great improvement*

Hospitals with major trauma units need pharmacists on hand to handle emergencies. But if there is a limited number of pharmacists who are trained and prepared to work in the intensive care unit (ICU) or emergency room then the hospital might come up short during a major crisis period.

This is one reason why it's a good idea to train staff pharmacists in emergency medicine.

"We have three ICUs at The Children's Hospital Denver [of Aurora, CO]," says **Pamela D. Reiter**, PharmD, clinical pharmacy specialist in the pediatric intensive care and trauma unit.

The hospital already had the pharmacy represented on the code and trauma team. The pediatric ICU pharmacist carries a pager, and there is a pharmacist available at all times.

But it would be an even greater benefit to the hospital if all pharmacists had even a basic training in handling code and trauma cases.

"Our expectation was that all pharmacists should be able to manage pharmacy responsibilities in a code or trauma," Reiter says. "We wanted to develop an educational competency program so all pharmacists could take this and maintain

their skills."

The key was to develop an education program that would train pharmacists to handle emergency cases in a confident and competent manner.

So the hospital asked pharmacists to voluntarily participate in a pediatric emergency training program.

"We had a sign-up sheet, asking everyone to participate in a self-scheduled learning module and mock code session," Reiter says. "They always took the computer module first."

Here's how the program worked:

• **Develop competency and confidence tool:** At baseline, the pharmacists took a 20-item competency and confidence survey, answering multiple choice questions about emergency department medications.[1]

The survey also asked pharmacists how they felt about their participation in trauma or code situations. And the exam asked about what would be the medicine of choice for a particular condition or disease and what were their duties in a code or trauma situation, Reiter says.

"We designed it ourselves, and it's particular to our institution," she says.

For instance, the exam includes questions about where in the hospital certain medications are stored.

"Right now we use the competency exam internally, but we have the potential to use it with our network hospitals," Reiter says. "We would need to change it a little, such as the location for some medications might be different, but this is an area that we could expand."

The results showed that pharmacists' test scores on average improved by 11% from baseline to after receiving the trauma and code training, Reiter says.

Some pharmacists scored 100% at baseline because they work in the intensive care unit routinely, she notes.

"At baseline, a competency test score of 83.7% was the mean score," Reiter says. "The range was 35% to 100%."

"What was particularly important to us was how well those pharmacists do who score the lowest at baseline," she adds. "And that group of pharmacists who score less than 80% at baseline had a mean increase of 23.5% after the intervention."

• **Provide training with slide show:** Pharmacists watched a 20-30 minute slide presentation that reviewed important points about national guidelines and institutional guidelines regarding the pharmacist's role in trauma and code situations, Reiter says.

"There might be 35 slides, and my voice was in the background," Reiter adds. "The slide presentation was a PowerPoint on DVD, and three or four people could watch it at one time."

• **Use a mock code exercise in training**: After watching the PowerPoint module, the pharmacists could participate in a mock code exercise in which two common scenarios were used and videotaped, Reiter says.

One scenario involved having a child patient who has seizures, and the second scenario was of a child patient who had suffered trauma and needed to be intubated, Reiter says.

"We made these as realistic as possible with a code cart and the mock code in a private room," Reiter says.

Also, pharmacists were expected to ask for information on the patient's weight and known drug allergies, and if they didn't ask for these essential details, they weren't given that information, she notes.

"We role-played two different situations, and they had to respond in an appropriate manner with the right dose, etc.," she says.

The key was for the pharmacist to anticipate the next medication that might be required and to know where to find the medication, draw it up, and label it," Reiter says.

It's common in a trauma and code situation for the physician to ask for a particular medication, and the pharmacist is supposed to know how much of the medicine is needed, she says.

"We have dosing tools to help us, and we introduced that to a lot of our pharmacy staff," Reiter says. "We have helper cards that The Children's Hospital creates with common emergency medication doses on there, so the question was: Do the pharmacists know where to go for this information if they don't know the answer off the top of their heads?"

In the second scenario, the child had been in a car accident and needed rapid sequence intubation, Reiter says.

"So the medical team wanted to place the child in a respirator, but we needed medicine to help the child not get too distressed with that procedure," she explains. "The pharmacist needed to know where to find the fentanyl, an opioid analgesic, and midazolam and rocuronium."

Pharmacists also needed to know the correct doses and had to demonstrate that they could draw it up right there and label it correctly, Reiter says.

"Some of these medications are in the

emergency drug cart, and we had that right there so they could access the medicine right there and then," she adds.

"We reviewed their performance afterwards and gave them immediate feedback, saying, 'You did this great.'"

If the pharmacist wasn't able to find the medication needed for the role-playing scenario, then the instructor told him or her where it would be.

After completing the training session, pharmacists took the exam again, and instructors reviewed their scores, looking for improvements, Reiter says.

"We found the training particularly made a difference to those pharmacists who had not used a code in a long time," she notes.

Although the hospital likely will continue to have a core group of pharmacists who will be the primary ones to respond to pediatric emergencies, now there are many more who could help if the need rose, Reiter says.

"Our goal is to make sure that all pharmacists — if they had to help out — could," she says. "So this program will continue and be part of our new pharmacists' orientation, new residents' orientation, and it will be an annual competency program."

### *Reference*

1. Small L, Schuman A, Reiter PD. Case studies: Training program for pharmacists in pediatric emergencies. *Am J Health Syst Pharm* 2008;65:649-654. ■

# Hospitals are encouraged to remove propoxyphene

*Florida hospital did so effortlessly*

It's time to take propoxyphene off the hospital's shelves, according to the recent clarion call issued by the American Society of Health-System Pharmacists (ASHP) of Bethesda, MD. ASHP called for the Food and Drug Administration (FDA) to remove the pain drug from the market.

Specifically, ASHP refers to the synthetic opioid propoxyphene, which is marketed as Darvon®, or propoxyphene plus acetaminophen, which is marketed as Darvocet®.

While some hospitals have discouraged use of propoxyphene for years, others might find that physicians resist requests to stop prescribing the drug because of their own and their patients' preferences.

But tradition isn't a good enough reason to keep prescribing a drug that research shows has more adverse effects than acetaminophen and no additional benefit.

There has been evidence for decades that propoxyphene has no place in a hospital pharmacy, says **Randy C. Hatton**, PharmD, FCCP, BCPS, co-director of the Drug Information and Pharmacy Resource Center at Shands at the University of Florida in Gainesville, FL. Hatton also is a clinical professor at the University of Florida in the college of pharmacy.

Shands in Gainesville removed propoxyphene from its shelves in the early 1980s, Hatton notes.

"For a long, long time we've taken an evidenced-based approach to our formulary," Hatton says. "In the early 1980s we looked at the literature available then, and there was a fair amount of literature that showed that propoxyphene with acetaminophen — or Darvocet — was no more effective than acetaminophen alone."

Also, the literature has shown for decades that propoxyphene increases the risks of adverse events and toxicities.

"So our evidence back in the early 1980s was that there were better therapeutic alternatives," Hatton says.

When Shands first removed propoxyphene from its formulary, there was some resistance.

Most of the pushback came from physicians who had prescribed the drug for years and found that patients liked the red pills, Hatton says.

"With pain medications there is a huge placebo response, and Darvocet in those days was a big red tablet," Hatton says. "People did find relief from it, but you get relief from acetaminophen too."

Since every formulary has options for non-formulary use, some physicians continued to prescribe propoxyphene in the two decades since the hospital made that change.

"Mainly it was prescribed for patients who were admitted on the drug," Hatton explains. "Some patients come in and have had chronic pain, taking pain medicine for years, if not decades, and they might be very insistent on using Darvocet."

The amounts that were prescribed were small and weren't tracked until a couple of years ago when the hospital's drug information center assessed its use, Hatton says.

"We evaluated it and decided we would not use it at all," Hatton says.

"We did a medication use evaluation over a

six-month period, collecting data on 30 patients receiving the drug," Hatton says. "We wanted to see the characteristics of the patients getting the drug."

The evaluation found that 43% of the patients were older than 65 years, and about half of the elderly patients were on propoxyphene before their hospital admission.[1]

Also, the evaluation focused on the prescribers to see if they might have the impression that the drug was a beneficial product, Hatton notes.

It did not appear that any one physician or hospital service had relied heavily on propoxyphene, so a more targeted education effort did not appear necessary, he adds.

If anyone had an issue with propoxyphene being pulled off shelves, Hatton would have gone over the literature and provided justification for the decision.

"We don't always use a medication use evaluation and audit, but if we think there might be some controversy about a decision, or if we think a drug might be used for something we're not considering, then this is an additional tool at our disposal," Hatton says. "An audit might reveal something we haven't thought of."

The data collected include the patient type, indication of use, the drug's typical dosage, issues regarding the drug's use, etc.

"You can go to the patient's chart and talk with the patient to find out specifically why the patient is taking that drug," Hatton says.

Once the hospital's formulary committee heard the data and approved the change, it was time to educate the hospital's prescribers and pharmacists about how the drug would no longer be made available.

A notice was put in the September, 2007, edition of the *Drugs & Therapy Bulletin*, which is edited by Hatton.

Another key to having a smooth transition to taking the drug off shelves was to offer physicians an alternative to prescribing propoxyphene, Hatton says.

"There's a psychology in the placebo effect with pain medications, and there's also psychology in trying to stop physicians from prescribing a drug," he explains. "It's very difficult to convince people to stop doing something by saying, 'Gee, don't do that.'"

In hospitals where propoxyphene use is high and popular among some physicians, it would be a good idea to meet with them prior to making the decision formal and learn about their concerns and issues, Hatton suggests.

"Providing an alternative is one of the best approaches," he says.

For example, physicians could prescribe tramadol (Ultram®), which is a unique pain medication that affects the neurotransmitter with a different mechanism of action, Hatton says.

"It's not a terribly potent medication, but it's at least as effective as propoxyphene and acetaminophen," he adds. "And it can be combined with acetaminophen (Ultracet®)."

While plain acetaminophen would be a good prescribing choice, its ubiquity makes it a less exciting drug to patients, so tramadol is an alternative that could work with some patients, Hatton says.

Also, there might be withdrawal symptoms among some long-term propoxyphene users, so part of the pharmacy's guidance for physicians was the suggestion that they could treat such symptoms with clonidine, Hatton says.

Since the drug has been removed there has been very little response from providers and patients.

The hospital's decision to remove propoxyphene from its shelves paralleled efforts by a neighboring veteran's administration hospital that was moving in the same direction, Hatton notes.

"The fact that they were doing the same thing helps," he says.

But there was one patient who was very upset when told he couldn't have the drug, and the pharmacy administrator called him to explain the hospital's rationale for the decision, Hatton recalls.

"One of the things we had going for us is that propoxyphene hasn't been in our formulary for 25 years and our use was relatively low," Hatton says. "That makes our situation a little bit easier than in some places that have had it in their formulary for a long time and their use is high."

### Reference

1. Hatton RC. Nonformulary and not available. *Drugs & Therapy Bulletin* 2007;21:1-3. ■

# Pharmacy sets up intranet site with answers, links

*Popular forms available on-line*

A hospital's drug information call center fielded numerous phone calls about finding

forms and regulatory or accreditation requirements. While the call center experts were happy to help out it took up a lot of time they could have been spending on more vital questions about medications.

So a pharmacy resident at the Stanford Hospital and Clinics Drug Information Service in Stanford, CA, came up with a solution: Develop an intranet site for the drug information service.

"I wanted to make things more accessible," says **Emily C. Costerison**, PharmD, an associate medical communications scientist with Genentech Inc. of South San Francisco, CA. Costerison had been working as a resident in the drug information center of a major hospital when she developed the intranet site.

"The thinking in the medical world is that we have all of these resources so do we really need a drug information center," Costerison says. "But, although we have these resources, it's hard to find things."

The drug information center has a call center to which physicians and nurses commonly called to ask how they might obtain a particular form or how they should use a database, she recalls.

"The forms weren't available on-line at that time," Costerison says. "They were available on our server, and pharmacists could access and print out the forms for themselves and physicians."

Physicians frequently requested the pharmacy and therapeutics form in which they could make a request that a new drug be added to the hospital's formulary, she says.

Also, nurses and physicians often asked to see the drug shortage list, which is updated each week, she adds.

Costerison decided to develop an intranet site with pharmacy information and updates and links to requested forms.

"We had a web team and already had Intranet available," Costerison says. "The web team gave me some examples to follow, and I developed a plan of how I wanted the Intranet site to look and what kind of information I wanted on it."

The Intranet site is accessible only by Stanford hospital and clinic personnel.

"Our main focus at Stanford was to provide service to our own health care providers," she says.

Costerison analyzed five months of the phone calls coming into the drug information center and identified trends, such as those that were repetitive and could easily be answered on a web site.

"We categorized each question," Costerison says. "So if you had a question on dosing, it'd be categorized as 'dosing'; an adverse event question would be categorized as 'adverse event'; if someone needed a form or had a question that was not a true drug information question, we categorized it as 'other.'"

Since the Intranet site has been on-line, there have been fewer calls to the drug information center that are categorized as "other," which may mean that people are finding their answers on the Intranet site, Costerison notes.

Since some calls requested information about where additional information could be found, Costerison created a table, containing questions and answers, for the Intranet site.

"I put together a table so that if you had a question about an adverse event it would provide you with the databases you'd need," she says.

The links include the Stanford University library databases and others, she notes.

"I did a rotation in the Stanford library, and we set up a portal just for the pharmacy where they could click on the portal/web page with its databases," Costerison says. "These are the free databases that would be the most helpful, giving professionals assistance when they narrow down where to go for information."

For dosing questions, Costerison created questions and answers for those that were simple and that a medical professional could answer on his or her own.

The Intranet site's links include the drug shortage list, two pharmacy and therapeutics forms for adding or deleting a drug from the pharmacy, forms for pharmacists about restricted drugs, and patient criteria standards.

"We have an "Ask the Pharmacist" page where they can e-mail a question and have a 24-hour turnaround time," Costerison says. "They can

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give their phone number in case it's an urgent question."

The frequently-asked-questions page includes these topics:

- How do I get to the database?
- Who do I contact if I need to order a certain drug?

"The main thing is we wanted to make sure the Intranet site is really easy to maintain," Costerison says. "We didn't want to put a lot of clinical information on the web site because it changes so frequently, so we put in the process information of how do I get this and who do I contact?"

After working on the Intranet site for four months, Costerison was ready to market the new resource.

She developed a brochure and had the marketing department review it.

The brochure describes the Intranet site and the drug information center's services.

"I have a couple of presentations about the Intranet site, trying to focus on places where we didn't have clinical pharmacists," Costerison says.

For example, Costerison visited a dermatology clinic that doesn't have a staff pharmacist, but whose clinicians might need access to forms that are available on the new Intranet site.





Also, Costerison told clinicians in places like the dermatology clinic that the drug information center has a staff pharmacist who is available to help them with any medication issues or questions.

"I went to a lunch meeting with physicians to discuss the Intranet site," Costerison adds. "And all of our pharmacy residents were told about the site, and they started using it and sharing it."

Although the main marketing efforts were directed toward the clinics, there was a little marketing to other hospital clinicians, she notes.

For example, the Intranet site and drug information center's services were featured in a monthly newsletter, and the hospital system's webmasters sent out e-mail notices.

"We didn't want to start out too big and have the drug information center overwhelmed with phone calls," Costerison says. "So we did a little advertising and watched how it was going and then re-evaluated it to see if we could do more."

They also tracked the hits on the Intranet site and found that from February 2007, when the main marketing campaign began, to a month into the campaign, the Intranet site's hits went from 107 hits to 398 hits, Costerison says.

"After the advertising, it went back down to about 100 hits per month," she adds. "We tell people about the Intranet site, and they visit it, but if you don't constantly remind them they stop visiting it as regularly." ■

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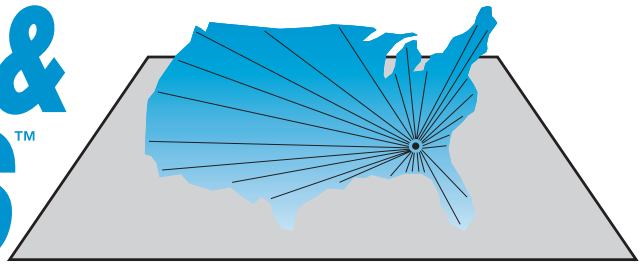

# New Therapies in HIV/AIDS Treatment

By **Justin Garmany**, PharmD Candidate, Harrison School of Pharmacy, Auburn University, and **Richard Cramer**, PharmD, Drug Information Coordinator, Department of Pharmacy, Hunstville (AL) Hospital

The human immunodeficiency virus (HIV) is the biological cause of the acquired immunodeficiency syndrome (AIDS), which was first recognized in the United States in 1981. HIV is an RNA retrovirus that violates the natural production course of DNA by producing DNA from RNA by utilization of a reverse transcriptase enzyme embedded in the virus. There are two types of HIV virus, HIV-1 and HIV-2, with HIV-1 being the primary cause of AIDS in the United States. HIV-2 is mostly seen in Western Africa and is less likely to be encountered in the Western world.

Since the first reports of HIV, more than 65 million people worldwide have been infected with HIV; 25 million have lost their lives to AIDS. At the end of 2005, the World Health Organization (WHO) estimated that 38 million people were living with HIV/AIDS worldwide with 64% of cases being from sub-Saharan Africa. In the United States, approximately 1 million persons are living with HIV/AIDS, with an estimated 40,000 new infections occurring annually. Of particular concern is that of the U.S. cases, 164,000-312,000 people are unaware that they are infected and experts suspect that the majority of new infections each year are acquired from these undiagnosed cases.

## The HIV Life Cycle

To comprehend current treatment modalities, it is important to understand HIV's complex life cycle. HIV targets cells involved with the immune response, specifically helper T cells (CD4 cells). The virus must first bind and penetrate the cell and it does so by utilization of an outer glycoprotein expressed on the virus that has high affinity for CD4 receptors. There are two types of CD4 coreceptors, CCR5 and CXCR4, which the virus targets for attachment. Viruses that prefer the CCR5 virus (R5 viruses) are generally seen in the majority of sexually transmitted cases and in early disease. Those viruses that preferentially use the CXCR4 receptor (X4 viruses) are usually seen in later stages of the disease. Although viruses can prefer one coreceptor over another, there can be a combination of both R5 and X4 viruses in some cases.

Once HIV attaches and penetrates the CD4 cell it uncoats and begins copying its genetic material. It does this by utilization of an enzyme unique to HIV called reverse transcriptase, which is capable of transcribing its RNA to form DNA. Once reverse transcription occurs, the newly formed viral DNA enters the nucleus and integrates into the host cell genome via another enzyme unique to HIV called integrase. Once integration occurs, the virus is able to establish a chronic infection. Now that the virus has integrated into the host cell genome, the cell produces messenger RNA (mRN) and subsequent viral proteins. The viral proteins then bud from the host cell through the plasma membrane where the virus matures via the HIV protease enzyme, thus forming functional viral proteins to produce a viable and complete new virus.

## Treatment Goals and Guidelines

The development of highly reactive antiretroviral therapy (HAART) has greatly changed the clinical course of HIV. People who acquire HIV no longer receive an instant death sentence but can now be managed in a way similar to other

chronic diseases. HAART has profoundly reduced morbidity, improved quality of life, and prolonged survival in HIV patients. The goals of therapy are to maintain a high CD4 cell count, reduce the viral load to undetectable levels for as long as possible, and ultimately reduce morbidity and mortality. According to the Department of Health and Human Services (DHHS) guidelines, treatment should be started in the following patients:

- Patient with a history of an AIDS defining illness (i.e., opportunistic infections)
- CD4 T-cell count < 350 cells/$mm^3$ (normal values: 600-1,500 cells/$mm^3$)
- Pregnant patients and those with HIV-associated nephropathy should start therapy regardless of CD4 T-cell counts
- Patients coinfected with hepatitis B (HBV) when treatment is indicated

## Available Therapies

Current available therapies for HIV/AIDS include nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), fusion inhibitors, CCR5 antagonists, and integrase inhibitors. Of these available agents, the CCR5 antagonists and integrase inhibitors are the newest classes of agents to be introduced to the market. These new drugs, both of which act by a different mechanism of action than other available antiretroviral therapies, are particularly important in the treatment of HIV due to the fast rate of resistance that develops against the traditional agents. It is estimated that 6-16% of newly infected HIV patients will already be resistant to one drug and 3-5% will have reduced susceptibility to drugs from more than one class.

The CCR5 antagonist maraviroc (Selzentry™) was FDA approved on Aug. 6, 2007, for the treatment of HIV-1 infection in combination with other antiretroviral agents in treatment-experienced adult patients who are infected only with CCR5-tropic HIV-1 and have evidence of viral replication. It is also indicated for treatment-experienced adult patients who have HIV-1 strains resistant to multiple antiretroviral agents. This agent opens up a whole new class of agents to help suppress viral load and prolong treatment in patients with few treatment options remaining due to multiple drug resistance. Maraviroc is currently available in 150 mg and 300 mg tablets and the usual recommended starting dose is 300 mg twice daily. It is recommended by the DHHS guidelines to perform a coreceptor tropism assay whenever the use of a CCR5 inhibitor is under consideration.

Maraviroc like most drugs for HIV/AIDS, has some limit adverse effects. One in particular is a black box warning for drug-induced hepatotoxicity with allergic-type features. It is recommended to consider discontinuation if signs/symptoms of hepatitis or an allergic reaction occur following drug administration. Other commonly reported adverse effects include fever, dizziness, cough, upper respiratory tract infection, rash, and abdominal pain. Maraviroc is a major substrate for CYP3A4 and so caution should be used when concurrently administering strong inducers or inhibitors of this enzyme system. As many of the current therapies for HIV/AIDS are inhibitors and inducers of the CYP3A4 enzyme, dosage adjustment recommendations are available.

Raltegravir (Isentress™) is the first integrase inhibitor, and was approved by the FDA on Oct. 12, 2007, for the treatment of HIV-1 infection in treatment-experienced patients with multi-drug resistance in combination with other antiretroviral agents. Like maraviroc, raltegravir provides another treatment option for patients who have few therapeutic alternatives due to drug resistant virus. Raltegravir is currently available in a 400 mg tablet with the recommended dose of 400 mg twice daily. The most commonly reported adverse effects are headache, fatigue, dizziness, increased blood glucose, lipodystrophy, vomiting, and increased liver enzymes.

Another drug of particular importance is the new second generation NNRTI etravirine (Intelence™) that was FDA approved on Jan. 18, 2008. Etravirine is indicated in conjunction with at least two other antiretroviral agents in treatment-experienced patients. It differs from other NNRTIs in that it possesses activity against HIV-1 strains resistant to others within the NNRTI class. Hepatic enzymes metabolize etravirine; primarily CYP3A4, 2C9, and 2C19, so drug interactions are a concern with this product. The most commonly reported adverse effects are rash, increased LDL-cholesterol and triglycerides, increased blood glucose, nausea, abdominal pain, and hypertension. Etravirine is available in a 100 mg tablet with a typical starting start dose of 200 mg twice daily.

The most recent addition to the PI class is

darunavir (Prezista™). It was approved by the FDA on June 23, 2006, for the treatment of HIV-1 infection in combination with ritonavir (Norvir®) and other antiretroviral agents. It is recommended that this drug be limited to treatment-experienced patients or patients resistant to multiple PIs. Ritonavir is another member of the PI class, which is coadministered frequently with other antiretroviral agents to increase their plasma concentrations due to its strong inhibitory effects on the CYP3A4 enzyme. Darunavir is a major substrate for CYP3A4, which does not reach appreciable plasma concentrations without the coadministration of ritonavir.

The most commonly reported adverse effects of darunavir therapy are increased triglycerides, nausea, diarrhea, vomiting, taste disturbances, increased GGT, and weakness. Darunavir is available in a 300 mg tablet with the starting dose being 600 mg of darunavir with 100 mg of ritonavir, both administered twice daily.

## Conclusion

Significant progress has been made in the management of HIV/AIDS since its recognition. There are several classes of agents available for treatment and more are likely to follow. However, despite great strides in HIV/AIDS therapy, many problems remain such as viral resistance and the inability to halt disease progression. More research on new agents and treatment strategies are needed to further improve quality of life and survival of patients with HIV/AIDS.

## Resources


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Merson MH. The HIV-AIDS pandemic at 25 — the global response. *N Engl J Med* 2006;354:2414-2417.

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# New FDA Approvals

The FDA has approved Relistor™ (methylnaltrexone bromide) to help **restore bowel function** in patients with late-stage, advanced illness who are receiving opioids on a continuous basis to help alleviate their pain.

Opioids are often prescribed on a continuous basis for patients with late-stage, advanced illness to help alleviate pain. This includes patients with a diagnosis of incurable cancer, end-stage Chronic Obstructive Pulmonary Disease (COPD) from emphysema, heart failure, Alzheimer's disease with dementia, HIV/AIDS, or other advanced illnesses.

Opioids can interfere with normal bowel elimination function by relaxing the intestinal smooth muscles and preventing them from contracting and pushing out waste products. Methylnaltrexone bromide acts by blocking opioid entrance into the cells, thus allowing the bowels to continue to function normally.

Methylnaltrexone bromide is an injectable medication. It can be administered as needed, but not to exceed one dose in a 24-hour period. The recommended starting schedule is one dose every other day as needed for patients with late-stage advanced illness. Methylnaltrexone bromide is not recommended for patients with known or suspected intestinal obstructions.

Common side effects include abdominal pain, gas, nausea, dizziness, and diarrhea. If severe diarrhea, vomiting, nausea, or abdominal pain occurs while taking methylnaltrexone bromide, patients should discontinue use of the medication in consultation with their health care professional.

The safety and effectiveness of the drug was demonstrated in clinical studies conducted by the sponsors. The two randomized, double-blind placebo-controlled studies involving a total of 287 participants were conducted over a four-month period. The median age of the study participants was 68 years, and 51% of the participants were women. In both studies, all patients had advanced late-stage illnesses with a life expectancy of less than six months. Prior to treatment with methylnaltrexone bromide, participants had either less than three bowel movements in the week prior to treatment or no bowel movement for more than two

days. Patients who were treated with methylnaltrexone bromide had a significantly higher rate of elimination than those receiving placebo. The safety and effectiveness of methylnaltrexone bromide have not been studied in pediatric populations.

Methylnaltrexone bromide is manufactured by Wyeth Pharmaceuticals Inc., Philadelphia, PA, and Progenics Pharmaceuticals, Tarrytown, NY.

Cimzia® (certolizumab pegol) has received approval from the FDA for adults with moderate-to-severe **Crohn's disease** who have not responded to conventional therapies. This product was approved with a Medication Guide.

Crohn's disease is a chronic, inflammatory bowel disease that affects more than one million men and women worldwide. It has no cure and its cause is unknown. Crohn's can cause diarrhea, fever, rectal bleeding, malnutrition, narrowing of the intestinal tract, obstructions, abscesses, cramping, and abdominal pain. It also can lead to abnormal connections (fistulas) leading from the intestine to the skin or internal organs.

Patients treated with certolizumab pegol will receive an injection every two weeks for the first three injections. Once benefit has been established, certolizumab pegol should be given once every four weeks.

The most common side effects of certolizumab pegol are headache, upper respiratory infections, abdominal pain, injection site reactions, and nausea.

Patients taking certolizumab pegol are at increased risk for serious adverse effects, including serious infections that can lead to hospitalization or death. Because certolizumab pegol affects the immune system, it can lower the body's ability to fight infections, such as tuberculosis and other opportunistic infections. Certolizumab pegol is a blocker of tumor necrosis factor and may cause lymphomas (a form of cancer) and other malignancies. Although an increased risk of tumors was not seen in studies of certolizumab pegol, the modest size and relatively short duration of the controlled studies prevents any firm conclusion. Post-marketing studies and clinical trials will be required to obtain long-term safety data.

Patients taking certolizumab pegol should be educated about how to identify an infection and be instructed to contact their health care professional at the first sign of infection while on certolizumab pegol. In cases of serious infections, the drug should be discontinued immediately.

Certolizumab pegol is manufactured by UCB, Inc., Smyrna, GA. ■

# CE *Questions*

Pharmacists participate in this continuing education program by reading the article, using the provided references for further research, and studying the CE questions. Participants should select what they believe to be the correct answers.

Participants must complete a post-test and evaluation form provided at the end of each semester (June and December) and return them in the reply envelopes provided. A statement of credit requires a passing score of 70% or higher. When a passing test and evaluation form are received, a statement of credit and answer guide will be mailed to the participant.

This CE program will improve participants' ability to:

- **Compare** the clinical efficacy and safety of one therapeutic agent over another used in the same setting.
- **Assess** clinical trial data and explain how the results influence formulary decision making.
- **Perform** cost-effectiveness analyses.

1. There are two types of HIV virus, HIV-1 and HIV-2, with HIV-1 being the primary cause of AIDS in the United States. HIV-2 is mostly seen in Western Africa and is less likely to be encountered in the Western world.
   A. True
   B. False

2. Approximately how many new cases of HIV/AIDS are diagnosed annually?
   A. 20,000
   B. 40,000
   C. 60,000
   D. 80,000

3. HIV targets cells involved with the immune response, specifically:
   A. cytokines.
   B. macrophages.
   C. CD4 cells.
   D. mast cells.

4. Which of the following agents have been introduced to the market most recently?
   A. Nucleoside reverse transcriptase inhibitors & non-nucleoside reverse transcriptase inhibitors
   B. Protease inhibitors
   C. Fusion inhibitors
   D. CCR5 antagonists & integrase inhibitors