FOR MORE THAN 20 YEARS

DRUG FORMULARY R•E•V•I•E•W™

Utilization, Criteria and Outcomes

AHC Media LLC

IN THIS ISSUE

Statement of Financial Disclosure:
Barry A. Browne, PharmD (Pharmacist Editor), John Hope (Editor), Lee Landenberger (Editorial Group Head), Paula Cousins (Managing Editor), and Spencer H. Durham and Sara Webster (Authors, insert) report no relationships with companies related to this field of study.

DECEMBER 2006
VOL. 22, NO. 12 • (pages 89-96)

Technology helps combat pharmacist shortage

Faced with the realization in the early years of this decade that 26 community pharmacies had recently closed and 12 more were at risk of closing, the North Dakota Board of Pharmacy started looking for a solution. A problem, according to North Dakota State University College of Pharmacy dean **Charles Peterson**, PharmD, was that many pharmacists in rural areas of the state were reaching retirement age and wanted to leave the profession. But there was great difficulty in finding replacements because of the pharmacist shortage generally and because of the difficult economic conditions in some of the rural areas.

"The board started talking with stakeholders in terms of a decision that had to be made," Peterson tells *Drug Formulary Review*. "Either we needed to find a creative solution or we could allow the situation to continue and become an even greater crisis."

Telepharmacy came up as a possible solution, he says, and the board agreed to a small pilot program to test it. That pilot turned out to be so successful that the board scrapped it in less than a year and wrote rules so the process could be implemented statewide.

North Dakota, like many states, had rules requiring that licensed pharmacists be present in the pharmacy when support personnel are performing the mechanical functions involved in dispensing a prescription. For telepharmacy to work, the pharmacy board had to take a leap of faith and accept that a registered pharmacist could supervise the work of a pharmacy technician from a remote site using real-time audio-video communications technology.

The project now is in the fifth year of a federal grant from the Health Resources and Services Administration's Office for the Advancement of Telehealth. It has grown to 57 participating sites, including 44 community pharmacies and 13 hospitals, and serves more than 40,000 rural citizens who otherwise would not be likely to have access to traditional pharmacy services. And the project has added an estimated $12.5 million to the economies of small towns in the state by adding jobs and restoring pharmacy services.

Under new rules established by the Board of Pharmacy, a pharmacist

at a central site supervises a registered pharmacy technician at a remote site through use of audio-video Internet conferencing equipment and digital imaging cameras. And, Peterson tells *DFR*, it is being done at a cost well below that of automated dispensing technology while still keeping pharmacists in the loop for the important job of consultation and professional expertise.

"It is important to understand when dispensing actually occurs in telepharmacy," Peterson wrote in a *Journal of Pharmacy Technology* report. "Dispensing of the product to the patient is always the professional function of a licensed pharmacist and must not be delegated to the technician. As with telemedicine, nobody would define surgery as being conducted by a technician who lays the patient on the table in preparation for the physician to operate the computer-assisted surgery equipment over the long distance communication link. Likewise, nobody would ever consider the radiology technician, who is assisting with a patient's scan (e.g., mobile MRI) at a remote location, to be doing the actual diagnosis of the scan. In the same manner, the dispensing of the pharmaceuticals (an important professional function in the practice of pharmacy) should not be assigned to the technician, when the duty is actually performed by the pharmacist, using the telepharmacy tools. The pharmacy technician prepares the prescription for final dispensing, and the pharmacist does the actual dispensing, at the same time the patient education is provided."

The distance from the central pharmacy site to the remote telepharmacy site ranges from 13 to 95 miles. The remote telepharmacies are staffed by one technician and one or two store clerks and generally dispense 15-55 prescriptions per day. The remote telepharmacy communities have populations ranging from 498 to 1,367 people, and have a medical clinic staffed work days by either a physician, physician's assistant, or nurse practitioner.

Ongoing dialog and supervision

A pharmacy technician at a remote site prepares a drug for dispensing, including entering the prescription and patient information into the pharmacy system, preparing the container label, and filling the medication container. The pharmacist is able to have an ongoing dialog with the technician, answer any questions, and verify the technician's work over the secure Internet connection.

Technicians also send the pharmacist digital images of the health care provider's written prescription, the medication's original manufacturer container, the prepared label, and one of the tablets or capsules, if appropriate. Peterson said receiving those images helps a pharmacist be sure the patient is receiving the correct medication in the correct dosage. And the digital photos can be stored for later recall if necessary.

Once the pharmacist has completed a final check of the prepared prescription, approval is given to the technician to release the medication to the patient care area.

Peterson tells *DFR* the use of technicians over the years has allowed pharmacists the time to concentrate on more professional tasks. While some have expressed concerns about patient safety in the telepharmacy model, Peterson insists the process is exactly the same as it would be if the pharmacist and technician were together in the same building. "Pharmacists in the store make the final check on

Drug Formulary Review (ISSN#1548-2790), including **Drug Criteria & Outcomes**™, is published monthly by AHC Media LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodical postage paid at Atlanta, GA 30304. POSTMASTER: Send address changes to **Drug Formulary Review**, P.O. Box 740059, Atlanta, GA 30374.

Subscriber Information

Customer Service: (800) 688-2421 or fax (800) 284-3291, (customerservice@ahcmedia.com) **Hours of operation:** 8:30 a.m.-6 p.m. Monday-Thursday; 8:30 a.m.-4:30 p.m. Friday.

Subscription rates: One year (12 issues), $499. Outside U.S., add $30 per year, total prepaid in U.S. funds. Discounts are available for multiple subscriptions. For pricing information, call Steve Vance at (404) 262-5511. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue date. **Back issues**, when available, are $83 each. (GST registration number R128870672.)

AHC Media LLC is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education. This program, #381-000-06-032-H01, will be available **January 1, 2006-December 31, 2007.**

AHC Media LLC has designated up to 6 contact hours annually for this program. Participants will receive statements of credit within 6 weeks after receipt of the post-test and evaluation form, provided a passing grade of at least 70% is achieved. Health system pharmacists and pharmacy benefits managers are the target audience of this activity; however, anyone involved in prescribing, dispensing, patient counseling, formulary selection, or reimbursement processes might benefit from participation.

Editor: **John Hope**.
Vice President/Group Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@ahcmedia.com).
Editorial Group Head: **Lee Landenberger**, (404) 262-5483, (lee.landenberger@ahcmedia.com).
Managing Editor: **Paula Cousins**, (816) 237-1833, (paula.cousins@ahcmedia.com).
Senior Production Editor: **Nancy McCreary**.

Editorial Questions

Questions or comments? Call **Lee Landenberger** at (404) 262-5483.

the technician's work," he says. "Why not do the same thing from a distance but with the same checks and balances? We're just using technology to make the same process work. The pharmacist can view all the work the technician does and have a constant dialog. In reality, the process is exactly the same as the standard procedure and protocol for filling prescriptions."

Remote site techs need more experience

Pharmacy technicians working at remote sites must be registered with the Board of Pharmacy and be a graduate of a training program accredited by the American Society of Health-System Pharmacists. Technicians also must have at least one year of work experience before practicing at a remote site.

Peterson told the *American Journal of Health-System Pharmacy* that he believes the telepharmacy model is actually safer than when a pharmacist in a large hospital's central pharmacy releases a medication from an automated dispensing machine because many of those units don't have the audio-video connection facilitating conversation between the pharmacist in the central pharmacy and the nurse or technician at the patient care unit. "And we think that's problematic," he said. "Part of the feature of the North Dakota telepharmacy model is to keep the pharmacist in the health care loop in providing professional expertise, counsel, and guidance related to proper drug selection and monitoring. And that requires a verbal conversation."

He also says the North Dakota project enhances patient safety because in pharmacies patients are free to reject offered pharmacist counseling, while at a remote site patients can't leave until they have received counseling from the pharmacist over the audio-video connection.

In addition to closure of community pharmacies in rural areas, communities also face severe pharmacist shortages in their hospitals. While experienced hospital pharmacists are a critical part of a hospital's health care team, bringing extensive knowledge on complex issues that arise when dealing with severely ill patients who are on multiple medications and have complicating health factors, attracting and keeping hospital pharmacists in rural communities is as difficult as attracting and keeping retail pharmacists.

When a hospital has only one pharmacist, Peterson says, there is severe pressure on that person to meet all the facility's needs and burnout is a real problem. The rate of pharmacy staff turnover in small hospitals is twice as large as it is in large hospitals.

Telepharmacy also is being used in North Dakota to help solve the hospital pharmacist shortage. Peterson says the state has 39 rural hospitals. Most have only one pharmacist and some are so small that they contract for pharmacy services from a local pharmacy. Regulations generally say that to promote patient safety, pharmacists should make a first dose review of all medications before they are dispensed. But this presents a nearly impossible challenge when facilities operate 24 hours a day, seven days a week, and there is only one pharmacist to do all that work.

"We now have a group of hospitals each having only one pharmacist that is cross-covering for each other," Peterson tells *Drug Formulary Review*. "They have created a telepharmacy network with audio-video links in their hospitals and also in their homes so they can cover for each other." He adds that the pharmacists are working out schedules so individuals can go to professional meetings or take some time off. And they're available to cover for each other if someone has to call in sick. In the harsh North Dakota winters, pharmacists who are stranded at home can still do their work via the secure audio-video link in their homes.

"This has not been easy to arrange," Peterson says. "Hospitals want to each maintain their own identity and administrators aren't always sure they want to allow competitors to work on behalf of their facility. They also all have their own procedures and rules and it was necessary to work out agreements so the pharmacists are doing things the way each hospital wants them done."

Can this model be expanded into other areas of the hospital? Because Peterson thinks it may be possible, he has been invited to submit a proposal to the state hospital association to explore other avenues of cooperation. "We're very excited about this proposal," he tells *DFR*. "We don't know where it will end up, but the possibilities are tremendous."

Peterson and his College of Pharmacy colleagues also are working with rural networks in other states that are looking for reasonable and responsible ways to satisfy new Joint Commission requirements.

Peterson has developed a step-by-step guide to creating a successful telepharmacy program, included in the article in the January 2004 *Journal of Pharmacy Technology*. Steps he identified include:

• **Becoming familiar with laws and regulations.** To operate a telepharmacy program, a state must have laws and rules in place for allowing

telepharmacy services to operate in the state, and remote sites must be properly licensed with the State Board of Pharmacy.

• **Assessing the need**. Questions to be asked include: Are pharmacy and pharmacist services currently available? Are health care providers authorized to prescribe medications sufficient to support a telepharmacy operation? Is there a convenient cost-effective location for a remote site? Is there stakeholder support for a telepharmacy project? Is there a licensed pharmacist available who is willing to take accountability for delivering remote services?

• **Developing community partners.** Peterson says that in choosing partners it is important to consider community need, interest, and investment in the project; availability of a pharmacist at a central pharmacy site in a nearby community willing to deliver telepharmacy services to the remote site; and support from the state Board of Pharmacy. It may be helpful, he says, to obtain feedback from individual patients, senior citizen groups, rural health clinic personnel, community business leaders, local community leaders, local government officials, pharmacists practicing in the area, the state Board of Pharmacy administrator, the state Pharmaceutical Association, and any School of Pharmacy in the state.

• **Securing a physical location.** Selection criteria, Peterson says, for choosing a site for a remote pharmacy should include convenient access for the public, proximity to other health clinic facilities, proximity to nursing homes, financing arrangements, and technology transfer or connectivity capabilities, such as the availability of high-speed Internet access.

• **Selecting personnel.** The North Dakota Board of Pharmacy has established higher standards for pharmacy technicians working in remote telepharmacy sites than for technicians working in traditional pharmacies where a licensed pharmacist is present. Pharmacists working at a central pharmacy are responsible for performing a final check of the prescription prepared by the technician, performing a complete drug utilization review on the patient's medication profile, and performing mandatory patient education counseling. Although Peterson reports that licensed pharmacists at central pharmacy sites have been very excited and quite positive about delivering telepharmacy services to another remote community, they have expressed concern about the significant extra workload falling on them. North Dakota's telepharmacy rules allow a pharmacist to manage up to four remote sites.

• **Considering patient response.** Peterson says it's important that patients be comfortable with the telepharmacy technology before receiving services. Consideration should be given, he says, to formally marketing the telepharmacy concept to the public before implementing services. Proper information and education of patients can assist in alleviating any questions or concerns on how it works and what it looks like, including the similarities and differences between telepharmacy services and traditional pharmacy services.

Peterson tells *Drug Formulary Review* that success is related to the availability of committed project partners who are willing to think outside the box and not believe it's always necessary to do things the way they have been done in the past. It's also necessary, he says, to have good patient support, because if they balk at using the technology, it will be impossible to implement a program.

"Any time you incorporate innovation and creativity it raises people's anxiety," Peterson concludes. "People need to be willing to face the rules and change them if necessary. They need to be willing to take charge of their own destiny."

Download Peterson's article from the Journal of Pharmacy Technology *at www.jpharmtechnol.com/abstracts/volume20/January-February/index.html. Contact Peterson at (701) 231-7609 or e-mail him at Charles.Peterson@ndsu.edu.* ■

Study: Adverse drug events cause ED visits

Some 700,000 U.S. residents go to hospital emergency departments (EDs) each year because of adverse drug events (ADE), according to research reported in the Oct. 18 issue of the *Journal of the American Medical Association*. One-sixth of those ED visits led to hospitalization of the patient in an inpatient care unit or ED observation bed.

The researchers said people ages 65 and older are more than twice as likely to be treated in an ED for an ADE than younger people, and are nearly seven times as likely to require hospitalization. ED visits for ADEs in the 65+ age group "were nearly as common as those for motor vehicle occupant injuries," the report said. They said their findings highlight the importance of directing ADE prevention efforts to that vulnerable population.

To reach their conclusions, researchers analyzed

data from the federal government's National Electronic Injury Surveillance System, which tracks information from a nationally representative sample of 63 hospitals. The study included data from January 2004 through December 2005. In this period, 21,298 ADE cases were reported. Based on those reports, the researchers estimated that 701,547 patients visited an ED each year as a result of an ADE.

Most of the hospitalizations from an ADE were attributed to unintentional overdoses of medication, the researchers said. Drugs that commonly require outpatient monitoring to prevent acute toxicity, such as antidiabetic agents, warfarin, anticonvulsants, digitalis glycosides, theophylline, and lithium, were involved in most of the unintentional overdoses, the authors said. Those drugs were implicated in 66% of estimated overdoses requiring hospitalization and 41.5% of all estimated hospitalizations, they said. However, among patients ages 65 and older, those drugs were implicated in 85.4% of estimated overdose ED visits, 87% of estimated overdoses requiring hospitalization, and 54.4% of all estimated hospitalizations for that age group.

Five common drug classes

Overall, the five most common drug classes implicated in ADE-connected hospitalizations were anticoagulants, insulins, opioid-containing analgesics, oral hypoglycemic agents, and antineoplastic agents, the researchers said.

Of the 18 medications most commonly involved in an ADE that led to an emergency room visit, 16 have been in clinical use for more than 20 years, they said.

More than 80% of the U.S. population in 2004 reported using at least one prescription medication, nonprescription drug, or dietary supplement, and 30% reported using five or more products. An aging population, a trend toward outpatient delivery service, development of new prescription medications, the transition of many prescription medications to nonprescription status, and the increasing use of drugs for chemoprevention will likely increase outpatient drug use, the authors said.

They said while much attention and effort have been directed to measuring, understanding, and preventing ADEs in hospitalized patients, "less attention has been focused on ADEs occurring outside of health care facilities. Efforts to reduce the burden of outpatient ADEs have been hampered by sparse data, except in selected health care systems or settings," the researchers concluded. ■

Nicotine replacement may hurt ICU patients

Mayo Clinics researchers say smokers admitted to intensive care units appear to be at higher risk of cardiovascular events and death if they are given nicotine replacement therapy to ameliorate acute nicotine withdrawal. The researchers presented their findings at the annual meeting of the American College of Chest Physicians.

Amy Lee, MD, and **Bekela Afessa**, MD, conducted a retrospective study of 224 heavy smokers admitted to the ICU; half received nicotine replacement therapy and half did not. Severity of illness was reported to be similar in the two groups, which also were matched for age, gender, and ethnicity. Median length of stay in the ICU and the hospital stay overall was not significantly different between the groups.

Although nicotine replacement therapy is not standard practice for ICU patients, some units have nurse-driven protocols for doing so, according to presentation materials.

There were 18 deaths (16.1%) in the nicotine replacement therapy group, compared with three deaths (2.7%) in the control group. The researchers noted that hemodynamic effects of nicotine withdrawal, including increased blood pressure, heart rate, and coronary artery constriction, can theoretically complicate management of a critically ill patient. Previous studies have shown that nicotine replacement therapy is safe for general medical patients.

"Our study showed that nicotine replacement therapy may not be safe in critically ill patients," the researchers told Reuters. "But this does not include general medical patients in the hospital or outpatients. However, even for the critically ill patient, we cannot confidently say it does harm because our study was retrospective with several limitations." ■

Pharmacists' role in critical pathway development

Pharmacists using new technology, new knowledge, and evidence-based medicine approaches can and should play a critical role in answering questions about the value of critical pathways,

according to members of the 2005 American College of Clinical Pharmacy (ACCP) Task Force on Critical Pathways.

Writing in an ACCP White Paper published in *Pharmacotherapy*, task force members said that as pharmacists continue to play a leading role in managed care, opportunities will be available for them in the critical pathway process that will be essential to ensure future success of critical pathways.

The White Paper says critical pathways represent comprehensive management plans that aim to optimize and streamline patient care. Some specific critical pathway goals include providing continuous quality improvement, decreasing service fragmentation through managed care, optimizing health care delivery cost-effectiveness, guiding a patient and family through expected treatment and progress, and increasing satisfaction of patients, families, staff, physicians, and third-party payers.

Critical pathways create targeted patient outcomes and quality endpoints that form a foundation for common expectations, shared responsibility, regular communication, and early problem detection and intervention among all members of the health care team, the White Paper says. Also, they identify specific time frames and desired outcomes associated with each care step, with the goals of minimizing delays and maximizing resource utilization.

Not treatment guidelines

Critical pathways are differentiated from clinical treatment guidelines. Clinical treatment guidelines may be intended to define appropriate care for a specific indication. The White Paper says the main difference between critical pathways and disease-specific guidelines is that critical pathways focus on targets of care for the clinical management of patient groups instead of addressing decisions on individual patient management.

Because pharmacotherapy is a central component of many critical pathways, pharmacists should take leadership roles in developing, implementing, and assessing critical pathways, the authors said. Critical pathways have been used to establish and document the valuable, accountable roles of pharmacists as essential members of the health care team. Official statements regarding practice guidelines and pharmacists' involvement in patient management, particularly drug therapy and outcomes, have been published by the ACCP and the American Society of Health-System Pharmacists.

"With the advances of clinical pharmacy and medicine, particularly new health care knowledge and technology, pharmacists have been extensively involved in various aspects of the critical pathway," the authors said. "Therefore, a more comprehensive and updated document is warranted to incorporate those changes." The intent of the White Paper was to review the steps in critical pathway development, to discuss the pharmacist's role in critical pathways, and to describe use of critical pathways to maximize delivery of health care while ensuring efficient and effective resource use.

The task force said the process of developing and implementing a critical pathway follows these steps to:

1) identify target patient population, procedure, or disease category;

2) educate staff about critical pathways;

3) convene a multidisciplinary group of care providers;

4) identify key outcomes and corresponding timelines for accomplishing key outcomes;

5) gather information, which may include chart audits;

6) develop critical pathways based on ideal, realistic, or current practice;

7) educate the staff about the critical pathway and its implementation plan;

8) implement the critical pathway;

9) evaluate the critical pathway periodically;

10) insert new alternatives, interventions, and plans into the critical pathway to improve performance;

11) reevaluate the critical pathway after each adjustment.

The report said the process also includes evaluating a health care facility's current process of care and review of medical evidence and external practices. Once a critical pathway is implemented, a follow-up assessment of its impact, using predefined outcomes and baseline observations, should be considered, according to the task force.

Seek support

Before undertaking development and implementation of a critical pathway, planners must take steps to ensure the support of the medical staff and the health system's administration. The authors said an interdisciplinary team must be formed to discuss and determine the goals of management of the selected disease state being addressed by the critical pathway. Team members should be aware of the current standard of care for whatever pathway is being pursued. Experts in the particular

specialty, as well as those who will use the pathway, should be consulted and included. Rational cost-effective therapy intended to achieve definite outcomes that improve a patient's quality of life is the goal from the pharmacist's standpoint, the White Paper said. Also, mechanisms to ensure efficacy and patient safety should be incorporated into a pathway.

Another element in developing a critical pathway is defining the desired clinical outcomes that can be achieved for most patients in the selected population. Thus, a desired clinical outcome might be curing a disease with no adverse effects, within a given time frame and for a given cost. "Critical pathway development offers an ideal opportunity to examine current practice habits for the selected patient population," the researchers said. "Before constructing the critical pathway, the best practice for the target population should be defined by using literature review and benchmarking."

This step, the report said, affords the pharmacist an opportunity to build rational and cost-effective drug therapy into the standard of practice for the selected patient population. At meetings of team members discussing best practices, pharmacists should be prepared to support their recommendations for drug therapy with scientific data, if available, and with benchmarking information and cost analyses. The researchers said impediments to pathway development include lack of data on current practices and outcomes with specific disease states, difficulty in gaining consensus from multiple practice groups, and time-intensive personnel requirements.

Because successful implementation of a critical pathway depends on health care provider education and understanding of the purpose and need for the pathway, a six-month pilot test of pathways is recommended by the researchers so providers can become familiar with using the pathway and the team can modify it as potential improvements are identified.

Because measuring a pathway's impact can be time-consuming, this is a good time to start thinking about how technology can assist the pathway process. The researchers said that automation will help ensure that policies and protocols already in place are followed. A key factor in designing critical pathways is to determine variables that will be measured before implementation. With outcome variables in mind, an institution may be able to create reports that would be beneficial to many areas of the health care system. Patient and financial outcomes need to be considered when measuring a critical pathway's impact, and outcome measures should consider approaches that allow easy retrieval of results or benchmarks from an electronic database.

Again, the report said, pharmacists play a key role in these processes. They should ensure that any software programs that are written are not prone to creating errors. They also should ensure that needed elements and links to other databases (such as allergy and reaction information, drug interaction information, dose range information, laboratory results, and problem lists or diagnoses) are built into the critical pathway to streamline the order entry process and promote practitioner ease of use and compliance.

Review, revise practices and protocol

As part of critical pathway development and implementation, pharmacists must review or revise current pharmacy practices and protocols and implement them to ensure practice consistency. The researchers said a pharmacist can "play an important role on a team evaluating a critical pathway that requires appropriate drug utilization, including those in which drugs are ancillary, such as diagnostic or surgical procedures.

Pharmacy services, including but not limited to pharmacotherapy consults and discharge drug counseling, should be integrated into the critical pathway, and documentation of such services should be incorporated into the overall care plan.

After a critical pathway is developed, those who will be using it need to be educated, and pharmacists can provide education to medical

COMING IN FUTURE MONTHS

- Adverse drug events in ICUs
- How pharmacist-managed diabetes care clinics lead to higher screening rates, attained treatment goals
- Optimal drug therapy for labor and delivery
- Satisfaction with Pharmacist-Managed Lipid Clinics
- Barriers to Glucose Control in ICUs

and nursing staff on protocols and drug therapies to be used or incorporated into the pathway. The groups should also be told of performance standards and goals pharmacy is measuring.

"The three Cs — communication, continuity, and consistency — cannot be overemphasized," the researchers said. "As pharmacists use a critical pathway, they can model and educate other clinicians about the pathway. Pharmacists should prospectively design drug use evaluations in such a way that areas of the critical pathway involving safety, adherence, variation, and efficacy, including specifically designated outcomes, can be assessed. Analysis of the results, with suggested alterations, should be shared with the groups who developed and use the pathway and appropriate clinical and/or administrative committees."

During the past decade, the researchers said, critical pathways have evolved and become common tools in providing health care. The onus is on health care professionals to intensify the validation and justification for using critical pathways in clinical practice, and pharmacists have an important role to play in that process.

Download the ACCP White Paper from www.accp.org. ■

New FDA Approvals

FDA recently approved these drugs:

• Pantheon's Zolinza (vorinostat) capsules were approved for treating **cutaneous T-cell lymphoma (CTCL)**, a type of skin cancer, to be used when the disease persists, gets worse, or comes back during or after treatment with other medicines. Vorinostat was approved under the agency's Orphan Drug program that gives drug companies financial incentives to develop medications for diseases affecting fewer than 200,000 American patients yearly.

The drug's safety and effectiveness were assessed in two clinical trials with 107 CTCL patients who received vorinostat after their disease had recurred following other treatments. A positive response (improvements on a scale scoring skin lesions) occurred in 30% of patients receiving vorinostat, and lasted for an average of 168 days.

The most common serious adverse events were pulmonary embolism, dehydration, deep vein thrombosis, and anemia. The most common other adverse events were gastrointestinal symptoms, fatigue, chills, and taste disorders.

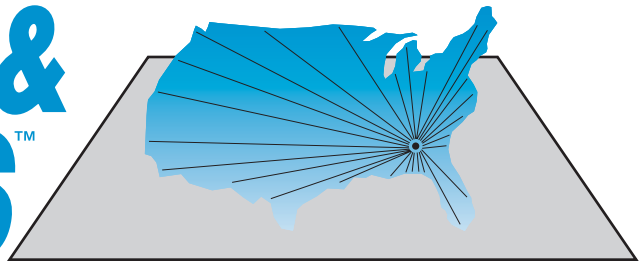
Although it has not been studied in pregnant women, results of animal studies suggest that the drug may cause fetal harm when administered during pregnancy.

• Merck's Januvia (sitagliptin phosphate) tablets were approved as the first diabetes treatment in a new class of **drugs known as DPP-4 inhibitors that enhance a body's own ability to lower elevated blood sugar**. FDA approved sitagliptin phosphate for use in addition to diet and exercise to improve blood sugar levels in patients with Type 2 diabetes, alone or in combination with two other commonly prescribed oral diabetes medications — metformin or a PPAR (peroxisome proliferator-activated receptor gamma) agonist, when either of the drugs, alone or along with diet and exercise, don't provide adequate sugar control.

• Sanofi-Aventis' Taxotere (docetaxel) injection concentrate was approved for use in combination with cisplatin and fluorouracil before radiotherapy for treating patients with **inoperable, locally advanced squamous cell carcinoma of the head and neck.**

• Novartis' Tyzeka (telbivudine) has been approved for treating adults with **chronic hepatitis B.** The agency said telbivudine is a new molecular entity. It is not a cure for hepatitis B. FDA said telbivudine was well tolerated and most reported adverse events were mild to moderate. ■

DRUG CRITERIA & OUTCOMES™



Iplex® and Increlex® Formulary Evaluation

By **Spencer H. Durham**, PharmD Candidate
Auburn (AL) University Harrison School of Pharmacy

Iplex® (mecasermin rinfabate) and Increlex® (mecasermine) are two recently approved agents for the treatment of short stature in pediatric patients. Mecasermin rinfabate is composed of human insulin-like growth factor-1 (IGF-1) and human insulin-like growth factor-binding protein-3 (IGFBP-3). Mecasermine is an aqueous preparation containing human insulin-like growth factor-1 (IGF-1).

Indication

Mecasermin rinfabate and mecasermine are indicated for treatment of growth failure in children with severe primary IGF-1 deficiency (also known as primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to growth hormone. Mecasermine is approved for long-term treatment but mecasermin rinfabate is not.

Mechanism of Action

The main role of IGF-1 in the body is to promote linear growth, and it also suppresses hepatic glucose production as well as stimulates peripheral glucose utilization. IGFBP-3 has no direct effect on growth promotion. It aids in the modulation of IGF-1 by binding to IGF-1 and circulating throughout the body; thus, it is thought to increase distribution of IGF-1 in the body.

Pharmacokinetics

The pharmacokinetic profiles of mecasermin rinfabate and mecasermine are presented in **Table 1**.

Dosage and Administration

Mecasermin rinfabate is supplied as a 36 mg/0.6 mL preservative-free sterile solution in single-dose glass vials. The initial dose is 0.5 mg/kg administered via subcutaneous injection. The maximum dose per day is 2 mg/kg, but the normal therapeutic dosing range is 1-2 mg/kg per day.

Mecasermine is supplied as a 10 mg/mL sterile solution in multiple-dose glass vials (40 mg/vial). The recommended starting dose is 0.04-0.08 mg/kg administered twice per day via subcutaneous injection. The dose may be increased by 0.04 mg/kg per dose up to a maximum dose of 0.12 mg/kg given twice per day.

Table 1
Pharmacokinetics

Drug	Absorption	Metabolism	Excretion
Mecasermin rinfabate	Because the drug is administered via subcutaneous injection, the bioavailability is thought to be 100%, but this has not been fully determined.	The kidney and liver are known to metabolize IGF-1.	For administration of 1 mg/kg, the half-life of IGF-1 is approximately 13.4 hours and the half-life of IGFBP-3 is approximately 54.1 hours.
Mecasermine	Because the drug is administered via subcutaneous injection, bioavailability is thought to be 100%, but this has not been fully demonstrated.	The kidney and liver are known to metabolize IGF-1.	Half-life is approximately 5.8 hours after administration of 0.12 mg/kg.

Contraindications

Mecasermin rinfabate and mecasermine are contraindicated in patients with closed epiphyses, patients who are allergic to any portion of the product formulation, and patients who have active or suspected neoplasia (mecasermine

should also be discontinued if a patient develops neoplasia). In addition, intravenous administration is contraindicated.

Warnings and Precautions

Mecasermin rinfabate has not been studied in patients younger than 3 years of age; use caution in this population.

Mecasermine contains benzyl alcohol, so it should not be used in neonates due to possible neurological toxicity.

Both agents must be administered only via subcutaneous injections.

Adverse Drug Effects

Adverse drug effects reported for mecasermin rinfabate include hypoglycemia (31%), arthralgia, injection site reactions, headaches (22%), lymphadenopathy, iron deficiency anemia, thyromegaly, hyperglycemia, arthralgia, bone pain, muscular atrophy, increased transaminases, papilledema, hematuria, and ovarian cysts.

Hypoglycemia (42%), arthralgia, injection site reactions, lipohypertrophy, bruising, otitis media, snoring, tonsillar hypertrophy, headache, dizziness, convulsions, vomiting, hypoacusis, ear pain, abnormal tympanometry, cardiac murmur, pain in extremities, thymus hypertrophy, and intracranial hypertension have been reported with mecasermine use.

Special Considerations

Studies have not been conducted in patients with renal or hepatic impairment; caution should be used in these patients.

Patients always should take mecasermin rinfabate and mecasermine with food to avoid hypoglycemia. Do not administer if patient cannot take with food.

Clinical Trials

The only information available about these drugs come from the package inserts, so critical evaluation is not possible.

Mecasermin rinfabate

Study Design and Treatment Regimen

• Prospective, open-label multicenter study involving 36 pediatric patients.

• Inclusion criteria: extremely short stature, low IGF-1, low IGFBP-3, and normal GH secretion.

• Patients were started on 0.5 mg/kg/day and titrated up to 2 mg/kg/day based on tolerability and serum IGF-1 levels.

Table 2

Comparison of Annual Cost by Weight

	10-kg Child	40-kg Child
Mecasermine	$12,319	$49,275
Mecasermin rinfabate	$32,850	$98,550

Results

• There was a statistically significant increase in height velocity ($P < 0.0001$) from baseline at both six months and 1 year.

• Patients had a significant increase in height from baseline; for children receiving ≤ 1 mg/kg/day, $P < 0.0001$ at six months and $P < 0.002$ at 1 year; for children receiving ≤ 2 mg/kg/day, $P < 0.001$.

Mecasermine

Study Design and Treatment Regimen

• Five clinical trials (one randomized, double-blind, controlled trial and four open-label trials) were conducted involving 71 pediatric patients. Data from these trials were combined to assess safety and efficacy.

• Inclusion criteria: extremely short stature, slow growth rates, low IGF-1 serum concentrations, and normal growth secretions.

• Patients were administered doses ranging from 0.06 mg/kg bid to 0.12 mg/kg bid for up to eight years.

Results

• Height velocity was significantly increased in years 1-6 of the study ($P < 0.0001$ in years 1-3, $P < 0.0045$ in year 4, $P < 0.0015$ in year 5, and $P < 0.0009$ in year 6).

• No significant increases in height in years 7 and 8.

Cost Comparison

In general, mecasermine is a cheaper option than mecasermin rinfabate, though both drugs cost thousands of dollars annually. **Table 2** compares the annual cost of both drugs. These numbers are based on mecasermine's multiuse 40 mg vial and an average wholesale price per vial of $562.50 and mecasermin rinfabate's single-use 36 mg vial and an average wholesale price per vial of $90.

Formulary Recommendation

At this time, neither mecasermin rinfabate nor mecasermine should be placed on formulary. It is

unlikely that these agents would be used to any significant extent in the hospital setting. If a case should arise that requires use of one of these agents, evaluate on a case-by-case basis.

Resources

• Iplex™. Package Insert. Glen Allen, VA: Insmed Inc.; 2006.
• Increlex™. Package Insert. Brisbane, CA: Tercica Inc.; 2005.
• Tercica Inc. Tercica's increlex pricing provides a significant competitive advantage, June 5, 2006. Available at: www.tercica.com. Accessed Oct. 4, 2006. ■

MTM: Another New Pharmacy Acronym?

By **Sara Webster**, PharmD Candidate
Auburn University Harrison School of Pharmacy

Medications taken incorrectly in the United States represent annual costs of more than $100 billion.[1] One possible solution, medication therapy management (MTM), is a distinct group of services that optimizes therapeutic outcomes for individual patients.[2,3] MTM services enhance patients' understanding of appropriate drug usage, increase compliance with medication therapy, and improve detection of adverse events. These services employ collaboration between the members of a multidisiplinary health team that include a physician, pharmacist, nurse practitioner, dietician, and disease-specific educator (e.g., diabetes).

MTM is expected to decrease overall medical costs by evaluating patients' current therapies, thereby reducing unexpected physician appointments, emergency department visits, and hospital stays.[4] These services include, but are not limited to:

• Performing or obtaining necessary assessments of patient's health status.

• Formulating a medication treatment plan.

• Selecting, initiating, modifying, or administering medication therapy.

• Monitoring and evaluating the patient's response to therapy, including safety and efficacy.

• Performing a comprehensive medication review to identify, resolve, and prevent medication-related problems including adverse drug events.

• Documenting the care delivered and communicating essential information to patient's other primary care providers.

• Providing verbal education and training designed to enhance patient understanding and appropriate use of his or her medications

• Providing information, support services, and resources designed to enhance patient understanding and adherence with his or her therapeutic regimen.

• Coordinating and integrating medication therapy management services within the broader health care management services being provided to the patient.[3,4]

Focus activities may include providing education and management of drug therapy for issues such as diabetes, hypertension, smoking cessation, pain control, asthma, anticoagulation, and immunizations.[3] Diabetes education classes may be offered, as well as instruction on glucose testing and insulin use. A physician's management of a patient's hypertension would benefit from regularly checking blood pressures and maintaining logs. Other possible services include assessing pain control and determining the most practical therapeutic options, educating on inhaler and peak flow meter use for asthma patients, and inoculating people with the influenza, pneumococcal, and other indicated vaccines.

In addition, monitoring could be utilized for osteoporosis, INR, cholesterol, and other medical needs.[3] With osteoporosis, a screening could be conducted to judge the need for a DEXA scan. Likewise, INRs could be tested regularly to help individualize warfarin dosing. Screening of cholesterol levels could be provided to determine efficacy of cholesterol-lowering medications.

Other medication-related services include developing comprehensive patient drug therapy information, which could be achieved by completing a medication review, a personal medication profile, and a drug therapy plan. In conjunction with this, intervention and referral, which consists of recommendations for medication changes, review of abnormal laboratory values, and reports of adverse drug events, are also possible by-products of MTM. Documentation and follow-up would be necessary to receive full benefit from all of these services. MTM service providers can make recommendations to patients, physicians, and other health care providers based on analysis of the patient's current issues. The increased attention given to a patient's current therapies through this education and monitoring also might increase his or her compliance. A personal medication profile could be created and updated listing the patient's medications, doses, indications, and monitoring results to discuss and evaluate during physician and pharmacy visits.[3]

MTM is covered by Medicare Part D for qualified patients who may receive pharmaceutical

care, cognitive services, and disease-state management.[5] Patients qualify if they have at least two chronic medical conditions, take at least two medications covered by Part D, and are likely to spend greater than $4,000 on medications annually.[4] MTM also is available to all interested patients, especially those who have issues with multiple and/or complicated disease states, polypharmacy issues, or have the desire to receive help in medication utilization.[3]

Currently, there is no specific model that defines which practitioners can provide these services or how to provide them. A good option is the team (or multidisiplinary) approach, in a "face-to-face" setting rather than by telephone or with printed materials.[3,4] A collaborative practice could exist between the nurse practitioner, physician, and pharmacist to eliminate excessive visits to physicians for medication purposes. For example, a pharmacist, during an MTM visit, could observe a patient for physical signs of an adverse drug reaction, drug interaction, or inappropriate therapy. The pharmacist would then be able to alert the physician of the issue and implement therapy adjustments. Another example would be a patient having problems controlling his or her diabetes; an MTM visit might allow the pharmacist to recommend changes in current therapy, or increase compliance to the prescribed regimen. These changes would help the patient better control his or her disease, as well as provide a plan for more frequent monitoring and maintain documentation of glucose readings for future reference.[3]

Many patients, regardless of whether they qualify for Part D, would benefit from receiving these services, and MTM will likely elicit more insurance providers to include reimbursement for these services as their patients' request and demand it. The financial aspects of these services are important to the patient in determining whether health or finance is put first. The availability of payment for this service could increase so that payment for MTM is available to more than only those who qualify under Part D. This allows patients with a need for MTM to have the opportunity to benefit from it.[2]

References

1. NexDose: A Unique Solution for Medication Therapy Management. NexDose web site. Available at: www.nexdose.com/for_hcp/MTM.htm. Accessed Nov. 6, 2006.

2. DaVanzo J, Dobson A, Koenig L, et al. Medication therapy management services: A critical review. *J Am Pharm Assoc* 2005;45:580-587.

3. Bennett M, Bertram C, Chater R, et al. Medication therapy management in community pharmacy practice: Core elements of an MTM service. American Pharmacists Association and National Association of Chain Drug Stores; Washington, DC, and Alexandria, VA; April 2005; 1-10.

4. Chen DF, Thompson KK. Proposed model for assuring quality of Medicare's medication therapy management. *Am J Health-System Pharm* 2006;63:1,167-1,171.

5. Pharmacist's Letter. October 2006; 22:1. ■

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.

21. Mecasermin rinfabate and mecasermine are indicated for treatment of growth failure in children with severe primary IGF-1 deficiency (also known as primary IGFD) or with growth hormone (GH) gene deletion who have developed neutralizing antibodies to growth hormone.

A. True
B. False

22. Which of the following is approved for long-term treatment?

A. Mecasermin rinfabate
B. Mecasermine

23. In the body, IGF-1 serves which of the following functions?

A. It promotes linear growth.
B. It suppresses hepatic glucose production.
C. It stimulates peripheral glucose utilization.
D. All of the above

24. Mecasermin rinfabate and mecasermine are contraindicated in which of the following patients?

A. Patients with closed epiphyses.
B. Patients who are allergic to any portion of the product formulation.
C. Patients who have active or suspected neoplasia.
D. All of the above

DRUG FORMULARY REVIEW™
Utilization, Criteria and Outcomes

2006 INDEX

Need back issues? Call our order department at (800) 688-2421; inside Georgia (404) 262-7436. E-mail: customerservice@ahcmedia.com. ***Managing Editor: Paula Cousins.***