diarrhea-predominant irritable bowel syndrome (IBS-D) for whom the benefits of therapy exceed the risks, and
- Communicate the risks of ischemic colitis and serious complications of constipation to patients, pharmacists, and prescribers.

Both FDA and Prometheus, in their briefing documents for the committee's meeting, state that the REMS is meeting both goals.

But the requirements for the prescriber-verification sticker and patient signature on the "Patient Acknowledgement Form" pose logistical burdens that do not further those goals, according to the company, which proposed eliminating both requirements but not the medication guide.

Committee member Brian Erstad, a professor at the University of Arizona College of Pharmacy in Tuscon, voted in favor of updating the prescriber-verification requirement.

And he spoke in favor of continuing to have patients, after a discussion with the prescriber, sign the form acknowledging they understand the risks of alosetron therapy and know the appropriate responses to certain symptoms.

No one, Erstad said, could "tease out the effective elements" from the whole REMS. Thus, FDA should make only one major change at a time to a strategy that is already considered effective.

T. Mark Woods, clinical coordinator for pharmacy at St. Luke's Hospital in Kansas City, Missouri, likewise voted in favor of updating the prescriber-verification requirement.

"Drugs we put REMS on have serious, serious problems," he said.

Yet the committee consistently hears about workarounds for elements in the REMS programs, he added.

With alosetron, Woods said, the sticker on prescriptions signals the dispensing pharmacist to give the situation extra attention.

Alosetron, a serotonin type 3-receptor antagonist, first entered the U.S. market in early 2000 and left later that year. GlaxoSmithKline withdrew the product because serious adverse gastrointestinal events, some fatal, had occurred in users. At the time, the product's labeled indication was the treatment of IBS-D in women; the recommended dosage was 1 mg twice daily.

The product returned to the market in 2002 with a risk management plan, a boxed warning in the labeling, and a narrower indication: women with severe IBS-D who have chronic symptoms, no anatomic or biochemical abnormalities of the gastrointestinal tract, and no response to conventional therapy. The labeling recommended an initial dosage of 1 mg once daily; a higher dosage, 1 mg twice daily, could be taken after four weeks if the initial dosage was well tolerated but insufficient to adequately control a patient's symptoms.

In 2008, after Prometheus acquired the product, the initial recommended dosage was changed to 0.5 mg twice daily.

According to Prometheus, which relied on an IMS Health database, a total of 48,544 patients have taken alosetron from 2002 through March 2013.

An FDA review of the agency's Adverse Event Reporting System for 2002 through 2012 revealed one case in which a patient died, and her gastroenterologist reported that the small-intestine perforation, which led to sepsis, was "possibly" due to alosetron. Two additional alosetron users underwent or were scheduled to undergo intestinal surgery.

The Prometheus-supported adjudicated review of adverse-event reports from 2002 through 2012 found no deaths related to alosetron use and one intestinal surgery for a "probable/possible" case of ischemic colon.

In 2000 alone, according to the company's report on GlaxoSmithKline's data, 11 alosetron users died of causes related to gastrointestinal events.

—Cheryl A. Thompson

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TB care poses challenges, opportunities

The pharmacist-managed tuberculosis (TB) compliance clinic at the University of Southern California (USC) serves students with latent TB infection and also showcases what could be a growing health care role for pharmacists.

Clinical pharmacist Jeffrey Goad said that before the pharmacy staff began managing the program, less than 5% of the students who came to the clinic completed the then-standard six-month course of isoniazid therapy for latent TB.

"We came in about 12 years ago and told [administration] that pharmacists can do a better job. We took it over, and we got the rate up to about 66%," Goad said.

Six pharmacists participate in the clinic, which is part of the university's outpatient pharmacy services.

"The pharmacists are in charge of giving that supply of the medications as the students come in. They check to make sure how much they've taken of the medication," Goad said. Pharmacists also monitor the students for medication-related adverse events and for signs and symptoms of active TB, which requires more extensive care than the clinic offers.

The Centers for Disease Control and Prevention (CDC) has recommended three drugs—isoniazid, rifampin, and rifapentine—for the treatment of latent TB. Treatment courses last for three, four, six, or nine months and require patients to take one or two medications daily, weekly, or twice weekly.

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The once- and twice-weekly regimens require directly observed therapy, meaning that the patient comes to the clinic and a pharmacist observes the patient taking the dose to ensure compliance.

"As more and more therapy moves to short course, we're going to have more need for directly observed therapy," Goad said. "It's a perfect service for pharmacists . . . for adherence, disease progression, and side-effect monitoring."

Tuberculosis typically affects the lungs but can involve any part of the body. In its active form, TB can be transmitted to others through airborne droplets when an infected person coughs, sneezes, or speaks.

According to the World Health Organization (WHO), more than 9 million new TB cases occur each year, and nearly 2 million people die of the disease annually. About a third of the world's population is estimated to be infected with TB, most with the latent form of the disease.

Without drug therapy, about 5–10% of these people will eventually progress to active TB, which requires up to two years of drug therapy.

Most U.S. cases of TB occur in non-U.S. nationals who acquired the infection in their home country, according to CDC.

USC's student population included 8,000 international students during the 2012–13 academic year, including about 3,000 from China and 1,300 from India. According to WHO, China and India account for about 40% of TB cases worldwide.

Goad said it's challenging to treat latent TB in international students who need to leave USC before completing their drug regimen.

"For our students who are graduating, or who are only there for a short program, we have to send them back [home] and instruct them to follow up, which probably won't happen," he said.

He said that's because latent TB isn't viewed as an urgent problem in many countries.

"In the United States, we have a larger problem with latent infections than we have with active infections. And in other countries, it's only active TB that they're really concerned about," because of resource constraints, Goad said.

According to CDC, the annual TB case rate for U.S.-born persons is 1.5 per 100,000 population. The burden is higher among some ethnic and racial groups, such as Native Americans, whose annual TB case rate is 5.6 per 100,000 population.

Kai Chiu, director of the pharmacist-managed latent TB clinic at the Phoenix Indian Medical Center, said pharmacists make treatment recommendations and monitor therapy for Native Americans who are referred to the clinic.

The clinic works with local public health officials who treat patients with active TB infection, and the staff participates in the treatment of people who have been exposed to active TB and are at high risk for infection.

Chiu said he is moderately concerned about drug-resistant TB in his practice setting, because people come to Phoenix from all over the world.

Of particular concern is multidrug-resistant (MDR) TB, which constitutes about 7% of new and 20% of previously treated TB cases worldwide, according to WHO.

MDR-TB is resistant to, at least, isoniazid and rifampin. Extensively drug-resistant (XDR) TB is a subset of MDR-TB that is resistant to isoniazid, rifampin, any fluoroquinolone, and amikacin, kanamycin, or capreomycin or another second-line injectable drug.

A total of 98 U.S. cases of MDR-TB, including 6 cases of XDR-TB, were reported to CDC in 2011, the most recent year for which full data are available. In all, MDR-TB accounted for 1.3% of all TB cases reported to CDC, a slight uptick from the previous year.

"Despite the fact that tuberculosis . . . is currently at an all time low in the United States, as long as TB remains a global problem, [resistance] will always remain a great concern," Chiu said.

News reports in March described an immigrant from Nepal with XDR-TB who is under quarantine in Texas. According to *The Wall Street Journal,* which first reported on the case, the Nepalese man is infected with a strain of *Mycobacterium tuberculosis* that is resistant to at least eight first-line anti-TB drugs.

Goad said the issue of drug resistance is "a little tricky" in his TB clinic because students are identified on the basis of a positive skin-test result and a negative chest x-ray. He said cultures aren't done because people with latent TB don't produce sputum to test for the presence of the organism.

"For all practical purposes, we treat all patients as if they have a susceptible infection," Goad said.

Goad said he is concerned about the public health implications of MDR-TB and the lack of new therapies for the disease.

Bedaquiline late last year became the first anti-TB drug with a new mechanism of action that FDA has approved in 40 years. The drug is indicated for the treatment of MDR-TB for which no other treatment options exist.

Other than bedaquiline, which isn't used at USC's clinic, "we're dealing with old drugs, and the mycobacterium has had plenty of years to get used to them," Goad said.

—Kate Traynor

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News Briefs

• ***The Annals of Pharmacotherapy*** and ***The Journal of Pharmacy Technology*** (JPT) are now published by Sage Publications. Milap C. Nahata remains the editor-in-chief of *Annals of Pharmacotherapy.* Eugene M. Sorkin, previously the associate editor of both journals, is now the managing editor of *Annals of Pharmacotherapy* and editor of *JPT*. The new publisher was announced in both journals' July–August issue. Harvey A. K. Whitney, Jr., is the journals' former publisher.

• **America's Essential Hospitals** is the new name for the National Association of Public Hospitals and Health Systems, which was founded in 1981.