FDA Launches New Transparency Task Force

BY JOYCE FRIEDEN

In one of her first public acts at the Food and Drug Administration, new commissioner Margaret Hamburg announced that the agency aims to be more transparent about its daily work and decision making process.

"Over the years, complaints have been made about FDA's lack of transparency," Dr. Hamburg said June 2 in announcing the launch of a transparency task force. "The agency has been referred to as a 'black box' that makes important decisions without disclosing them. The agency can and should communicate in a way that provides more transparency, not less."

"On President Obama's first day in office, he pledged to strengthen democracy … by creating an unprecedented level of openness" in government, noted Dr. Hamburg, who took over at FDA on May 22. "This will be an agency-wide effort charged with figuring out how to make the FDA and its processes more transparent to the public."

The transparency task force will include the directors of all FDA centers as well as the agency's associate commissioner for regulatory affairs, its chief counsel, and its chief scientist. Its first public meeting was held June 24; another will take place in the fall. The task force "expects to submit a written report to the commissioner about 6 months from now," according to Dr. Joshua Sharfstein, FDA principal deputy commissioner and task force chair.

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Clarity is one area of interest for Dr. Sharfstein. "People don't understand why the FDA may have done something or not done something," he said. "In many cases, the agency has an explanation, but you don't necessarily hear that explanation very clearly."

Dr. Hamburg said she expects that a wide range of recommendations could emerge from the task force's work. Some recommendations "will be in areas that we can implement swiftly, but there may be other types of information that will take more time, and there may be some areas where we have limitations within the current law and need to examine whether appropriate changes can and should be made," she said.

Dr. Hamburg and Dr. Sharfstein emphasized that a balance will need to be struck between providing more information and the appropriate use of confidentiality.

"There are other policy goals besides transparency, and one of the other questions is what information should remain confidential," Dr. Sharfstein said. "The secret formula for how to make X pill may be legitimately confidential information."

Another balancing act will come in terms of clinical trials, Dr. Sharfstein said. "What is the argument for different amounts of data [being disclosed] at different points in the drug development process, and on the other side, what are the confidentiality concerns and the reasons for them?"

The call for transparency comes at a time when the FDA has a backlog of requests under the Freedom of Information Act. Asked how she planned to handle personnel needs while the agency is behind in its work, Dr. Hamburg said, "When the recommendations come in, I will work with the task force and others on implementation. Some activity may result in more work, and some may result in decreased work. If we make more information available, there may be fewer Freedom of Information Act requests and citizen petitions." ■

The Federal Register notice announcing the task force's formation is available online at www.federalregister.gov/OFRUpload/OFRData/2009-12902_PI.pdf. Comments on the task force's mission are being accepted through Aug. 7.

Propylthiouracil Use Associated With Hepatotoxicity in Graves' Disease

BY ELIZABETH MECHCATIE

The antithyroid drug propylthiouracil (PTU) has been associated with severe liver injuries and deaths in patients and should be reserved for those in the first trimester of pregnancy or those who are intolerant of or allergic to methimazole, according to a warning by the Food and Drug Administration.

"If PTU therapy is chosen, the patient should be closely monitored for symptoms and signs of liver injury, especially during the first 6 months after initiating therapy," Dr. Amy Egan, deputy director for safety at the FDA's division of metabolism and endocrinology products at the Center for Drug Evaluation and Research, said in a statement that was posted on the agency's MedWatch Web site. From 1969, when the agency's adverse event reporting program was established, through October 2008, 32 cases of serious liver injury associated with PTU were reported to the FDA. Of these cases, 22 were in adults, and included 12 fatalities and 5 liver transplants. Among the 10 pediatric cases, there was 1 fatality and 6 reports of liver transplants.

Based on an analysis of these reports, the FDA determined that the risk of hepatotoxicity is greater with PTU than with methimazole (MMI). Like PTU, MMI is indicated for the treatment of hyperthyroidism caused by Graves' disease. The FDA received only five reports of serious liver injury associated with MMI, which was approved in 1950.

PTU, approved in 1947, is considered a second-line therapy for patients with Graves' disease, with the exception of those who are intolerant of or allergic to MMI. But because of rare cases of embryopathy reported in association with MMI treatment during pregnancy, PTU "may be more appropriate" for treating women with Graves' disease in the first trimester of pregnancy, according to the FDA.

The FDA plans to change the prescribing information for PTU to reflect the hepatotoxicity warning, and said that the American Thyroid Association (ATA) plans to update its Graves' disease treatment guidelines.

In April, PTU-induced liver failure was among the topics on the agenda at a public meeting on the role of PTU in managing Graves' disease in adults. The ATA/American Association of Clinical Endocrinologists Hyperthyroidism Guidelines Task Force is finalizing recommendations on the use of antithyroid drugs, including during pregnancy and childhood, and will cover the role of monitoring hepatic function in patients on PTU, according to the ATA.

Hepatoxicity has been recognized as one of the more serious but rare side effects associated with PTU, Dr. David Cooper, professor of medicine at Johns Hopkins University, Baltimore, said in an interview. MMI also can be hepatotoxic, but is usually associated with cholestatic dysfunction, while PTU causes hepatocellular necrosis.

With input from the ATA, the FDA decided to issue the warning, said Dr. Cooper, who directs the Johns Hopkins thyroid clinic. He and Dr. Scott Rivkees of the Yale Pediatric Thyroid Center, New Haven, Conn., coauthored an editorial in which they wrote, "one could reasonably conclude that PTU should never be used as a first line agent in either children or adults, with the possible exception of pregnant women and patients with life-threatening thyrotoxicosis" (J. Clin. Endocrinol. Metab. 2009; 94:1881-2).

Dr. Cooper said that most patients who can't take MMI should be treated with radioactive iodine or surgery. Patients who develop jaundice, fatigue, or other symptoms should stop PTU immediately, and contact their physicians. White blood cell count and bilirubin, alkaline phosphatase, and transaminase levels should be checked in such patients, he said. ■

A link to the FDA's alert is available at www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm162701.htm. Serious adverse events associated with PTU products can be reported to MedWatch at 800-332-1088 or www.fda.gov/MedWatch/report.htm.

Stolen Insulin Vials Pose Health Threat

BY MIRIAM E. TUCKER

The Food and Drug Administration has issued an advisory about stolen vials of Levemir that have now resurfaced.

Three separate lots totaling approximately 129,000 10-mL vials of the long-acting basal insulin analogue, made by Novo Nordisk, were stolen in North Carolina and are now being sold in the U.S. market. Some vials from one of the lots were discovered at a medical center in Houston.

These stolen insulin vials may not have been stored or handled properly and may be dangerous to patients. The FDA has received one report of a patient who suffered an adverse event due to poor glucose control after using a vial from one of the lots.

The agency advises the following for patients who use Levemir:

► Determine if you have Levemir from one of the following lots: **XZF0036**, **XZF0037**, or **XZF0038**. Lot numbers are located on the side of the box of insulin and also on the side of the vial.

► If the Levemir is from one of these lots, replace it with a vial of Levemir from another lot. Do not switch to a different brand of insulin without first contacting your health care provider, because another insulin product may require dosing adjustments.

► Always visually inspect your insulin before using it. Levemir is a clear and colorless solution.

► Contact the Novo Nordisk Customer Care Center at 800-727-6500 for instructions on what to do with vials from these lots, or if you have any other questions.

"The safety of our patients is of paramount concern and we are working with our partners, the pharmacy, the FDA, and law enforcement authorities to investigate the situation and take immediate steps to maintain the highest standard of safety and quality for our products," Novo Nordisk said in a statement. ■