New Drug Labels Make Pediatric Info Easier to Find

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ROCKVILLE, MD. — Pediatric information in drug labels is expected to be easier to find and less confusing because of a new approach to incorporating pediatric information into the revised drug label design that is required for all new drugs approved since June last year.

At a meeting of the Food and Drug Administration's Pediatric Advisory Committee held to review pediatric adverse event reports for several drugs, Iris Masucci, Pharm.D., of the FDA's Center for Drug Evaluation and Research (CDER), provided an overview of the elements of the revised drug label.

A physician labeling rule implemented in June 2006 requires that drug labels be revised to make them more user friendly than the previous format. The label, or package insert, of any newly approved drug or biologic or supplemental efficacy approval of a drug submitted to the FDA after June 30, 2006, is required to be in the new format. Drugs approved in the 5 years before this implementation date are required to update their labeling to the new format according to a stepped timeline.

Drugs approved before that time are not required to make the change, but may do so voluntarily. The new labeling requirements also apply to biologics.

The approach on where to incorporate pediatric information into labels is a separate initiative from the new labeling format requirements. Rather, it is a more clearly defined paradigm than what has been used in the past, which will make labels more consistent in terms of how and where pediatric information is added, Dr. Masucci said in an interview.

A major change in the newly designed label is the highlights section, designed in response to feedback from physicians on what they wanted in a drug label, which appears at the beginning of the label. This is a half-page summary that provides the main information on a drug in a simple format with bullets and tables, Dr. Masucci said at the meeting.

This section includes the name of the product with the date of the initial U.S. approval; a boxed warning (if there is one); indications (which include the pharmacologic class of the drug); usage, dosage, and administration information; major changes recently made to the label; as well as dosage forms and strengths, contraindications, warning and precautions, adverse reactions, and drug interactions.

Also included is a patient counseling information statement and a section on use in specific populations, such as children.

The contents of the label include numbered sections with a specific number that corresponds to a particular section, which will be consistent for all drugs. For example, section 2 will always pertain to dosage and administration, and section 8 will always pertain to use in specific populations, which includes pediatric patients.

Other features of the new label include the consolidation of the warnings and precautions sections. Sections on drug interactions, use in specific populations, and patient counseling information—which appears in the precautions section in the old label—are now separate sections. Also, sections on clinical studies and nonclinical toxicology, previously optional, are now required, she said.

Contact information for the FDA's adverse event reporting program, MedWatch, and the drug's manufacturer for reporting adverse events are now also included in the label.

With the old format, it is difficult to determine if a drug is actually approved for pediatric use, Dr. Masucci said, noting that for example, in some tables, a pediatric dose may be listed but no pediatric data are listed.

If the new data are adequate to warrant a pediatric indication, the pediatric information is included in the applicable sections: indications and usage, dosage and administration, adverse reactions, use in specific populations, pharmacokinetics and pharmacodynamics, and clinical studies.

However, if the data are not adequate to support pediatric approval, all pediatric information on the drug appears in the section on "Use in specific populations-Pediatric Use," which she said "will avoid the implication of approval." ■

Example of Highlights for a Fictitious Drug

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Imdicon safely and effectively. See full prescribing information for Imdicon.

IMDICON® (cholinasol) CAPSULES
Initial U.S. Approval: 2000

----------DOSAGE FORMS AND STRENGTHS----------
Capsules: 50 mg (3)

----------CONTRAINDICATIONS----------
- Hematopoietic disorders or a history of TTP or aplastic anemia (4)
- Hemostatic disorder or active bleeding (4)

----------USE IN SPECIFIC POPULATIONS----------
Hepatic impairment: Dose may need adjustment. Contraindicated in severe hepatic disease (4, 8.7, 12.3)
Renal impairment: Dose may need adjustment (2.3, 8.6, 12.3)

----------INDICATIONS AND USAGE----------
Imdicon is an adenosine diphosphate (ADP) antagonist platelet aggregation inhibitor indicated for:
- Reducing the risk of thrombotic stroke in patients who have experienced stroke precursors or who have had a completed thrombotic stroke (1.1)
- Reducing the incidence of subacute coronary stent thrombosis, when used with aspirin (1.2)

Important limitations:
- For stroke, Imdicon should be reserved for patients who are intolerant of or allergic to aspirin or who have failed aspirin therapy (1.1)

----------DOSAGE AND ADMINISTRATION----------
- Stroke: 50 mg once daily with food. (2.1)
- Coronary Stenting: 50 mg once daily with food, with antiplatelet doses of aspirin, for up to 30 days following stent implantation (2.2)

Discontinue in renally impaired patients if hemorrhagic or hematopoietic problems are encountered (2.3, 8.6, 12.3)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling

SOURCE: DR. MASUCCI/ELSEVIER GLOBAL MEDICAL NEWS

FDA Seeks $87 Million More in Fees From Drug Manufacturers

BY ALICIA AULT
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The Food and Drug Administration on Jan. 11 proposed greatly increasing the fees its drug division collects from pharmaceutical manufacturers, saying that current fees collected under the Prescription Drug User Fee Act have not kept pace with inflation or the agency's growing workload.

Most of the additional money would be used to upgrade the agency's postmarketing drug safety monitoring. The FDA also is proposing to create a separate program to collect fees from companies that want their direct-to-consumer television ads reviewed by the agency.

The FDA published its proposals in the Jan. 11 Federal Register and planned to collect comments on them at a public meeting on Feb. 16. The final proposal will be sent to Congress later this year, said Jane Axelrad, associate director for policy at the Center for Drug Evaluation and Research (CDER), in a teleconference sponsored by the FDA.

Time is of the essence, as PDUFA—first established in 1992 and reauthorized in 5-year increments—is due to expire on Sept. 30, 2007.

Under PDUFA, the FDA charges prescription drug makers a set fee to review the safety and efficacy of products submitted under a new drug application. In return, the agency has to meet deadlines for review and approval.

The law has helped FDA to reduce review times and increase its postmarketing oversight, said Dr. Steven K. Galson, CDER director, during the teleconference.

Under the new proposal, FDA seeks to collect $393 million annually, $87 million more than it currently takes in each year. Drug user fees account for about half of CDER's budget, said Dr. Galson, adding that he could not say whether that would hold true going forward, since the agency has not yet received its appropriation for fiscal 2007 or a budget for fiscal 2008.

However, Ms. Axelrad said that drug user fees represent an increasing proportion of CDER's budget.

Public Citizen's Health Research Group criticized that trend, saying that the agency should not receive so much of its funding from the industry it regulates.

"The FDA's crucial drug regulatory functions are too important to be tainted and compromised by direct funding from the very companies whose drugs the agency reviews for safety," said Dr. Sidney Wolfe, director of the advocacy group, in a statement.

The biotechnology and pharmaceutical industries praised the FDA proposal.

"The PDUFA recommendations announced today are a win-win," said Jim Greenwood, president and CEO of the Biotechnology Industry Organization, in a statement. "If enacted, they will help enhance and improve drug safety while providing resources to continue to enable efficient and comprehensive review of new drugs."

The largest portion of the increase, $29 million, would be devoted to postmarketing safety. With those funds, the agency said it could hire 82 new employees, and acquire the best tools and databases for improving the detection and analysis of safety signals. The agency also will institute new programs to reduce medication errors, in response to an Institute of Medicine report issued in September 2006 calling for drug safety improvements at the agency.

Some $20 million would go to cover expenses incurred in the last few years to facilitate drug makers' requests for formal meetings about their products. Sheila Mullin, FDA assistant commissioner for planning, said that in fiscal 2005, the agency held 1,800 formal meetings at manufacturers' request.

About $4 million would be devoted to improving information technology for drug reviews, with the goal of moving to "an all-electronic environment," according to the FDA proposal.

"Reviewing data electronically helps to improve the efficiency of the drug approval process and expedites getting important new drugs to the patients who need them," said Billy Tauzin, president and CEO of the Pharmaceutical Research and Manufacturers of America, in a statement.

The agency is proposing to create a new user fee program solely to fund the review of direct-to-consumer television ads. Currently, companies can voluntarily submit their ads for review, but the FDA has not been able to keep up with the growing workload, said Dr. Galson.

The FDA anticipates charging $6 million in the first year of the program, which would subsidize the hiring of 27 new employees. Another $6 million would be collected for a reserve fund, to cope with unanticipated increases in volume of advertisements.

PhRMA lauded the new program.

"The FDA would have more resources to develop comments for companies before their ads are broadcast, which would help to ensure the advertising's accuracy, balance and compliance with all regulatory requirements," said Mr. Tauzin. ■