FDA News

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FDA Approves Updated Warfarin (Coumadin) Prescribing Information

New Genetic Information May Help Providers Improve Initial Dosing Estimates of the Anticoagulant for Individual Patients

The U.S. Food and Drug Administration announced today the approval of updated labeling for the widely used blood-thinning drug, Coumadin, to explain that people's genetic makeup may influence how they respond to the drug.

Manufacturers of warfarin, the generic version of Coumadin, are to add similar information to their products' labeling, FDA said.

The labeling change highlights the opportunity for healthcare providers to use genetic tests to improve their initial estimate of what is a reasonable warfarin dose for individual patients. Testing may help optimize the use of warfarin and lower the risk of bleeding complications from the drug.

These labeling updates are based on an analysis of recent studies that found people respond to the drug differently based, in part, on whether they have variations of certain genes.

FDA estimates that 2 million persons start taking warfarin in the United States every year to prevent blood clots, heart attacks and stroke. Warfarin is a difficult drug to use because the optimal dose varies and depends on many risk factors including a patient's diet, age, and the use of other medications.

Patients who take a dose larger than they can tolerate are at risk of life-threatening bleeding. Those who receive too low a dose are at risk of equally dangerous blood clots. Dosing is particularly important at the beginning of therapy, when problems in adjusting the dose can lead to complications such as bleeding.

Warfarin is the second most common drug – after insulin –implicated in emergency room visits for adverse drug events.

Physicians and other health care professionals who prescribe warfarin regularly check to see if the drug is working properly by ordering a test called the PT or prothrombin time that evaluates the blood's ability to clot properly. The results are measured in seconds and compared with the expected value in healthy people, known as the International Normalized Ratio or INR.

"Today's approved labeling change is one step in our commitment to personalized medicine. By using modern science to get the right drug in the right dose for the right patient, FDA will further enhance the safety and effectiveness of the medicines Americans depend on," said Commissioner of Food and Drugs Andrew C. von Eschenbach, M.D.

The FDA's "personalized medicine" initiative makes use of pharmacogenomics—the science that predicts a response to drugs based upon a person's genetic makeup. This effort supports the personalized health program spearheaded by Health and Human Services Secretary Mike Leavitt.

A person's genes "encode" enzymes and differences in the sequence of a gene can cause differences in enzyme activity or sensitivity. That is why different people process the same drug differently.

One-third of patients receiving warfarin metabolize it quite differently than expected. Research has shown that some of the unexpected response to warfarin depends on a patient's variants of the genes CYP2C9 and VKORC1.

"Although genetic testing can currently identify who has these genetic variants, more studies are needed to explore the precise starting dose for these patients," said Larry Lesko, Ph.D., director of the FDA's Office of Clinical Pharmacology. "FDA has been working with other government agencies and organizations to develop such studies under the auspices of our three-year-old Critical Path Initiative, which addresses the challenges of moving promising medical products from discovery to patient use."

FDA's Critical Path Initiative has funded a research project with the University of Utah and the Critical Path Institute of Tucson, Ariz., to develop genetically based instructions for warfarin dosing. The Initiative has also facilitated meetings and planning with the National Heart, Lung and Blood Institute for a clinical trial that will study warfarin dosing based on genetic test information and is helping to pay for another clinical study being conducted by Harvard Partners that will derive personalized warfarin dosing algorithms for patients new to the drug.

The dosage and administration of warfarin must be individualized for each patient according to the particular patient's PT/INR response to the drug. The specific dose recommendations are described in the warfarin product labeling, along with the new information regarding the impact of genetic information upon the initial dose and the response to warfarin. Ongoing warfarin therapy should be guided by continued INR monitoring.

Bristol-Myers Squibb Co. of Princeton, N.J., is the manufacturer of Coumadin.

For more information see New Labeling Information for Warfarin.

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