Physician calls for more rigorous standards for drugs up for FDA approval

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A hospitalist at the University of Rochester Medical Center calls for more stringent Federal guidelines governing the approval of potential new drugs, in a commentary in the March 10 issue of the *Journal of the American Medical Association*.

Alec B. O'Connor, M.D., M.P.H., associate professor in the Hospital Medicine Division of the Department of Medicine, says that while the U.S. Food and Drug Administration does an "incredible job, considering its long list of responsibilities and budget constraints," the agency should be empowered to demand more detailed data when a new drug is being considered for approval.

O'Connor's main point is that the FDA should require studies comparing the effectiveness and safety of a new drug to an established first-line drug when considering a drug for approval. Currently the agency does not require such studies, known as "active comparator trials," though some large studies of new drugs do include them. In many cases, to gain approval, the main criterion besides safety is that a new drug must be shown to be more effective than placebo.

"When new medications have been compared only to placebo, not to drugs already on the market, it's very difficult to know whether and how we should prescribe them to patients," O'Connor said. "For example, if a new medication to treat depression is approved based only on placebo comparisons, it's very difficult to know how the new drug compares with the dozens of medications already approved for depression. Faced with

the extensive and very successful marketing undertaken by the drug manufacturer, oftentimes physicians will assume that the newer drug is more effective or has important advantages over older treatments, even though there may be no evidence showing that to be so."

"The current system makes it very difficult to evaluate a new, more expensive treatment against an established, less expensive option," added O'Connor. "We should consider a different standard for approval - that a drug not just outperform placebo, but that it also undergo direct comparison with at least one treatment considered the standard of care. In this way we can ensure that new, less effective treatments do not replace older, more effective and cheaper ones. Requiring new drugs to be compared with established treatments before drug approval would also decrease the amount of federally funded comparative effectiveness research required down the road."

O'Connor began studying issues related to drug approval a few years ago, when he began a meta-analysis of the effectiveness of approved medications to treat severe nerve pain, known as neuropathic pain. With the help of colleagues, he was able to unearth a great deal of information from unpublished studies available deep within the FDA web site. Oftentimes these studies contained negative data about new medications - information that was largely unknown in the medical community.

In his commentary, O'Connor calls for revisions to the Code of Federal Regulations, which spells out the guidelines FDA uses to evaluate new medications. O'Connor notes that Congress, not FDA, sets the guidelines that FDA follows.

Last year O'Connor published another commentary in *JAMA* drawing attention to the availability of information about new drugs through FDA and suggesting ways to make the data easier to find for physicians and others.

"The FDA has its own statisticians who analyze data and arrive at their own conclusions regarding studies," said O'Connor. "They have no financial conflict of interest, and there is no pressure to produce favorable results for a drug. Such an independent analysis is a gold mine for researchers and physicians seeking information about the safety and efficacy of a medication that has recently been approved.

"I have a huge amount of respect for FDA. The amount of time and effort the agency puts into each new drug review is incredible. They do an incredible task with a finite amount of time and resources. The FDA is an ally in maintaining public health and protecting our patients," he added.

Provided by University of Rochester Medical Center