

FDA Takes Caution on Approving New Drugs

By LINDA A. JOHNSON, AP Business Writer August 17, 2007

Under growing scrutiny since the blockbuster painkiller Vioxx was pulled from the market, the Food and Drug Administration in recent months has rejected a slew of experimental drugs or delayed their approval and required more data.

Besides keeping drugs some patients might desperately need off the market, the rejections have battered drug company stock prices and are expected to increase the cost and time it takes to develop a new drug, not to mention the price of developing future ones.

Denials and delays have hit everyone from pharmaceutical giants such as GlaxoSmithKline PLC, Merck & Co., Novartis AG, Sanofi-Aventis and Wyeth down to struggling startups trying to get their first drug on the market. The FDA also has recently stiffened warnings on several drugs, most prominently diabetes drugs Avandia and Actos, and five months ago made Novartis withdraw its constipation drug, Zelnorm.

"There have been no systematic changes in how we are approaching the approval standards for new applications," FDA spokesman Christopher Kelly said in an e-mail. "Whether the current public debate and criticism of FDA on drug safety has played any role in our actions is very hard to quantify."

But Chris Milne, associate director of the Tufts Center for the Study of Drug Development, said Friday the FDA has systematically implemented more controls for scrutinizing drugs, particularly for heart and liver side effects. While he thinks the trend on approvals is not yet clear, he said the FDA now is requiring experimental drugs similar to ones already on sale to be more effective and safer than their predecessors.

Some experts say they already see a trend toward increased rejections, although drugs for life-threatening diseases or conditions with no good current treatment are generally being approved.

"The FDA is being more cautious," analyst Steve Brozak of WBB Securities said, explaining that FDA staff now realize new drugs will be used by many patients beyond those intended -- known as off-label use because the drug is taken for another condition than the one it was approved to treat. That often boosts the chances that some patients will be harmed by side effects.

He sees the FDA mentality now as: "It's got to be so safe that we're not going to be criticized ever" for approving a drug.

The agency has approved 61 percent of drug applications through mid-August, down from 73 percent in the same period last year, according to BioMedTracker, a biotech and pharmaceutical research service.

James Kumpel at Friedman, Billings, Ramsey & Co. just published a report showing FDA approvals of "new molecular entities" -- drugs made from new chemical compounds rather than just twists on existing drugs -- so far this year are at their lowest level in at least a decade. Only seven were approved through the end of July, versus an average of 12 over the first seven months of each year since 1998.

"The FDA certainly has made it more difficult for pharmaceutical companies by pushing for more data and for more participants and for longer studies," said Kumpel, barriers he said will start limiting the number of new blockbusters.

Already, the average cost of shepherding a potential drug from discovery through approval is \$980 million, up from \$802 million in 2000, and the process takes 14.2 years on average, according to Tufts.

"It appears that FDA has been on defense since 2004," Kumpel said.

That's when Merck withdrew its blockbuster painkiller Vioxx from the market because of increased risk of heart attacks and strokes, making Vioxx an instant poster child for drug safety issues.

Last April, the FDA rejected Merck's Arcoxia, a long-planned successor to Vioxx on sale in many other countries.

Just Friday, Endo Pharmaceuticals Holdings Inc. said the FDA for the second time asked for more time to review its approved migraine drug Frova for a new use, preventing menstrual migraines.

In between, the FDA has cited safety or effectiveness questions in rejecting or delaying approval for experimental drugs including Novartis' diabetes drug Galvus, Sanofi-Aventis' weight-loss drug Zimulti, and even a higher dose of GlaxoSmithKline's Advair Diskus for bronchitis and emphysema symptoms. Also shot down: Wyeth's experimental schizophrenia drug bifeprunox and Wyeth's Pristiq, which would have been the first nonhormonal drug for menopause symptoms.

Likewise, small pharmaceutical companies have been hurt. One, Pozen Inc., this month got its second FDA request for more information about a migraine treatment called Trexima it is jointly developing with GlaxoSmithKline. That news sent Pozen shares down 46 percent.

Scott Gottlieb, an American Enterprise Institute fellow who was FDA deputy commissioner until January, said drug companies have long complained that FDA was too conservative. Now, there's even more uncertainty both at the agency and in the industry.

For drugs where benefits don't strongly outweigh risks, Gottlieb said, "The agency errs on the side of caution."