The Push for Additional Orphan Drugs

Can the FDA Do More to Encourage Their Development?

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AstraZeneca’s failed attempts to convince the Food and Drug Administration (FDA) and a federal court to require extra labeling on the slew of generic versions of Crestor that became available this summer illustrate the lengths to which brand-drug companies will go to protect orphan drug prices and profits. In May, the FDA approved AstraZeneca’s Crestor (rosuvastatin calcium) as a treatment for a rare condition called homozygous familial hypercholesterolemia (HoFH). As a result, AstraZeneca gained seven-year orphan market exclusivity for Crestor for that indication. Its broader patent expired in July.

Then AstraZeneca tried to force the FDA and a U.S. District Court to require the agency to mandate that the new Crestor generics include pediatric HoFH labeling that would prevent safety problems if physicians prescribed generic Crestor off-label for pediatric HoFH. The agency and a judge rejected AstraZeneca’s demand. Other brand-drug companies have tried unsuccessfully to use the same tactic.

The global orphan drug market is estimated at $170 billion a year and is growing at 12% annually, according to consultant EvaluatePharma. Patient advocacy groups, such as Global Genes and the National Organization for Rare Disorders (NORD), say there are 7,000 rare diseases, and only 326 drugs have been approved for them since the Orphan Drug Act was passed in 1983. Given the profits that orphan drugs generate, one might wonder why more aren’t on the market. Still, 80% of all rare-disease patients are affected by approximately 350 rare diseases. If each of the 326 drugs had been approved for one of those 350 rare diseases, one might assume that many people with rare diseases already have a drug treatment. So what’s the problem?

Patient advocacy groups would like to see an effective drug made available at a reasonable price for every rare disease, defined by the FDA as one affecting fewer than 200,000 people in the United States. Congress is sensitive to those desires. The House included a provision in its 21st Century Cures Act, passed in July 2015, that would add six months of market exclusivity to the seven years already granted to an orphan drug when the company added a second orphan indication. The Senate has not passed a 21st Century Cures bill, and none of the disparate Senate bills that could be packaged into a 21st Century Cures companion act contains a similar provision.

The Senate did pass a bill in late September to extend an orphan-drug development voucher program to the end of 2016. In March, the Government Accountability Office (GAO) published a report questioning the effectiveness of the vouchers, which Congress established in 2012. The program awards a pediatric orphan voucher to companies that market a new pediatric orphan drug. The voucher authorization expired at the end of September, and the FDA opposed extending it because “they have seen no evidence that the program is effective,” according to the GAO.

The FDA approved 21 orphan drugs in 2015—almost half of all its approvals. “We believe the FDA is using a historic amount of flexibility in reviewing orphan therapies, something we are very thankful for,” says Paul Melmeyer, Associate Director of Public Policy at NORD. “While the FDA is doing quite well overall, we are still aware of situations in which the FDA will request extra confirmatory trials, particular endpoints, limited inclusion criteria, or other clinical trial structures or requests that our patient organization members that participate in such trials deem inappropriate.”

The FDA has included potentially significant orphan-drug enhancements in its “commitment letter” laying out what the agency will do in conjunction with Congress’ expected approval of the next version of the Prescription Drug User Fee Act (PDUFA) when the current law expires in September 2017. The PDUFA specifies the fees companies pay the FDA to support the drug approval process, and the commitment letter outlines improvements the FDA plans in the approval process, in part to justify higher fees.

One proposed initiative would expand the Rare Diseases Program by integrating rare disease specialists in each review division. “I think the addition of the rare disease specialists into the review teams is helpful from an overall understanding of clinical development programs in the context of a rare disease; however, the scientific expertise will still lie with the clinical review personnel,” says Lisa N. Pitt, PharmD, Vice President of Global Regulatory Affairs at Premier Research.

One thing seems certain. If Congress allowed companies such as AstraZeneca to tack on extra six months of market exclusivity onto goldmines like Crestor, there would be an explosion of private sector research and development on orphan drugs. But Congress may not pass even the much more anemic incentive in the House bill.

REFERENCES


