FDA Warns Merck About Its Diabetes Drugs

March 5, 2012 by Patrick A. Malone

Merck can't say it wasn't warned.

In what the FDA Law Blog calls the first of its kind, the FDA last month sent the pharmaceutical manufacturer notification that it violated its promise to conduct postmarket research (PMR) on its diabetes drugs Januvia and Janumet.

The letter represents new authority Congress granted the FDA to compel the pharmaceutical industry to conduct followup studies to assure a drug's long-term safety after problems have been reported. Violations of this obligation can result in charges of misbranding, and in fines of $250,000 and potentially more if they continue.

This is crucial to patient safety, because what many patients don't realize, but is openly acknowledged in the drug and device industry, is that the first few years a new product is on the market is a crucial test of how safe the new drug or device really is. And keeping track of bad events is really important, but scarcely done well in the United States, at least up to now.

The Merck drugs were approved in 2006 and 2007 respectively. The FDA's Adverse Event Reporting System (AERS), an information database and postmarketing safety surveillance program for all approved drug and therapeutic biologic products, received reports of pancreatitis associated with the use of the drugs.

Patrick A. Malone
Patrick Malone & Associates, P.C.
1331 H Street N.W.
Suite 902
Washington, DC 20005

pmalone@patrickmalonelaw.com
www.patrickmalonelaw.com
202-742-1500
202-742-1515 (fax)

In 2009, the FDA recommended that doctors monitor patients for signs of pancreatitis (inflammation of the pancreas) after initiating treatment with Januvia or Janumet, or after increasing their dosage. The feds had found that 58 of 88 cases of pancreatitis in the drugs' users required hospitalization, four in intensive care. And last year a study in the journal Gastroenterology found that Januvia might increase the risk of pancreatic cancer as well.

In light of the adverse events reported, Merck agreed to conduct PMRs via a three-month pancreatic safety study with rats. The final report was due last June.

But Merck's study results were rejected because the FDA had not approved its design. The agency implied that the studies hadn't reached sufficient levels of exposure to properly evaluate the safety concern.

The Warning Letter orders Merck to submit a plan for the study within 30 days of its issue. The trial must begin within six months of the agency's approval of the plan.

The FDA was hardly demure in its Merck smack down: "You have not provided an adequate explanation for the cause of the delay of either of the milestones in the timetable for completion of the postmarketing requirement, nor did you propose to revise the agreed-upon timeline," read a passage in the Warning Letter. "[Y]ou are more than 20 months late in achieving the June 15, 2010 final protocol submission milestone and more than 8 months late in achieving the final protocol submission milestone in the timetable, and you have not demonstrated good cause for these delays."

The agency concluded that Merck's drugs were misbranded, and threatened it with financial penalties and the wrath of "other federal agencies" that might consider Merck's recalcitrance "when considering the award of contracts."

When Big Pharma acts only in its own interests, ignoring that of the patients who consume its drugs, it appears the feds are more willing to treat it as the dangerous scofflaw it is. As the Law Blog reported, only days after the Warning Letter was issued last month, the FDA issued a Notice to Industry that read, "Once FDA notifies a drug sponsor of the need for a postmarketing study or clinical trial, the company is required to provide a timetable for completion, including study milestones, and periodic status reports on progress toward completion of the PMRs. If a company fails to comply with the timetable, FDA is authorized to take enforcement action against the company, unless the company can demonstrate good cause for the failures."

Impressive expression of force. But given Congress' generally weak-kneed submission to the medical industrial complex's financial power, is there bite behind this bark? Merck hopes not. We hope so.

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