

Biogen and F.D.A. Issue Drug Warning



By ANDREW POLLACK
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Biogen Idec's multiple sclerosis drug Avonex might cause severe liver damage in rare cases, the company and the Food and Drug Administration said yesterday.

The warning was another blow, though probably only a glancing one, to Biogen, which is already reeling from the halt in sales of its other multiple sclerosis drug, Tysabri, which was linked to a rare brain infection.

In a related development, GlaxoSmithKline said yesterday that the F.D.A. had ordered it to halt a trial of its multiple sclerosis drug, which works in a similar way as Tysabri.

A Glaxo spokesman said the company understood that a halt was made as a precaution in trials of all drugs in the same class as Tysabri. A spokeswoman for the F.D.A. said the agency could not comment because of confidentiality about clinical trials.

In a letter that was posted on the F.D.A. Web site, Biogen said that severe liver injury, including liver failure, "has been reported rarely in patients taking Avonex." It said doctors should especially consider the risk when Avonex is used along with other drugs that can cause liver damage, or by patients who drink alcohol.

Amy Ryan, a spokeswoman for Biogen, which is based in Cambridge, Mass., said there had been only a handful of cases among the 130,000 patients using Avonex, which has been on the market since 1996. She said a "minor update" was being made to the drug's label, upgrading liver damage from a "precaution" to a stronger "warning."

It is not uncommon to find new side effects of drugs as they are more widely used. The label of Rebif, a drug very similar to Avonex that is made by Serono, already comes with a warning about liver problems.

Still, with Tysabri off the market at least temporarily, Biogen will become more dependent for growth on Avonex, its biggest product, which had sales of \$1.4 billion last year. Its shares fell 88 cents, to \$37.19.

Both Ms. Ryan and Kathleen Quinn, a spokeswoman for the F.D.A., said that there was no connection between the Avonex warning and the Tysabri withdrawal, and that the timing was coincidental.

Biogen and Elan, its partner on Tysabri, suspended sales of that drug on Feb. 28 after two patients in clinical trials came down with a rare viral brain infection, progressive multifocal leukoencephalopathy. The two patients, one of whom died, had been taking both Tysabri and Avonex for more than two years in a clinical trial.

Tysabri, which was approved in November, works by stopping certain infection-fighting white blood cells from leaving the bloodstream to enter the brain. That helps stop the cells from attacking nerve cell insulation in people with multiple sclerosis but also might leave them more vulnerable to brain infections, some specialists say.

Glaxo was in Phase 2, the middle stage of testing, of its drug, 683699, which blocks the same protein as Tysabri. The drugs are different chemically and the Glaxo drug was not being tested in combination with Avonex.

Glaxo's drug, being developed with Tanabe Seiyaku of Japan, appears to be the most advanced in trials of drugs that work by blocking that protein, called alpha 4 integrin. Antisense Therapeutics, an Australian company, said last week that it was halting an early Phase 2 trial of its alpha 4 integrin drug, ATL1102, to assess the situation.

Pharmaprojects, a British database that tracks pharmaceutical development, said in a news release yesterday that 12 such drugs were in development, mostly for asthma; 5 are being developed for multiple sclerosis.

Meanwhile, Biogen's chief executive, James C. Mullen, said yesterday that there were "no other indications" of the viral infection beyond the first two patients. In a Webcast presentation at the SG Cowen Health Care Conference in Boston, he said that as time elapsed, "the absence of negative news one can view as positive."

Still, he said, it would take weeks to check the medical records of all the patients in Tysabri trials and to give them new MRI scans and other tests.

He did not say when, or if, he thought the drug could return to the market. But he said that if no more cases arose, the drug might be able to return without extensive new clinical trials. Biogen for now is keeping its sales force intact and continuing to manufacture Tysabri, though at a slower rate than before, he said.