No Lipodystrophy Approval for Serostim

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The U.S. Food and Drug Administration (FDA) declined this week to approve EMD Serono's Serostim for the treatment of HIV-associated adipose redistribution syndrome (HARS)—the accumulation of fat associated with lipodystrophy. Patients with HARS hoping to gain access to the drug, approved since 1996 for the treatment of AIDS-related wasting syndrome, will likely have a difficult time doing so without an official indication from the agency.

"All of us were pretty surprised by this," says Martin Delaney, founding director of Project Inform in San Francisco. "There had been every indication that this was going to be approved—partly because the data support it and because there's really nothing else for this particular indication."

Instead of approval, the company is being permitted to amend Serostim's labeling—the drug's package insert—to include safety and efficacy data from two HARS clinical trials.

"The label change is not an approval of Serostim for the treatment of HARS," a company spokesperson confirms.

According to Richard Klein of the FDA's Office of Special Health Issues and a frequent point person regarding drug approvals for HIV/AIDS, the agency felt that the potential benefit of Serostim for HARS did not outweigh its potential risk. He did caution that he was unable to address the FDA's decision in detail, as he had not yet consulted with key faculty at the agency.

The denial of approval ultimately prevents EMD Serono from marketing or advertising the drug for HARS and will likely mean that patients will have a hard time securing access to it. "Because it's not getting the full indication and doing this goofy label thing instead," Delaney says, "one of the effects of that is that the company cannot support it with the patient assistance program."

Like the patient assistance program (PAP) in place for people with AIDS-related wasting syndrome hoping to use the drug, the HARS program would help patients secure access to the drug through private insurance, public payers (e.g., Medicaid or Medicare), or charitable distribution.

Delaney also suspects that the lack of approval will prevent the manufacturer form negotiating with state AIDS drug assistance programs (ADAPs), further limiting affordable access to a high-cost medication (a 12-week course of Serostim for AIDS-related wasting syndrome costs approximately $21,000).

In two clinical trials conducted to date, Serostim—using a 4 mg daily dose for 12 weeks, followed by 4 mg every other day thereafter—achieved and maintained significantly greater reductions in belly fat compared to placebo in patients with HARS. However, patients in these studies receiving Serostim were also more likely to experience increase in their blood glucose levels in the trial, potentially increasing the risk of diabetes and cardiovascular problems.

“My understanding,” Klein says, “is that there was marginal short-term change in fat. That improvement was offset by cardiovascular and diabetic risk shown by laboratory tests in the analysis of the study.”

Delaney questions the FDA’s logic. The agency, he says, is attempting to answer “a long-term question about whether there is an increased risk of diabetes. It is not based on actual findings of either cardiovascular or diabetes in patients. Unless there’s real hard evidence it’s causing harm, the choice ought to be up to the patient as to just what level of theoretical risk they accept in return for some possible benefits.”

With respect to EMD Serono being allowed to include HARS clinical trial data in the package insert, Delaney says that the agency is “talking out of both sides of its mouth. That really is the strangest thing of all. What’s the point? How is a physician supposed to read that and think ‘OK, but I shouldn’t use it for that purpose.’”

EMD Serono says it will continue working with the FDA to further highlight the overall benefit/risk profile of Serostim and to secure a HARS indication for the drug.

Delaney adds that others are also interested in pushing for dialogue with the FDA. “I’ve talked to a couple of the investigators,” he says, referring to independent experts associated with the Serostim HARS studies. “They don’t agree with this decision. They’re going to sit down and strategize. There may even be further meetings on the community’s part with the FDA.”
