Scrutiny of HGH Could Bring New Restrictions

BY ALICIA AULT
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WASHINGTON — Congress is taking a tough look at the use of human growth hormone for a wide variety of conditions, including fibromylagia, which is prompting some concern that payers may react by limiting reimbursement for legitimate purposes.

Human growth hormone (HGH) has been touted as an antiaging cure, and increasingly appears to be used by athletes of all ages in the belief that it helps them improve performance and recover from injuries faster. It has been legitimately studied for injury recovery in the elderly, and also is being investigated as a potential therapy for conditions such as fibromyalgia and chronic fatigue syndrome. But this field of inquiry is relatively new.

Insurers are already reluctant to cover scientifically validated uses of HGH, Dr. Richard Hellman, president of the American Association of Clinical Endocrinologists, said in an interview. The drug can cost $10,000-$20,000 a year. The continuing use for purposes that have little-to-no evidence of safety and effectiveness may ultimately endanger patients who genuinely need HGH, said Dr. Hellman, a clinical professor of medicine at the University of Missouri, Kansas City.

Congress is taking a closer look at HGH and other alleged performance-enhancing substances in the wake of the December report issued by former Sen. George Mitchell that exposed a culture of acceptance for off-label and unproven uses of HGH and anabolic steroids in Major League Baseball.

In mid-February, the House Committee on Oversight and Government Reform held a hearing on what it called "myths and facts" about HGH, vitamin B_{12}, and other substances. The hearing was essentially a warm-up for subsequent panel meetings on the use of such substances in baseball and other professional sports that were scheduled for February, but it touched on issues of interest to physicians.

The hearing provided "an opportunity to provide essential and accurate information not just to professional athletes, but to high school kids, senior citizens, baby boomers turning 60, and everyone in between," according to Rep. Henry Waxman (D-Calif.), chairman of the oversight committee.

All of these uses are illegal. HGH is the only Food and Drug Administration (FDA) approved product that can only be prescribed for the approved indications. In children, the approved indications are to treat: growth hormone deficiency, chronic kidney disease, Turner syndrome, small for gestational age infants who do not catch up to normal range, Prader-Willi syndrome, idiopathic short stature; SHOX gene haploinsufficiency, and Noonan syndrome. In adults, HGH is legal for AIDS-related wasting syndrome, short-bowel syndrome, and growth hormone deficiency.

Distribution of HGH, or possession with intent to distribute, for any off-label use is a felony, punishable with up to 5 years in prison and fines.

"Without question, those attempting to market or distribute HGH claiming it will aid healing, slow or reverse the aging process, assist in weight loss, or cure depression are scamming consumers and breaking the law," warned Rep. Tom Davis (R-Va.), the oversight committee's ranking Republican member.

And yet, some estimate that illegal HGH sales far outweigh the sanctioned market. Dr. Thomas Perls told the House committee in February that anti-aging sales amount to $2 billion a year. "I personally have found Web sites of 279 antiaging clinics that advertise HGH treatment, and 26 pharmacies that distribute the drug to these clinics or sometimes directly to users," said Dr. Perls of Boston University. "I have certainly discovered only a fraction of what exists out there," he added.

In a JAMA article in 2005, Dr. Perls said that legal sales of HGH in 2004 amounted to about $622 million annually, for a little more than 200,000 initial and refill prescriptions, according to data from IMS Health, a market research company (JAMA 2005;294:2086-90).

Dr. Alan Rogol, a professor of clinical pediatrics at the University of Virginia, Charlottesville, also expressed dismay at the House hearing at what appears to be the growing misuse of HGH. Off-label use comes with increased risk of side effects such as acromegaly, and increased insulin resistance or diabetes, said Dr. Rogol. He also said that in many cases, HGH purchasers were getting something other than HGH. The prices being advertised are too low and, "many of these preparations are taken orally and cannot be the protein hormone HGH, for it is not active by this route," said Dr. Rogol, who testified on behalf of the Endocrine Society.

Another potential danger is that many of the illicit sales are of human tissue-derived pituitary growth hormone, which has been removed from the market because it has the potential to contain the pathogen that causes Creutzfeldt-Jakob disease. And yet, some of this type of hormone is still available in Eastern Europe and through the Internet.

"It is my opinion for an adult there are no legitimate off-label uses," Dr. Rogol emphasized in an interview.

But both Dr. Rogol and Dr. Hellman acknowledged that there are no central data on how much HGH is being used illicitly, by either nonphysician or physician prescribers. It's in the public interest to keep a registry or to create some other way to keep track of HGH use, Dr. Hellman said. Physicians legitimately using HGH "should have no problem having their work scrutinized," he said.

Both endocrinologists also said they were open to considering data on new uses of HGH, as long as it came from a validated scientific process.

The Endocrine Society and AACE both have published guidelines on HGH. The Endocrine Society guidelines, published in 2006, only pertained to treating adult growth hormone deficiency (J. Clin. Endocrinol. Metab. 2006;91:1621-34).

AACE last published guidelines in 2003. That report took a broad look at HGH uses and highlighted concerns that off-label prescribing or abuse could lead to reimbursement issues for legitimate patients (Endocr. Pract. 2003;9:64-76). ■

Long-Term Adalimumab Safe, Effective in PsA

BY SHARON WORCESTER
Southeast Bureau

SAN ANTONIO — Adalimumab proved safe and effective when used for up to 2 years for the treatment of psoriatic arthritis in a phase III open-label extension study, according to results reported at the annual meeting of the American Academy of Dermatology.

The agent safely controlled skin and joint symptoms in some patients through 2 years of use.

DR. MEASE

In 395 patients who completed 2 years of treatment with adalimumab (Humira) for the 120-week multinational trial, treatment showed rapid efficacy for psoriatic arthritis (PsA), and the effect was sustained through the duration of the study, said Dr. Philip Mease of the Swedish Medical Center in Seattle.

Among the measures used in the study to assess disease signs and symptoms were the American College of Rheumatology's ACR 20, ACR 50, and ACR 70 response rates, and the Psoriatic Arthritis Response Criteria (PsARC). The percentages of PsARC responders at weeks 48 and 104 were 77% and 81%, respectively, Dr. Mease reported.

Psoriasis disease activity was measured in those with at least a 3% body surface area involvement using the Psoriasis Activity Severity Index (PASI) 50, 75, and 90 and the Physician's Global Assessment of Psoriasis.

The percentage of patients achieving PASI 50, 75, and 90 scores at weeks 48 and 104 were 84%, 69%, and 55%; and 83%, 70%, and 53%, respectively, Dr. Mease said during a poster discussion at the conference. The percentages of patients with a Physician's Global Assessment of clear or almost clear at those time points were 38% and 30%, and 40% and 31%, respectively.

Patients in the study, which was funded by Abbott Laboratories, were participants in either the 24-week Adalimumab Effectiveness in Psoriatic Arthritis Trial or a similar 12-week trial of the drug. Both trials were placebo-controlled trials comparing placebo with 40 mg of adalimumab every other week, and both showed that adalimumab provided statistically and clinically significant improvement, compared with placebo.

Quality of life was also evaluated using a variety of measures. Among them was the Health Assessment Questionnaire, which measures disability. The mean change at both weeks 48 and 104 was –0.4, which surpassed the "minimum clinically important difference level" of –0.3, Dr. Mease noted.

As for safety, a total of 10.6 serious adverse events per 100 patient-years occurred during the course of the study. There were 2.4 serious infectious adverse events per 100 patient-years, 0.5 malignancies other than nonmelanoma skin cancer per 100 patient-years, 0.78 nonmelanoma skin cancers per 100 patient-years, and two deaths—neither of which was thought to be due to adalimumab treatment, Dr. Mease said. "Overall, the take-home message was that safety issues were similar to those in rheumatoid arthritis trials." The current findings demonstrate that adalimumab is safe, efficacious, and well tolerated for both skin and joint manifestations through 2 years in patients with psoriatic arthritis, Dr. Mease said. ■

Unapproved IV Colchicine Drugs Face FDA's Teeth

Companies marketing unapproved drugs that contain injectable colchicine to treat gout have 30 days to stop manufacturing and 180 days to stop shipping the drug, which has caused 23 reported deaths, according to the U.S. Food and Drug Administration.

All injectable colchicine drugs on the market 180 days after the FDA's announcement on Feb. 6 must have the agency's approval. Refusal could result in regulatory action, including seizure, injunction, or other legal action, according to the FDA statement. The enforcement measure marks the seventh action taken by the agency against companies marketing and selling unapproved drugs since issuing its Compliance Policy Guide. Colchicine tablets will remain on the market for now.

Injectable colchicine has been approved for treatment of gout in the U.S. since the 1950s. It is rarely administered because its use results in harmful adverse events or death.

For more information on the FDA's action, please go to http://www.fda.gov/cder/drug/unapproved_drugs/colchicine_qa.htm.

—Becky Jungbauer

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