# Novel Procedure Relieves Pain in Plantar Fasciitis

BY PATRICE WENDLING
*Chicago Bureau*

CHICAGO — The combination of ultrasound-guided dry-needling and steroid injection was 95% effective in relieving the heel pain associated with plantar fasciitis in a study of 44 patients.

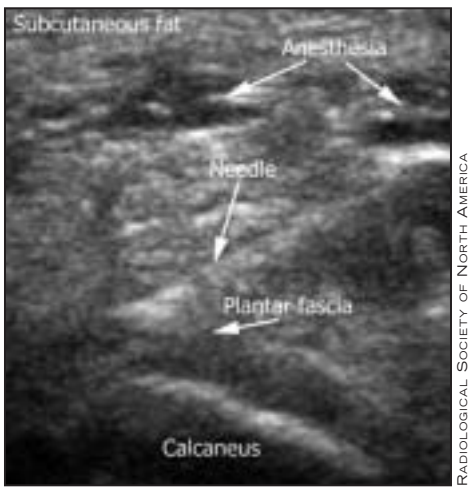
Within 2 to 3 weeks of treatment, symptoms disappeared completely 39 patients, initial worsening was followed by progressive disappearance of symptoms in 3 patients, and no response occured in 2 patients, Dr. Luca Maria Sconfienza reported at the annual meeting of the Radiological Society of North America.

The one-time outpatient procedure took about 15 minutes and required no time off work or in the hospital, said Dr. Sconfienza, a radiologist with the department of experimental medicine at Genova (Italy) University.

At 6 months' follow-up, 41 patients were "very satisfied," 1 was "satisfied," and 2 were "unsatisfied." No adverse events or recurrences have been reported in the patients, whose plantar fasciitis was previously unresponsive to traditional medical therapy. The majority of patients were female (89%), and their mean age was 48 years.

There is no widely accepted treatment for plantar fasciitis, a common condition that results from thickening and inflammation of the plantar fascia and causes stabbing or burning pain. Many patients are treated with shock waves, but this painful approach typically requires three sessions with 14 days off between sessions, and its long-term effectiveness is not fully documented, Dr. Sconfienza told reporters at a press briefing during the meeting. At $450, shock wave therapy also costs five times the $90 price of the new combination therapy.

"There is less pain, less time, and less money" with combination therapy, Dr. Sconfienza said. In an interview, he added, "The procedure can be performed anywhere and by anyone who underwent a basic training in interventional ultrasound."



RADIOLOGICAL SOCIETY OF NORTH AMERICA

**Ultrasound guidance ensures steroids are not injected into the plantar fascia.**

The technique involves injecting a small amount of local anesthesia and, under ultrasound guidance, repeatedly inserting a needle into the plantar fascia and on the periostium. The technique produces a small amount of local bleeding. The needle is then retracted to reach the perifascial soft tissue, where a small amount of steroid (1 mL of triamcinolone acetonide 40 mg/mL) is injected. Ultrasound guidance allows the provider to avoid injecting the drugs directly into the plantar fascia, which could lead to a complete rupture, he said.

The steroid reduces inflammation in the plantar fascia, while the local bleeding takes advantage of growth enzymes in the platelets that promote tissue healing. "We allow nature to work for us. This could be useful for other pathologies like tennis elbow," he said. Orthotic plantar support is strongly encouraged after treatment.

When asked if steroids or dry needling alone could produce similar results, Dr. Sconfienza acknowledged the lack of a control group in the study, but said previous experience has shown that steroids and dry needling are less effective when used as monotherapy. Future studies are needed to validate the findings, he said.

The investigators reported no conflicts of interest. ■

# Panel Backs Febuxostat Despite Cardiovascular Safety Concerns

BY ELIZABETH MECHCATIE
*Senior Writer*

SILVER SPRING, MD. — Approval of a long-awaited alternative to allopurinol for people with gout is likely now that febuxostat has received a nearly unanimous vote for support by a federal advisory panel.

The Food and Drug Administration's Arthritis Drugs Advisory Committee voted 12-0, with 1 abstention, recommending approval of the xanthine oxidase inhibitor febuxostat for the treatment of chronic gout, but recommended that studies further evaluating the drug's cardiovascular safety be conducted after approval.

The panel agreed that the available data on febuxostat at doses of 40 mg/day and 80 mg/day provided evidence that it would be useful as a treatment for patients with gout and would meet an unmet need for treating hyperuricemia in patients who are intolerant to or allergic to allopurinol and in those patients with renal impairment, who have to take a reduced, less-effective dose of allopurinol. The panel met last month.

Panelist Dr. John Cush, director of clinical rheumatology, Baylor Research Institute, Baylor College of Medicine, Dallas, said febuxostat would be a useful addition to the available treatments because of its potent urate-lowering effect. The drug requires less dose adjustment than does allopurinol and has been easier to tolerate than is allopurinol.

Like other panelists, he did not believe the issue regarding the potential cardiovascular safety signal seen in the two initial phase III studies of febuxostat had been completely resolved. That could be addressed with postmarketing studies, he said, adding it should not hold up approval.

Because of new legislation, the FDA now has more clout in getting companies to adhere to their postmarketing study commitments, which influenced some panelists to vote for approval. The FDA usually follows the recommendations of its advisory panels, which are not binding.

The manufacturer, Takeda Pharmaceuticals, has proposed that febuxostat, taken orally, at a dosage of 40 mg/day or 80 mg/day, be approved for treating hyperuricemia in patients with gout. The higher dosage would be recommended for patients with higher serum uric acid levels and for patients with tophi. If approved, febuxostat, a nonpurine selective inhibitor of xanthine oxidase that reduces the formation of uric acid, would be the second xanthine oxidase inhibitor approved for gout in the United States. Allopurinol, available since 1964, is a nonselective xanthine oxidase inhibitor.

Takeda presented the results of the phase III study of 2,269 mostly male patients with hyperuricemia, who had had gout for a mean of 11 years, conducted to prospectively evaluate the cardiovascular safety of febuxostat. Their mean age was 53 years; about 20% were older than 65 years, 53% had hypertension, 42% had hyperlipidemia, and 12% had atherosclerotic disease. Patients with mildly or moderately impaired renal function (about 66%) were also enrolled. At 6 months, the rates of cardiovascular events, blindly adjudicated by an independent expert committee, were similar in those on 40 mg/day or 80 mg/day of febuxostat and those on allopurinol (200-300 mg/day).

The FDA asked the company to conduct this study after the agency's review of the two phase III trials that were initially submitted to it for approval in 2004 suggested there was a cardiovascular safety signal associated with the 80-mg and 120-mg doses of febuxostat, compared with allopurinol. In the studies, the rates of cardiovascular thromboembolic events were higher in patients treated with 80 or 120 mg of febuxostat daily, compared with those on allopurinol or placebo, though the number of events was small. The company dropped development of the 120-mg dose and focused on the two lower doses.

The FDA held the panel meeting to review the drug's safety; efficacy was not an issue. In the three phase III studies, which enrolled patients with a diagnosis of gout and a baseline serum uric acid of 8.0 mg/dL or more, the 80-mg dose of febuxostat was significantly more effective than allopurinol, and the 40-mg dose was as effective as allopurinol, in lowering and maintaining serum uric acid below 6.0 mg/dL. Patients in all three groups experienced flares, which were higher in patients on the higher febuxostat doses but gradually decreased over time, said Takeda. The two doses of febuxostat were also effective in patients with renal impairment, who require a lower, usually suboptimal dose of allopurinol, and no safety signal was seen in this population. Febuxostat had no effects on blood pressure, glucose, lipids, or weight.

In two open-label extension studies that followed patients in phase II and the initial phase III studies for 3-5 years, gout flares fell to almost zero, said Takeda.

A cardiologist on the panel, Dr. Robert Harrington, professor of medicine, Duke University, Durham, N.C., said the database on febuxostat was insufficient to draw an inference about cardiovascular risk in patients with cardiovascular disease and that some of the issues regarding cardiovascular risk "still need to be better clarified." He noted that most of the subjects were middle-aged, overweight men, and that 6 months was not enough time to detect a cardiovascular risk for a drug that will be taken for a lifetime. He said his vote in favor of approval was influenced by the FDA's increased authority in requiring companies to meet their postmarketing study commitments.

The panelist who abstained, Dr. Curt Furberg, professor in the department of public health sciences, Wake Forest University, Winston-Salem, N.C., said that the febuxostat package insert should include a statement in the precautions section that safety in patients with cardiovascular disease was not known. He recommended a long-term trial of febuxostat's safety in people with gout who are at high risk for cardiovascular disease, as well as in older patients and those with cardiovascular disease.

In an interview, Dr. Robert Wortmann, professor of medicine and rheumatology, Dartmouth-Hitchcock Medical Center, Lebanon, N.H., noted that it has been 4 years since febuxostat's manufacturer filed for FDA approval and said the delay has been frustrating for clinicians who treat gout. He was not at the meeting but has been a consultant to Takeda and TAP Pharmaceutical Products Inc., which was acquired by Takeda, since 1998, and was involved in the design of febuxostat studies.

"The No. 1advantage in my opinion is that we [will] now have an alternative xanthine oxidase inhibitor for people who can't tolerate allopurinol," he said. Another benefit is that it can be used in patients with mild to moderate renal dysfunction, without modifying the dosage, as opposed to allopurinol, he added.

Allopurinol is effective if used appropriately, and it is inexpensive, but it is often underdosed, so many patients on allopurinol do not reach target urate level below 6 mg/ dL, he pointed out. Although allopurinol is approved at dosages up to 800 mg/day, most prescriptions are written for 300 mg or less, a dosage that does not adequately control urate in half to two-thirds of patients, he added, noting that there is not much experience with higher allopurinol doses.

The febuxostat studies were conducted in the United States and Canada; about 30% of the patients enrolled were treated by rheumatologists, and the rest were treated by primary care physicians, reflecting clinical practice. Gout is largely diagnosed and managed by primary care and emergency physicians; rheumatologists tend to treat those with more severe gout. If the drug is approved, Takeda plans to market it as Uloric. ■