**Febuxostat Found Safe in Renal-Impaired Patients**

*By Timothy F. Kirn*

**San Diego** — Febuxostat was more effective than allopurinol in management of gout, even in patients with moderate renal impairment, according to data from a company-sponsored trial.

The 28-week trial, Febuxostat vs. Allopurinol and Placebo in Subjects With Hyperuricemia and Gout, known as APEX, revealed that 4 of 9 gout patients with moderate renal impairment (serum creatinine between 1.6 and 2 mg/dL) who received febuxostat at a dose of 80 mg/day achieved a serum urate level less than 6 mg/dL in their final three measurements, as did 2 of 11 patients who received 120 mg/day and 3 of 5 patients who received 240 mg/day.

None of the 10 patients with moderate renal impairment who received allopurinol, at 100 mg a day, achieved that goal, Dr. H. Ralph Schumacher said at the annual meeting of the American College of Rheumatology. The presentation at the most recent ACR annual meeting included data on more patients as well as on those with renal impairment; the trial was shorter than the earlier investigation.

Dr. Schumacher’s new report included data on 1,067 patients with gout and a serum urate level greater than 8 mg/dL followed for 28 weeks. Last year’s report was based on 120 patients and followed for 12 weeks.

The new results were very similar to last year’s: Febuxostat at a dose of 80 mg a day decreased serum urate levels below 6 mg/dL in the last three measurements in 48% of patients. A dose of 120 mg a day reduced the last three measurements below 6 mg/dL in 65% of patients, and 240 mg a day reduced the last three measurements below 6 mg/dL in 69%.

The patients without renal impairment who received allopurinol received a dose of 300 mg a day, and, in those patients, the allopurinol reduced the last three measurements below 6 mg/dL in 20% of the group.

None of the patients on placebo had a serum urate measurement below 6 mg/dL during the trial. That compared with 40% of those on allopurinol and none on placebo.

Of the subjects on 240 mg a day of febuxostat, 75% got at least one serum urate measurement below 4 mg/dL. Although the increase was smaller in size on patients on either active treat-

ment, but the change was more significant among patients taking febuxostat, said Dr. Schumacher, professor of medicine at the University of Pennsylvania, Philadelphia.

Types of adverse events were similar in the patients with and without moderate renal impairment; dose of febuxostat did not have an effect on adverse events, he added.

Gastrointestinal adverse events were most common and included diarrhea in 2%-4% of the patients on febuxostat and 7%-9% of those on allopurinol.

Liver function abnormalities occurred in some patients and were deemed to be the result of colchicine use, used to manage gout flares and of little clinical concern, Dr. Schumacher said. Patients in all the groups had flares, particularly those on the highest dose of febuxostat, though the flares decreased over time.

Serum creatinine levels did increase slightly with febuxostat treatment. But those levels did not increase to any greater degree in the patients with moderate renal impairment as they did without febuxostat, the renal impairment, he added. Dr. Schu-
macher received funding from the company that makes febuxostat, TAP Pharma-
cutical Products Inc., Lake Forest, Ill.

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**Allopurinol Doesn’t Work? Here’s How to Lower Urate**

*By Bruce Jancin*

**Vienna** — A wealth of hard-earned off-label tricks of the trade for serum urate lowering in gout patients who can’t tolerate allopurinol may soon fall by the wayside, according to data from a company-sponsored trial.

The new results were very similar to last year’s. Febuxostat at a dose of 80 mg a day decreased serum urate levels below 6 mg/dL in 20% of the group. A dose of 120 mg a day reduced the last three measurements below 6 mg/dL in 76% of patients. A dose of 240 mg a day reduced the last three measurements below 6 mg/dL in 48% of patients.

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**View Asymptomatic Hyperuricemia As a Flag for Cardiovascular Risk**

*By Bruce Jancin*

**Vienna** — The time has come for a change in thinking regarding nongouty asymptomatic hyperuricemia, traditionally dismissed as a clinically irrelevant laboratory abnormality, Dr. George Nuki asserted at the annual European Congress of Rheumatology. Dr. H. Ralph Schumacher said at the annual meeting of the American College of Rheumatology.

Another good choice in patients with cardio-

vascular disease or hyperlipidemia.

Dr. Bardin said. Patients in all the groups had flares, particularly those on the highest dose of febuxostat, though the flares decreased over time.

Serum creatinine levels did increase slightly with febuxostat treatment. But those levels did not increase to any greater degree in the patients with moderate renal impairment as they did without febuxostat, the renal impairment, he added. Dr. Schu-
macher received funding from the company that makes febuxostat, TAP Pharma-
cutical Products Inc., Lake Forest, Ill.

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**What are the alternatives?**

- **Probenecid.** Having long taken a back seat to allopurinol because of its weaker urate-lowering effect, probenecid is being rediscovered by physicians. It should be started at 250 mg bid, gradually increasing the dose every 2-3 weeks up to a target of 2 g/day.

- **Losartan.** Has a rapid effect, similar to probenecid. Urate lowering is not an ACE inhibitor class effect but is limited to losar-
tan. The drug has the side benefit of re-
duced uric acid pH, thereby lessening the risk of uric acid stone formation. An excellent drug in gout patients with comorbid car-
diovascular disease or hypertension.

- **Fenofibrate.** Doubles uric acid clearance. Another good choice in patients with car-
diovascular disease or with hyperlipidemia.

Dr. Bardin often uses it together with allop-
urinol in patients who don’t target the serum uric acid level of less than 6 mg/dL.

Other fibrates don’t share fenofibrate’s urate-lowering effect.

- **Switch antirejection drugs in transplant recipients.** Azathioprine, 6-mercaptop-
turone, and cyclosporine are often con-
sidered contraindicated to allopurinol therapy because of harmful drug interactions.

Dr. Bardin has persuaded transplant physicians to substitute mycophenolate mofetil with good results in gout patients he wants on allopurinol.

- **Desensitization therapy.** An option that can enable patients with cutaneous re-
tactions to successfully go back on allopurinol. But it’s a difficult, complicated, and both-
ersome procedure. “In the literature, you’ll find a few cases of hypersensitivity syn-
drome occurring during desensitization. There’s no need for K. Nääksjärvi, professor of medicine at Kuopio (Finland) Universi-
ty, and coworkers found that men in the top one-third in terms of baseline