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

**BY BRUCE JANCIN
Denver Bureau**

**VIENNA** — A wealth of hard-earned off-label tricks of the trade for serum urate lowering in gout patients who can’t take allopurinol may soon fall by the wayside, forgotten in the rush to embrace an anticipated batch of new agents.

A variety of novel hypouricemic drugs intended to earn an indication for gout management are moving through the developmental pipeline. Furthest along is febuxostat, a nonpurine selective inhibitor of xanthine oxidase that has been submitted to the Food and Drug Administration for market approval. Also, looking good in phase II clinical trials for long-term urate lowering to prevent recurrent attacks of gout is a pegylated form of urate oxidase, Dr. Thomas Bardin noted at the annual European Congress of Rheumatology.

Febuxostat was more effective than allopurinol 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 3 of 5 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 300 mg/day achieved a serum urate level below 6 mg/dL.

Results show that at a dose of 80 mg/day, serum urate levels fell below 6 mg/dL 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 24% of the group. None of the patients on placebo had a reduction below 6 mg/dL in their last three measurements.

Dr. Schumacher noted that 90% of the patients on febuxostat had at least one 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.

Febuxostat was also better tolerated. Flares decreased over time.

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

**BY BRUCE JANCIN
Denver Bureau**

**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.

“We actually need at this time a paradigm shift in thinking about the significance of asymptomatic hyperuricemia,” said Dr. Nuki, professor of medicine at the University of Edinburgh.

Serum uric acid can be measured simply and inexpensively. But the central question regarding its clinical significance in asymptomatic individuals remains unanswered: Is it an independent risk factor for cardiovascular disease and mortality, or merely a marker for other more causal risk factors?

The evidence remains conflicting. A Framingham Study analysis concluded that asymptomatic hyperuricemia was not an independent cardiovascular risk factor. But it’s a difficult, complicated, and both expensive and time-consuming matter. “In the literature, you’ll find a few cases of hypersensitivity syndrome occurring during desensitization. These cases need to be scrutinized and the risks, and that the drug should be stopped immediately in the event of skin rash,” Dr. Bardin said.

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

**BY TIMOTHY F. KIRN
Sacramento Bureau**

**SAN DIEGO** — Febuxostat was more effective than allopurinol 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 3 of 5 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 300 mg/day achieved a serum urate level below 6 mg/dL.

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 who received allopurinol than in those without renal impairment, he added. Dr. Schumacher received funding from the company that makes febuxostat, TAP Pharmaceutical Products Inc., Lake Forest, Ill.