Febuxostat or Allopurinol for Gout? It Depends

BY MITCHEL L. ZOLER

Estimates of how many patients with gout should be treated with febuxostat range from just 5% to millions, according to experts interviewed for this article.

Febuxostat is clearly the second-line agent behind allopurinol, those same experts agreed. Allopurinol retains the top spot because of its substantially larger and longer track record and its dramatically lower cost.

Febuxostat received a warm welcome from gout specialists following its approval by the Food and Drug Administration 6 months ago. They cheered the arrival of the first new gout drug in decades, and early U.S. sales numbers for the drug were in line with expectations of Takeda Pharmaceuticals North America Inc., the company that markets febuxostat (Uloric), said Heather Dean, Takeda’s marketing director for the drug.

Despite that, the type of gout patient who is a good candidate for febuxostat treatment remains controversial. At one end are some experts who say only a few gout patients—those who are truly intolerant of or unresponsive to maximum allopurinol treatment—are appropriate candidates. At the other end are specialists who say that febuxostat is the preferred drug for any gout patient who has moderate renal failure or who fails to respond to 300 mg/day of allopurinol, categories that encompass a sizeable number of symptomatic gout patients.

The decision to treat with allopurinol or febuxostat may be guided by some of the following considerations:

► Allopurinol (or more accurately, its active form in blood, oxypurinol) is excreted by the kidney, so patients with impaired renal function have higher blood levels of oxypurinol than do patients with normal kidneys. Allopurinol doses must be adjusted for these patients.

► Allopurinol is ineffective at the standard dosage of 300 mg/day for perhaps half of gout patients, but in most of these cases it’s effective when the dose is raised; however, not all specialists are willing to prescribe the labeled maximum dosage of 800 mg/day.

► Febuxostat does not require any dosage adjustment in patients with renal impairment, and is labeled for use only at either 40 mg or 80 mg/day.

► Internet-based drugstores sell febuxostat at a cost of more than $5 a day, compared with an Internet cost as low as $0.10/day for allopurinol.

Patients With Renal Insufficiency

“About half the patients with chronic gout have significant impairment of renal function,” said Dr. Peter A. Simkin, a rheumatologist at the University of Washington in Seattle.

But Dr. Simkin doesn’t see impaired renal function as a barrier to allopurinol use. “It’s both safe and appropriate to use allopurinol in patients with renal insufficiency,” he said in an interview.

“You start with a low dose and escalate slowly, but that’s what we do with allopurinol for any patient.” High blood levels of oxypurinol that can occur in patients with renal impairment were avoided because they boost the risk of a hypersensitivity reaction, milder allergic reactions, or other forms of intolerance. Dr. Simkin said he had no disclosures relevant to febuxostat and allopurinol.

Other specialists say that now that febuxostat is an option, they’ll avoid potential problems by immediately jumping to the new drug for patients with impaired renal function. “Allopurinol should be first-line therapy in treating patients with hyperuricemia and gout unless their renal function prohibits use of allopurinol,” said Dr. Robin K. Dore, a rheumatologist at the University of California, Los Angeles. Dr. Dore said she has been a consultant to and has been on the speaker’s bureau of Takeda, and she participated in some febuxostat studies.

But febuxostat should not be considered completely free from renal concerns, said Dr. Ted R. Mikuls, a rheumatologist at the University of Nebraska in Omaha. “Studies of febuxostat have not included patients with a serum creatinine level of more than 2 mg/dL, that I’m aware of,” he said in an interview. “The medical community must demand a lot more data before using febuxostat widely in patients with renal failure.” Dr. Mikuls said he had no disclosures relevant to febuxostat and allopurinol.

“I am not convinced that careful allopurinol dose titration cannot achieve successful management of patients with impaired renal function,” said Dr. Michael A. Becker, a rheumatologist at the University of Chicago. Dr. Becker said he has been a consultant to Takeda, and he was a coinvestigator on several of the febuxostat pivotal trials.

Lack of Efficacy With Allopurinol

For symptomatic gout, the guiding number is a baseline serum level of uric acid. When the level drops below 6 mg/dL, existing uric acid crystals disappear by dissolving into the blood, thereby alleviating symptoms.

Although many patients respond to an allopurinol dosage of less than or up to 300 mg/day, most patients need more than 300 mg/day, Dr. Simkin said. “It’s appropriate to use up to 800 mg/day, and although dosages of 300-800 mg/day are usually effective, doses this high are not often prescribed. ‘The main reason [why patients have uncontrolled gout] is misuse of allopurinol. Patients don’t get treated with adequate doses.’”

Patients who don’t respond to high allopurinol doses are “very rare,” Dr. Simkin noted. He currently has “two such patients, and they’re doing better on febuxostat,” he said.

“A majority of the current gout patient population does not achieve a goal serum urate range of less than 6 mg/dL on 300 mg allopurinol,” Dr. Becker agreed. However, “there is little evidence for allopurinol safety and efficacy [in dosages] greater than 300 mg/day,” he said. Despite the lack of data, “I suspect that very few patients fail treatment with an allopurinol dosage of 600 mg or 800 mg/day,” Dr. Becker said. Patients who do fail at these higher dosages are “probably not likely” to do any better on febuxostat, he added.

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