Febuxostat or Allopurinol for Gout? It Depends

By Mitchel L. Zoler

E
timates of how many patients with
gout should be treated with
tFebuxostat range from just 5% to
millions, according to experts inter-
viewed for this article.

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

Febuxostat received a warm welcome
from gout specialists following its ap-
proval by the Food and Drug Adminis-
tration 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 widely debated. At one
end are some experts who say only a few
gout patients—those who are truly in-
tolerant of or unresponsive to maximum
allopurinol treatment—are appropriate
candidates. At the other end are special-
ists who say that febuxostat is the pre-
ferred drug for any gout patient who has
moderate renal failure or who fails to re-
spond to 300 mg/day of allopurinol, cat-
egories that encompass a sizeable num-
ber 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 ex-
crated by the kidney, so patients with im-
paired 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 per-
haps 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 maxi-
mum dosage of 800 mg/day. 

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

► Internet-based drugstores sell febuxo-
stat at a cost of more than $5 a day, com-
pared 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 re-
nal function,” said Dr. Per A. Simkin,
a rheumatologist at the University of
Washington in Seattle.

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

“You start with a low dose and es-
calate slowly, but that’s what we do
with allopurinol for any patient.”

High blood levels of oxy-
purinol that can occur in patients
with renal impairment may be avoided because they boost the
risk of a hypersensitivity reac-
tion, milder allergic reactions, or
other forms of intolerance. Dr.
Simkin said he had no disclosures re-
vant to febuxostat and allopurinol.

Other specialists say that now that
febuxostat is an option, they’ll avoid po-
tonial problems by immediately jump-
ing to the new drug for patients with im-
paired renal function. “Allopurinol
should be first-line therapy in treating pa-
tients with hyperuricemia and gout un-
less their renal function prohibits use of
allopurinol,” said Dr. Robin K. Dore,
a rheumatologist at the University of Cal-
ifornia, Los Angeles. Dr. Dore said she
has been a consultant to and has been on
the speakers bureau of Takeda, and she
participated in some febuxostat studies.

But febuxostat should not be consid-
ered completely free from renal con-
cerns, said Dr. Ted R. Mikuls, a rheuma-
tologist 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.”

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vant to febuxostat and allopurinol.

“I am not convinced that careful al-
lopurinol 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.

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Lack of Efficacy With Allopurinol

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Allopurinol Intolerance

An estimated 5%-10% of gout patients are intolerant of allopurinol. Intolerance
can range from a serious hypersensitivi-
ty reaction to a milder allergic reaction
or another form of adverse event, such
as gastrointestinal distress. A patient with
hypersensitivity to allopurinol is some-
one for whom “febuxostat could be re-
ally helpful,” but this is “pretty rare,” Dr.
Mikuls said. Problems such as stomach
upset may occur in 5%-10% of patients,
and this is another group of patients for
whom “febuxostat can be really impor-
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