

patient can be rapid and because such patients with early bacterial infections cannot be reliably distinguished from noninfected patients at presentation, empirical antibiotic treatment should be administered promptly to all neutropenic patients at the onset of fever. Afebrile patients who are neutropenic but who have signs or symptoms compatible with an infection should also have empirical antibiotic treatment beginning in same manner as do febrile patients. In the selection of the initial antibiotic regime, one should consider the most probable pathogen and antibiotic susceptibility of bacterial isolates recovered from other patients at the same hospital. The use of antibiotic by the oral route may be considered only for patients who have no focus of bacterial infection or symptoms or signs suggesting systemic infection other than fever. Several studies have shown no striking differences between monotherapy and multidrug treatment combination for empirical treatment uncomplicated episodes of fever in neutropenic patients¹⁰. Advantages of combination treatment are synergistic effects against some gram-negative bacilli and minimal emergence of drug resistance.

Before modern management, the all cause mortality among high-risk neutropenic patients with bacteremia was 84% in 1965; it decreased to 44% in 1972 with the introduction of early empirical broad-spectrum antibiotic treatment and to 20%-36% more recently¹¹. In our study, 30% mortality was seen. In randomized controlled trials, mortality rates are lower, reflecting patient selection, but the same improvement in survival can be observed. In a series of trials conducted by EORTC between 1978 and 1994, the all cause mortality among neutropenic patients with bacteremia decreased from 21% to 7%.⁹

In our study, 40% of patients who presented with ANC<100/mm³

expired, while in patients who had an ANC>500/mm³ at presentation, 25 mortality was noted. The result were in close comparison with that observed by Schimpff¹² who noted that when neutrophils are less than 100/mm³, sepsis was lethal in 47% of infected patients versus 14%, when neutrophils were >1000/mm³.

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DRUG PROFILE

Febuxostat

Febuxostat is an orally administered, non-purine, selective inhibitor of xanthine oxidase approved for the management of chronic hyperuricaemia in patients with gout. In a randomized, double-blind, dose-ranging study in patients with gout and hyperuricaemia, significantly more recipient of febuxostat 40-120 mg/day than placebo had serum urate levels of <6.0 mg/dL after 4 weeks of treatment. Serum urate levels were reduced below 6.0 mg/dL at the last three monthly observations in a significantly greater proportion of patients with gout and hyperuricaemia receiving febuxostat 80 or 120 mg once daily than in those receiving allopurinol 300 mg once daily in a 52-week, randomized, double-blind trial (FACT). Similarly, febuxostat 80, 120 or 240 mg once daily showed significantly greater urate-lowering efficacy than allopurinol 100 or 300 mg once daily in a 28-week, randomized, double-blind, placebo-controlled trial (APEX) in patients with gout and hyperuricaemia. Long-term treatment with febuxostat for up to 4 years or more reduced the incidence of gout flares to (or close to) zero. **Dosage & Administration:** The recommended dosage of febuxostat is 80 mg orally once daily without regard to food, and the therapeutic target is to reduce and maintain sUA below 6.0 mg/dL. Urate-lowering therapy is typically initiated 2-8 weeks after resolution of an acute gout attack [8,9]. Anti-inflammatory therapy with low-dose, oral colchicines or an NSAID is recommended during the first few months of maintenance treatment and may be required for 12 months or more, depending on the sUA level. [8,9] Urate-lowering maintenance treatment of gout is effective only if it is continuous (not intermittent) and life long, an sUA level of <6 mg/dL is regarded as a suitable goal of urate-lowering therapy. However, reduction of sUA levels below 5 mg/dL might be necessary to promote resorption of tophi (urate deposits). **Drug Interaction:** Febuxostat has no clinically significant interactions with colchicine, indomethacin, hydrochlorothiazide or warfarin in adults in randomized, crossover studies. Although coadministration of naproxen 500 mg twice daily with febuxostat 80 mg once daily increased the C_{max} and AUC₂₄ of febuxostat by 28% and 41%. **Adverse Effect:** The most frequent adverse events (>5 events/100 patient-years) were upper respiratory tract infections, musculoskeletal, connective tissue or joint signs and symptoms, headache and diarrhoea; the incidences of events were similar in febuxostat and allopurinol recipients. The incidences of serious adverse events were also similar between febuxostat (10 events /100 patient – years) and allopurinol (11 events /100 patients-years) recipients. In each group, cardiac disorders (3 events/ 100 patient- years) were the most common serious adverse events.