

Action: The mechanism of action is unknown. In addition to its analgesic and antipyretic effects, the drug may act on the renal tubules to inhibit the reabsorption of urate and to increase the reabsorption of sodium.

Use: The usefulness of this drug is limited by its toxicity. Phenylbutazone is not recommended for prolonged administration, but it has some usefulness when given for very short periods (2 or 3 days) in the treatment of acute musculoskeletal disorders such as gout or bursitis.

Untoward effects: In 1955, Mauer (1) found 22 deaths due to this drug in the literature and added a case of his own. Since then other deaths have been recorded. Fifty serious complications and 18 deaths were reported in the United Kingdom during a 20-month period in 1964-1965.

Incidence of adverse reactions with this drug is 40%. In general, untoward effects are more apt to occur with high dosage or prolonged administration. However, death has occurred from small doses and short-term therapy. *The most frequent reactions are* nausea, edema, rash, epigastric pain, vertigo, and stomatitis. *The most serious are* reactivation of peptic ulcer—sometimes with severe hemorrhage, agranulocytosis, thrombocytopenia, aplastic anemia, exfoliative dermatitis, C.N.S. stimulation or depression—occasionally with psychosis or visual hallucinations, hypertension, and toxic hepatitis. In addition, *acute renal failure* has been reported in a healthy man on the sixth day of treatment for back pain (2). This complication has also been noted before (3, 4). "Allergic granulomas" may occur. Rash, fever, lymphadenopathy, and hepatosplenomegaly were reported after 200mg daily for six weeks; biopsy showed "sarcoid-like" granulomas which disappeared in four months after the drug was stopped (5). Another patient had rash and generalized lymphadenopathy on three separate occasions when the drug was given—after taking it for six weeks, for a few days, and after only one tablet (6). Another patient had painful swelling of parotid and submaxillary glands on two occasions after taking phenylbutazone (7). It is suggested that "allergic granulomas" may also occur in the heart.

In 1957, two fatal cases of phenylbutazone-induced cardiac complications were reported—one with pericardial effusion and interstitial myocarditis; the other with multiple focal perivascular granuloma (8). A woman who had taken the drug for one week developed pericarditis and recovered (9). One patient developed phenylbutazone skin rash and died; at autopsy, extensive perivascular granuloma-like lesions were found in the heart (10).

Phenylbutazone depresses the bone marrow in some patients and causes leukemoid reactions in others. In 1960, Bean (11) reported six cases of leukemia in patients who had taken this drug and suggested a cause and effect relationship—which has not been proved although many additional cases have been reported. The only statistical study comes from Western Australia where eight of 55 patients with acute leukemia had taken phenylbutazone. Since rheumatoid arthritis may be associated with leukemia, Innis (13) cautioned against incriminating phenylbutazone until the incidence of leukemia in rheumatoid arthritis treated with and without phenylbutazone was studied. However, cases of leukemia in non-rheumatoid patients are of interest, along with cases who developed sensitivity reactions to phenylbutazone followed in a short time by the onset of leukemia (14, 15, 16, 17).

Timing of Therapeutic Effect: The pain of acute gout is usually relieved within 24 hours after phenylbutazone administration, but joint swelling usually does not subside for 3 or 4 days. The drug is slowly excreted over a 7-10 day period.

Dosage & Administration: The smallest effective dose should be used for the shortest amount of time possible. The patient should be closely followed for signs of toxicity. The drug is given orally.

Adult Dose: 600 to 800 mg daily in 3 or 4 divided doses for 2 or 3 days. Maintenance therapy is not recommended.

How Supplied: Tablets: 100 mg

Approx. Retail Cost: About \$10.00 for 100 tablets (100 mg).

Special drug request forms must accompany orders for this drug because of toxicity.

REFERENCES

1. Mauer, *N.E.J.M.*, 253:404, 1955.
2. Richardson, et al, *N.E.J.M.*, 268:809, 1963.
3. Lipset & Goldman, *Ann. Int. Med.*, 41:1075, 1954.
4. Miatello, et al, *Pres. Med. Argen.*, 46:2551, 1959.
5. Goldstein, *Ann. Int. Med.*, 59:97, 1963.