

Untoward Effects of Furosemide

Adverse effects related to the drug's potency include rapid massive diuresis, hypokalemia, hyponatremia, and hypochloremic alkalosis. Excessive diuresis may result in hypovolemia and shock which may lead to arterial thromboses—particularly in elderly patients. Sometimes a marked fall in plasma volume results in decreased renal function—this is a result of the potent diuresis rather than a toxic effect of furosemide.

Electrolyte disturbances may be manifested as lethargy, weakness, dizziness, leg cramps, anorexia, vomiting, and/or mental disturbances (2). Hypokalemia may be a special problem in patients with cirrhosis of the liver and may precipitate hepatic encephalopathy. Cardiac patients being treated with digitalis may develop arrhythmias if hypokalemia occurs. Some patients may complain of epigastric discomfort when therapy with furosemide is started; this may disappear with continued treatment or may necessitate stopping the medication.

Skin rash, paresthesias, blurring of vision, pruritus, postural hypotension, and diarrhea may also occur. Hyperurecemia (6) and acute gouty attacks (2,6) have been reported. Hyperglycemia may also complicate treatment with furosemide (4). One case of thrombocytopenia and several of leukopenia have been reported in patients taking this drug.

Absorption and Excretion of Furosemide: Furosemide is well absorbed from the GI tract. About 40% of the drug is excreted in the stool, 10% in the urine, and small amounts in the bile and milk (6).

Timing of Therapeutic Effect With Furosemide

After oral administration, diuresis begins within 1 hour and lasts for 3 to 5 hours. Maximal effectiveness, if this is desired, can be obtained by giving the drug every 4 to 6 hours. In most instances, 1 dose per day is sufficient.

After I.V. administration, the drug acts within about 5 to 30 minutes and lasts from 1½ to 4 hours. (NOTE: an I.V. preparation is being tested and is not yet available commercially.)

Dosage and Administration of Furosemide: Furosemide is given orally. The patient should be carefully followed and excessive weight loss should be avoided.

Usual Adult Dose: Use the smallest effective dose. Begin with one dose of 40 to 80 mg in the morning. If the diuretic response over the next 4 to 5 hours is inadequate, a second dose of 40 to 80 mg can be given 6 to 8 hours after the first dose.

For More Resistant Cases: Up to 300 mg daily may be given.

For Maintenance Therapy: The dosage should be adjusted according to the patient's requirements for continued diuresis and his serum electrolyte levels. 40 to 80 mg every other day may be safe and adequate.

Children's Dose: At this time furosemide is not recommended for children.

How Supplied: Tablets 40 mg.

Approx. Retail Cost: About \$8.40 for 100 tablets.

REFERENCES

1. Early, *N.E.J.M.*, 276: 966, April, 1967
2. Stokes & Nunn, *Brit. M. J.*, 910, Oct., 1964
3. Robson, et al., *Lancet*, 1085, Nov., 1964
4. Hutcheson, et al., *Arch. Int. Med.*, 115: 542, May, 1965
5. Muth, *JAMA*, 195: 1066, March, 1966
6. Wertheimer, et al., *Arch. Int. Med.*, 119: 189, Feb., 1967

EXHIBIT B

[Page from the Los Angeles County General Hospital Formulary]

PHENYLBUTAZONE
(GENERIC NAME)

Brand name: Butazolidin (Geigy)

Category: Analgesic; antipyretic

Description: Phenylbutazone is a potent analgesic and antipyretic drug. Like aminopyrine, from which it is derived, phenylbutazone may be toxic to the bone marrow and may cause severe and even fatal reactions.