Phenylbutazone ("bute", PBZ)

Pharmacology
Phenylbutazone (PBZ) has analgesic (pain relieving), anti-inflammatory, and antipyretic (fever reducing) activity from inhibition of cyclooxygenase. It is available in many intravenous and oral formulations (powder, paste, gel, tablets). The injectable formulation must be given by careful intravenous injection, otherwise it causes severe tissue damage if given intramuscularly or subcutaneously. Following oral administration, PBZ is well absorbed, but time it takes to reach peak blood levels is delayed by feeding the horse, as the PBZ sticks to feed particles. In the blood, greater than 99% of the PBZ is carried bound to blood proteins. Phenylbutazone is converted by the liver to oxyphenbutazone, a metabolite with the same action as PBZ, but removed slower from the body than PBZ. The capacity of the liver to process PBZ becomes overwhelmed at relatively low drug doses. Therefore, increasing doses of PBZ can easily result in toxicity. In the horse, the therapeutic effect of PBZ lasts for more than 24 hours, due to the slow excretion of the oxyphenbutazone metabolite. PBZ and oxyphenbutazone will cross the placenta and are excreted in mare's milk.

Uses/indications
Phenylbutazone is used extensively in horses for a variety of common musculoskeletal disorders including navicular disease, laminitis, osteoarthritis and degenerative joint disease. It is economical and many brands are available. The use of PBZ in performance horses is very controversial, and it is highly regulated by individual performance associations. It is less effective in the therapy of colic and endotoxemia than flunixin meglumine (Banamine®). Phenylbutazone has less anti-clotting activity than aspirin and clinical use is not associated with increased bleeding. An initial dose of 4.4 mg/kg every 12 hours for the first day of therapy is followed by 2.2 mg/kg once a day for several days. Due to drug accumulation from the slow excretion of oxyphenbutazone, long-term PBZ therapy for chronic lameness conditions should be on an every other day basis with the lowest effective dose.

Adverse effects
Gastrointestinal effects are the most important adverse effects of PBZ therapy in horses. Clinical signs include loss of appetite, depression, colic, weight loss, ventral edema, hypoproteinemia (low blood protein), and diarrhea. Hemorrhages and ulcers may occur in the mouth, esophagus, stomach, cecum and right dorsal colon. These toxic effects are related to the dose of PBZ given. Horses that receive less than 0.4 g/100 lbs of body weight per day for 4 days (4 grams to a 1000 lb horse) or 0.1-0.2 g/100 lbs of body weight per day for up to 50 days remain clinically normal. Horses that receive more than 0.4 g/100 lbs of body weight per day for 4 days develop toxicity. In a study, horses that received approximately 7 g of PBZ developed gastrointestinal ulcers within 24 hours. Ulcer formation is thought to be predominantly due to PBZ-induced blood vessel constriction to the mucosal lining of the gastrointestinal tract. PBZ also causes kidney damage from inhibiting the prostaglandins that maintain kidney blood flow. Because of its mechanism of action against prostaglandins, PBZ toxicity occurs whether the drug is administered intravenously or orally. Dehydration contributes to the toxicity potential of PBZ by reducing the blood flow to the kidney, therefore it is very important that horses on PBZ therapy have adequate water intake.