NEW YORK STATE OF OPPORTUNITY. Gaming Commission

OFFICE OF THE EQUINE MEDICAL DIRECTOR

GENERAL ADVISORY – BISPHOSPHONATES

March 28, 2019

Equine Medical Director Scott E. Palmer, V.M.D., recommends that no bisphosphonate be administered to a racehorse that is less than four years old.

Further, no bisphosphonate should be administered to any racehorse except as may be prescribed by an attending veterinarian and taking into consideration the risk associated with concurrent use of NSAIDs or in horses with mineral or electrolyte imbalance or renal dysfunction.

Background Information

Bisphosphonates are substances used to treat osteoclast-mediated osteoporosis in humans. Bisphosphonates have a high affinity for bone where they inhibit calcification and hydroxyapatite breakdown, suppress bone resorption and their intracellular accumulation is cytotoxic to osteoclasts.[1] The use of bisphosphonates in younger animals is contraindicated because bisphosphonates inhibit osteoclast-mediated bone resorption, resulting in the accumulation of trabecular microdamage that can compromise the mechanical and regenerative properties of bone.[2] These effects predispose affected bone to delayed union and fractures.[3,4]

Tiludronate disodium (Tildren®) and Clodronate disodium (Osphos®) are two first-generation bisphosphonates currently approved by the FDA for treatment of equine navicular disease in horses four or more years old. The manufacturer's guidelines for both products include the following indications, warnings and precautions:

> Tildren® / Osphos® is indicated for the control of clinical signs associated with navicular syndrome in horses. The safe use of Tildren® /Osphos® has not been evaluated in horses less than 4 years of age. The effect of bisphosphonates on the skeleton of growing horses has not been studied; however, bisphosphonates inhibit osteoclast activity which impacts bone turnover and may affect bone growth.

According to the manufacturers of Tildren® / Osphos®, the use of bisphosphonates is not recommended in <u>any horse</u> with conditions affecting renal function or mineral or electrolyte homeostasis, and bisphosphonates should not be administered concurrently with non-steroidal anti-inflammatory drugs (*e.g.*, phenylbutazone, flunixin) as this may increase the risk of renal toxicity and acute renal failure. If treatment for discomfort is required after bisphosphonate administration, a non-NSAID treatment should be used.

A number of prescription medications are used “off label” in the horse, meaning that the drug is prescribed for treatment of a condition not listed on the FDA-approved package insert. Use of bisphosphonates outside of the approved age group as specified by the drug manufacturers, however, is not a good general practice due to the risk for serious unintended consequences, particularly in young racehorses.

Veterinary Care Recommendation

Given the scientific evidence that bisphosphonates are potentially harmful to the normal modeling of bone in horses less than four years of age, the absence of FDA approval or manufacturer’s label recommendations for the use of Tildren® / Osphos® in any horse less than four years old, and in consultation with other leading equine veterinarians, the Equine Medical Director recommends that no bisphosphonate should be administered, under any circumstances, to a racehorse less than four years old.

An administration of a bisphosphonate for any reason to a racehorse less than four years old poses an unacceptably high risk of serious injury or death from deleterious effects on bone growth and strength as a consequence of such use.

Equine Medical Director Scott E. Palmer, V.M.D., recommends further that no race horse, even a horse that is four or more years old, should be treated with Tildren® / Osphos® or similar bisphosphonate substances either concurrently with any non-steroidal anti-inflammatory drug (*e.g.*, phenylbutazone, flunixin) or if the horse has a condition affecting normal renal function or mineral or electrolyte homeostasis.

References:

[1]Drake MT, Clarke BL and Khosla S. Bisphosphonates: Mechanism of Action and Role in Clinical Practice. Mayo Clinical Proc. 2008;83(9):1032-1045.

[2] Einhorn TA. The cell and molecular biology of fracture healing. Clin Orthop & Related Res.1998 Oct;355 (Suppl):S7-21.

[3] Mashiba T, Mori S, Burr DB, Komatsubara S, Cao Y et al. The effects of suppressed bone remodeling by bisphosphonates on microdamage accumulation and degree of mineralization in the cortical bone of dog rib. J Bone & Mineral Metabolism. 2005;23(S1):36-42.

[4] Odvina CV, Zerwekh JE, Rao DS, Maalouf N, Gottschalk FA, et al. Severely suppressed bone turnover: a potential complication of alendronate therapy. J Clin Endocrinology & Metabolism. 2005 Mar;90(3):1294-1301.