



OFFICE OF THE EQUINE MEDICAL DIRECTOR

ADVISORY WARNING – BISPHOSPHONATES

March 28, 2019

Thoroughbred horse owners, trainers and/or veterinarians who are responsible for causing or failing to guard against an administration of a bisphosphonate to a racehorse less than four years old will be investigated for a violation of 9 NYCRR § 4043.12(c) for which a fine of \$25,000 may be imposed and the person's occupational license shall be revoked.

The New York State Gaming Commission has determined that there is no generally accepted medical use of a bisphosphonate in a racehorse that is less than four years old; that bisphosphonates are "other doping agents" within the meaning of 9 NYCRR § 4043.12(c)(1); and that any such administration shall violate 9 NYCRR § 4043.12(c).

This limitation applies to any Thoroughbred horse engaged in activities, including training, related to competing in pari-mutuel racing in New York. This includes without limitation any horses that are training outside the jurisdiction to participate in racing in New York who subsequently race in New York and all horses that are training in the jurisdiction.

An administration occurs, within the meaning of 9 NYCRR § 4043.12(c), whenever a substance is introduced into the body of a horse, not only by deliberate introduction of the substance, but also by unintentional acts or omissions.

Summary of Advisory Warning

Any administration of a bisphosphonate to a racehorse less than four years old is an unacceptable practice because of an unacceptably high risk of serious injury or death from deleterious effects on bone growth and strength as a consequence of such use.

Responsibility

Trainers are responsible to guard their horses and to prevent the administration of any substance in violation of Commission rules pursuant to 9 NYCRR § 4043.4(a). Owners and veterinarians are responsible for their acts or omissions that cause such violations. A violation of this rule shall result in exclusion of the horse from racing and the license revocation of any responsible person. 9 NYCRR § 4043.12(e). No bisphosphonate shall be administered to a horse without a veterinary prescription. 9 NYCRR § 4043.16.

Therapeutic Exception for Certain Horses

It is not a violation to administer a bisphosphonate to a racehorse pursuant to a valid therapeutic, evidence-based treatment plan. A therapeutic, evidence-based treatment

plan is a planned course of treatment written and prescribed by an attending veterinarian before the horse is treated that describes the medical need of the horse for the treatment, the evidence-based scientific or clinical justification for using the bisphosphonate, and a determination that recognized therapeutic alternates do not exist. 9 NYCRR § 4043.12(c)(3). This exception does not permit bisphosphonate possession on the grounds of a licensed racetrack in New York. *It is strongly recommended that any such plan be submitted to the Equine Medical Director before any use, including for horses that might ship into New York.*

Basis of Advisory Warning

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.

Further, the Equine Medical Director has consulted with other leading equine veterinarians, who concur that the use of bisphosphonates to treat race horses less than four years old is not a generally accepted veterinary practice.

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 consultation with other leading equine veterinarians, the Commission has determined that an administration of a bisphosphonate to a racehorse less than four years old shall be investigated as an unlawful and prohibited practice.

Additional Information

No drug may be administered, under any circumstances, to a racehorse engaged in activities, including training, related to participating in pari-mutuel racing in New York, without appropriate veterinary approval. 9 NYCRR § 4043.16. This requires a valid veterinarian-client-patient relationship between an attending veterinarian, the horse

owner (who may be represented by the trainer or other agent) and the horse, including:

- (1) the veterinarian, with the consent of the owner, has accepted responsibility for making medical judgments about the health of the horse;
- (2) the veterinarian has sufficient knowledge of the horse to make a preliminary diagnosis of the medical condition of the horse;
- (3) the veterinarian has performed an examination of the horse and is acquainted with the keeping and care of the horse;
- (4) the veterinarian is available to evaluate and oversee treatment outcomes, or has made appropriate arrangements for continuing care and treatment;
- (5) the relationship is maintained by veterinary visits as needed, and
- (6) the veterinary judgments of the veterinarian are independent and are not dictated by the trainer or owner of the horse.

9 NYCRR 4043.16(a). Further, no prescription drug may be administered except as prescribed by an attending veterinarian. 9 NYCRR § 4043.16(b).

According to the manufacturers of Tildren® / Osphos®, the use of bisphosphonates is not recommended in any horse 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.

Equine Medical Director Scott E. Palmer, V.M.D., therefore, recommends that no racehorse be treated with Tildren® / Osphos® or similar bisphosphonate substances, except after the attending veterinarian has taken into account the foregoing information.

References:

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

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

³Mashiba 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.

⁴Odvina 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.