Horsemen's Bulletin

April 20, 2020

1. Medroxyprogesterone

The RMTC recommends that medroxyprogesterone, often known as Depo Provera, not be used. It has been administered to mares in an attempt to control behavior during heat (estrus) but its use has been associated with serious and life-threatening allergic reactions and in some cases has resulted in sudden death. The United States Equestrian Federation (USEF) established medroxyprogesterone as a prohibited substance as of December 1, 2019. The American Association of Equine Practitioners (AAEP) issued the following statement in 2019:

> *Medroxyprogesterone acetate (MPA) is a synthetic progestin hormone administered to mares off-label in an attempt to suppress behavioral estrus. However, a controlled research study found that MPA was not effective at suppression of behavioral estrus. (1) Many veterinarians believe MPA modifies behavior by producing a calming effect in the horse and does not have a therapeutic benefit that goes beyond this behavior modification. Therefore, the AAEP recommends that MPA should not be administered to horses in competition.*

Altrenogest (Regumate) has FDA approval for use in the suppression of estrus and its use is permitted in fillies and mares in training and racing (in compliance with restricted administration times as required by individual racing jurisdictions).

2. Updates to the Uniform Classification of Foreign Substances

Acetylcysteine is used in racehorses as a mucolytic agent, decreasing the thickness of mucus in the trachea and lungs. It is available in FDA-approved formulations for oral, inhalation, or injectable use. Acetylcysteine has been assigned a classification of 4/C consistent with other mucolytics, such as guaifenesin, having FDA-approval.

Ethamsylate is an anti-thrombolytic agent used to promote blood clotting. Ethamsylate has been recognized by international racing regulatory authorities as an illicit substance in controlling EIPH. Ethamsylate has been detected in a post-race sample in a North American racing jurisdiction. There are no ethamsylate containing products that carry FDA approval and so it is assigned a classification of 4/B.

Botulinum toxin is a muscle paralyzing agent produced by the bacteria *Clostridium botulinum*. It is used human cosmetic medicine to decrease facial wrinkles and is also used to treat several other medical problems such as chronic migraine. Veterinary research has identified botulinum toxin as an aid in the treatment of laminitis, specifically in preventing rotation of the coffin bone. A botulinum toxin product labelled for use in the horse in the treatment of laminitis is anticipated to receive FDA approval within the next 12-18 months. A horse with laminitis

should not be in training or entered to race. For this reason, there is no legitimate justification for botulinum toxin to be administered to a horse or in the possession of any individual at a facility under the jurisdiction of a racing regulatory authority. Botulinum toxin is assigned a classification of 2/A

Selective Androgen Receptor Modulators (SARMs) are a class of drug that elicit androgenic (male characteristics), anabolic (muscle building) effects. Within the SARMs class, specific drugs can be developed to have differing ranges of anabolic and androgenic effects. SARMs are on the World Anti-Doping Agency's Prohibited Substance list and are also included in the ARCI's Prohibited Substances List. Specific examples of SARMs are andarine, ostarine, ligandrol, and testolone. Many other SARMs in varying stages of research and development are designated only by letters and numbers (for example, LG121071). SARMs have been used in human clinical trials, but no FDA-approved product exists. SARMs, both as a drug class, and individually as andarine, ostarine, ligandrol, and testolone are assigned a 2/A classification.

Bisphosphonates are a class of drug that inactivate osteoclasts, the cells responsible for removing damaged bone. Tildren (tiludronate sodium) and OsPhos (clodronate), FDA approved for use in the horse, are labelled for the treatment of navicular disease in horses 4 years of age and older. No other bisphosphonates are approved for use in the horse.

Serious concern has been raised about the potential for bisphosphonates to impede or prevent bone remodeling associated with high-speed exercise in young horses. Failure to adapt and remodel in response to high-speed exercise is associated with an increased risk of fatal bone fracture. ARCI-011-015 (Prohibited Practices) requires that FDA-approved Bisphosphonates be used only in accordance with label specifications. Veterinarians and horsemen are advised to consult their regulatory authority prior to bisphosphonate administration to insure that treatment requirements are met. All bisphosphonates, both FDA-approved and not approved, are assigned a classification of 3/A.

Altrenogest is a synthetic hormone with FDA approval for the suppression of heat (estrus) in mares. Off-label use has included short-term administrations to intact males to suppress aggression and other adverse reproductive behavior. Altrenogest also exerts an anabolic effect, and therefore its use is currently prohibited in geldings, stallions, and ridglings engaged in training and racing. Spayed mares have been added to the list of horses in which altrenogest is prohibited.