



Horsemen's Bulletin October 12, 2020

1. Ciclesonide

Ciclesonide (ARCI Drug Classification 4/C) is the corticosteroid in Aservo EquiHaler™ (Boehringer-Ingelheim). This product received FDA-approval for the treatment of equine asthma (also known as Recurrent Airway Obstruction and Summer Pasture Associated Pulmonary Disease) and is now commercially available by veterinary prescription.

Ciclesonide is administered by an inhalation device and is converted to its active form in the horse's lungs. Ciclesonide's effects occur almost exclusively in the lungs unlike other corticosteroids that can have effects throughout the body. Because of this focused effect, ciclesonide treatment is not likely to result in side effects such as a suppressed immune system. Ciclesonide is poorly absorbed from the intestinal tract; oral administration is likely to be ineffective.

In order to provide guidance on the use of this product the RMTC Scientific Advisory Committee reviewed results from a study performed by the manufacturer where horses were treated for ten days. Days 1-5 horses received 8 actuations twice daily. Days 6-10 horses received 12 actuations once daily. Based on this treatment schedule, the data support a 48-hour **Detection Time**.

Horsemen should consult their veterinarians to determine an appropriate withdrawal interval.

For more information, please refer to the RMTC's Ciclesonide Advisory (October 12, 2020).

2. Definitions and Distinctions:

Detection Time is first time point after a medication is administered where it is undetectable in all samples collected from the research horses.

Detection times are determined from analysis of samples collected at specific time points following an administration of a medication to group of, potentially as few as 4, test horses.

For example, if a substance is detected in 3 of 6 samples at 24 hours post-administration, 1 of 6 at 48 hours, and 0 of 6 at 72 hours, the Detection Time is 72 hours.

Detection times represent the foundation for a longer withdrawal interval that must also consider other factors such as: owner or trainer risk aversion, the health of the individual horse, other medications administered, and variability that could be expected to normally occur in a larger population.

The withdrawal interval used for a medication should always be longer than its detection time.

Restricted Administration Time (RAT) is a specified interval during which the treated horse cannot race (enter to race, or participate other regulated exercise as specified by a rule or regulation).

Enforcement can include surveillance, review of treatment reports or medical records, and out-of-competition testing, in addition to standard post-race testing. Evidence that a substance was administered during the restricted administration period establishes that a rule violation occurred.

An example of a treatment controlled by a combination of RAT, threshold and dose specifications is race day furosemide (Lasix). Lasix administration at less than 4 hours to a horse's post time is prohibited.

Evidence that a horse was treated with Lasix at less than 4 hours, regardless of dose administered or concentration detected in a post-race sample, is sufficient to determine that a rule has been violated.

Stand Down Period is a specified period after treatment during which the horse cannot race (enter to race or participate other regulated exercise as defined by rule or regulation).

Stand down periods and restricted administration times accomplish essentially the same thing—a mandatory interval between a treatment and an event (e.g. racing or training).

An example of a stand down period is the ARCI's Model Rule on Prohibited Practices (4)(c) establishing that a horse having received Extra Corporeal Shock Wave treatment ... "shall not be permitted to race or breeze for a minimum of 10 days following treatment."

Withdrawal Guidance is provided by regulators to assist licensees in complying with regulatory thresholds. Withdrawal guidance is a recommendation for a minimum interval between a treatment and racing. It is specific to the administration of a single medication, at a specified dose, route of administration (e.g. oral, intravenous, intra-articular, topical), and treatment schedule.

Withdrawal guidance is typically developed through a statistical analysis of data from a controlled research study.

The administration of a substance contrary to the withdrawal guidance does not, in and of itself, constitute a violation but may represent increased risk for a violation. A longer withdrawal interval, or clearance testing should be considered when the treatment differs from that described with the withdrawal guidance.

*As an example of how to use withdrawal guidance: A veterinarian has prescribed dantrolene capsules (Dantrium™) in a pre-race protocol for a horse with a history of tying up. The veterinarian selects a dose of 1,000 mg. Withdrawal guidance of 48 hours is provided for one 500 mg oral dose. In order to avoid risk of an overage the veterinarian recommends the 48-hour withdrawal interval be increased by one half-life, 4 hours**, to accommodate dosing at 2x that provided in the withdrawal guidance.*

** Knych, H.K., et al., *Pharmacokinetics and Metabolism of Dantrolene in Horses*, J. Vet Pharmacol. Therap., 2010; 34:238-246.