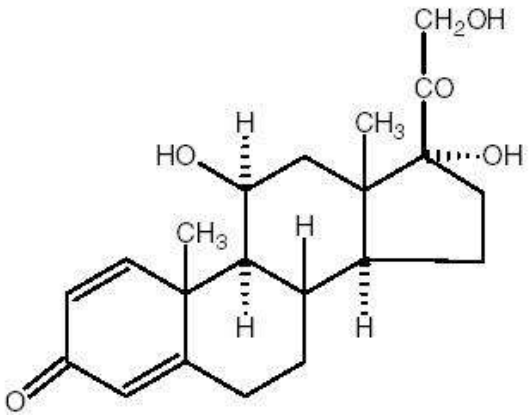
CONTROLLED THERAPEUTIC MEDICATIONS
MONOGRAPH SERIES

Prednisolone

Background

Prednisolone is a short acting corticosteroid. It is assigned 4/C in the ARCI's Uniform Classification of Foreign Substances. Prednisolone is a synthetic glucocorticoid, derived from cortisol, that is used to treat a variety of inflammatory and auto-immune conditions.[i] It is often used to treat allergies, allergic reactions, COPD, and general inflammation in equines.



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Prednisolone is a prescription medication and can only be dispensed from or upon the request of a veterinarian. It is commercially available in a variety of formulations including Medrol® Tablets.[ii] Prednisolone can be administered orally, intramuscularly, and intravenously.

Prednisolone's structure differs from cortisol by the presence of a $C_{1\text{-}2}$ double bond. This difference leads to a four-fold higher glucocorticoid or anti-inflammatory activity of prednisolone when compared to cortisol.[iii]

Prednisolone has been demonstrated to be much more effective as an oral anti-inflammatory than prednisone because it is absorbed in a pharmacologically active form and does not require metabolism as prednisone does.[iv]

Administration Studies

Through a confidentiality agreement with the European Horseracing Scientific Liaison Committee the RMTC Scientific Advisory Committee (SAC) was able to review data from an administration study where 6 horses were administered 1 mg/kg of prednisolone (Prednidale; Dechra, Shrewsbury, UK) orally once a day for 5 days. A 95/95 Tolerance Interval calculation was performed on data from samples collected at various time points.

Scientific Advisory Committee (SAC) Recommendation

The SAC determined that it did not wish to be permissive of the administration of prednisolone at less than 48 hours to a horse's race. The SAC rounded up the 95/95 TI value at 48 hours of

0.89 ng/mL to a threshold recommendation of 1.0 ng/mL of prednisolone in serum or plasma corresponding to withdrawal guidance of 48 hours for a 1 mg/kg oral dose.

Practice Tips

Withdrawal guidance is specific to dose and route of administration. Different formulations of prednisolone, administration of higher doses, use of other routes of administration, or combinations of prednisolone with other substances represent unknown risk for a concentration in excess of the threshold and therefore an extended withdrawal time is recommended. Veterinarians are advised to use caution when deviating from doses and routes that have been studied and to use an extended withdrawal time and/or submit a sample for analysis prior to competition.

Specifically, the withdrawal time recommendations do not apply to prednisolone acetate administered intramuscularly. This route of administration was not studied as there is no FDA-approved formulation for intramuscular administration. Other corticosteroids (e.g. triamcinolone and methylprednisolone) have demonstrated extended elimination periods when administered intramuscularly and therefore require longer withdrawal intervals. Similar caution is advised for the intramuscular administration of prednisolone.

Note: In 2019 the ARCI adopted a Model Rule prohibiting the stacking of corticosteroids (i.e. detection of two or more corticosteroids in a blood and/or urine sample). In order to provide analytical support for the stacking prohibition, the threshold was withdrawn, with prednisolone regulated by LOD in serum or plasma and a screening limit of 0.01 mcg/mL of free prednisolone in urine.

References

[i] Fidani, M., *Population Study of Free Predisolone in Horse Urine,* ICRAV 2014 presentation.

[ii] FDA Green Book. Avaliable at: https://animaldrugsatfda.fda.gov/adafda/views/#/search (Enter prednisolone in the search box)

[iii] Fidani, M., *et al, Investigation of the Presence of Endogenous Prednisolone in Equine Urine by High-performance Liquid Chromatography Mass Spectrometry and High-resolution Mass Spectrometry,* Rapid Commun. Mass Spectrom., 2012, 26: 879-886

[iv] Peroni, D.L., *et al*, *Prednisone Per Os is Likely to Have Limited Efficacy in Horses,* Equine Vet. J., 2002, 34(3): 283-287.