

## Norethisterone for the control of oestrus in females to be introduced as an exempted substance into the Greyhounds Australasia Rules

Notice to trainers – Norethisterone usage in greyhounds

On 1 August 2018, Greyhounds Australasia will introduce norethisterone to the list of *Exempted Substances* within GAR 1 Definitions as follows:

"Ethyloestrenol or norethisterone when administered orally to a female greyhound and where it has been prescribed by a veterinary surgeon for the sole purpose of regulating or preventing oestrus in that female greyhound."

Female greyhounds are unable to race whilst in season, which can occur up to twice a year and reduce their available racing career. Since the introduction of a ban on previously used anabolic androgenic steroids (AAS), oestrus control has been limited to the use of ethyloestrenol. Following a review, including research with The University of Nottingham and the Greyhound Board of Great Britain where norethisterone is used successfully, Greyhounds Australasia has agreed to allow norethisterone as an alternative non-AAS means of postponing oestrus in females.

Participants are encouraged to discuss with their veterinarian the options available for regulating or preventing oestrus in their greyhounds in order to make an informed decision. Options available include no treatment (allow natural cycling), spaying (permanent surgical option), or medication with ethyloestrenol or norethisterone.

Norethisterone is a synthetic form of progesterone and belongs to a class of drugs known as progestins, and is commonly used in human contraceptive pills. Progestins prevent oestrus by inhibiting the hormone that causes ovulation i.e. they act on the pituitary gland to reduce its responsiveness to gonadotrophin releasing hormone (GnRH) and blocking the effect of oestradiol on GnRH receptor expression. This leads to a suppression of reproductive cyclicity and prevents oestrus.

From a survey of UK trainers, norethisterone effectively and temporarily postpones oestrus in most females, but some side effects were reported including frequent urination, clitoral enlargement or a behaviour change. A separate review of performance data found that greyhounds performed up to one length slower if treated with norethisterone. These are similar to those side effects reported when using ethyloestrenol and were less likely at decreased doses (2.5mg/day compared to 5mg/day). The performance decrease found is similar to that seen when progesterone is naturally elevated during a normal oestrus cycle.

There are two products that are registered with the Therapeutic Goods Administration (TGA) that contain only norethisterone - Primolut  $N^{TM}$  and Noriday 28 Day<sup>TM</sup>. Given the low dose contained in the latter product, Primolut  $N^{TM}$  is likely to be an easier and more economic method of controlling oestrus for trainers. The cost per day of  $\frac{1}{2}$  - 1 tablet once daily of Primolut N is similar to ethyloestrenol at 45 - 90 cents.

Many products contain norethisterone in combination with other substances (e.g. ethinylestradiol - *an oestrogen not to be confused with ethyloestrenol*) - these additional substances are not exempted from being a prohibited substance and can cause a positive swab. Trainers administering these combination products do so at their own risk.

There are no longer any Australian Pesticides and Veterinary Medicines Authority (APVMA) registered products containing ethyloestrenol available in Australia. There is however one product containing ethyloestrenol (Orabolin) which has been produced under APVMA permit for several years. Unless a fully registered product returns to the market, the reliable ongoing supply of ethyloestrenol may be at risk.

Like ethyloestrenol, norethisterone must only be used for the purposes of regulating or preventing oestrus and can only be prescribed by a registered Veterinary Surgeon to an animal under his or her care after establishing a therapeutic need for that substance. That veterinary surgeon would be prescribing the product 'off-label' as neither substance is registered for the control of oestrus in canines. The product must be labelled in accordance with regulatory legalisation.

As both exempted substances are a Schedule 4 (Prescription Only) substance, trainers are reminded of their obligations under GAR 83A Raceday Treatment (i.e. do not administer on the day of an event until home after racing) and under GAR 84A Treatment Records (i.e. record administrations to each greyhound in their treatment book).

For further information please contact your state controlling body.