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Suprelorin®

Active Ingredient
Deslorelin acetate

Product Type
GnRH agonist

Manufacturer
Virbac Australia

Product information
Suprelorin (deslorelin), a GnRH agonist, effects contraception by temporarily suppressing the reproductive endocrine system and preventing production of pituitary (FSH and LH) and gonadal hormones (estradiol and progesterone in females and testosterone in males). The observed effects are similar to those following ovariectomy or castration, but can reverse after the hormone content of the implant is depleted or the implant is removed. As an agonist, deslorelin first stimulates the reproductive system, which can result in estrus and ovulation in females or temporary enhancement of testosterone and semen production in males. Then, down-regulation follows the initial period of stimulation.

Although deslorelin can also be an effective contraceptive in males of some species, it is used primarily in females. Monitoring efficacy by suppression of estrous behavior or of gonadal steroids in feces of females is more straightforward than ensuring continued absence of sperm in males, since most institutions cannot perform regular semen collections. It can, however, be used to ameliorate aggression in males of some species, but higher dosages are usually needed.

Deslorelin implants are available in two formulations: 4.7mg for a minimum of 6-months, and 9.4mg for a minimum of 12-months of contraception. Because deslorelin was tested first in domestic dogs and cats, it was considered most suitable for carnivores but is now used successfully in females of many other taxa (Agnew et al., 2021). It has also been successful in reducing aggression in some male primates, but it appears not to be effective in suppressing testosterone or spermatogenesis in some male bovids (e.g., antelope) (Penfold et. al., 2002) or marsupials.

Ordering
Deslorelin implants are available to AZA-accredited institutions as part of a research trial coordinated by the AZA Reproductive Management Center as part of an agreement with Virbac, Australia. The RMC will also work with AZA Sustainability Partners to supply implants for animals that are part of an SSP managed population. All other facilities interested in using Suprelorin can contact the RMC for important information about the product, but we do not distribute implants to non-AZA institutions or individuals. Suprelorin F® is commercially available in the United States, but solely for the treatment of ferret adrenal disease. For institutions outside of the U.S., Suprelorin is commercially available in the U.K., Europe, Australia, and New Zealand.

To order implants, AZA-accredited institutions in the U.S. should submit the Suprelorin Registration Form to the person listed below. The 4.7mg formulation costs $35/implant and the 9.4mg formulation costs $65/implant.

Storage

Implants should be stored at refrigeration temperatures (4°C). Expiration date ("place before" date) is stamped on individual implant packages. If the implant would expire prior to placement, contact Ashley Franklin (franklin@stlzoo.org) for advice.

Insertion/Administration

The area should be clipped and cleaned using standard surgical prep techniques. A fold of skin should be lifted and held between the thumb and fingers, as the trocar (supplied with the implant) is inserted. To prevent implant breakage during insertion, create a tunnel with the trocar, then slowly withdraw the trocar, while depressing the plunger, leaving the implant in place in the tunnel. The implant should be held in place through the skin as the trocar is removed to ensure release of the implant so that it remains in place under the skin.

Implant Placement and/or Removal Tips

The implant comes pre-loaded in an insertion device. The Suprelorin product insert instructs the veterinarian to place the implant subcutaneously (SQ) between the shoulder blades. That site is still appropriate if removal will not be needed, but because removal is desirable in most cases, the RMC recommends implant placement in alternative locations to facilitate later removal (Cowl et al., 2018). The implants were not designed to be removed, and they do become more porous and prone to breakage with time, as deslorelin diffuses out, but they do not dissolve. Thus, with careful placement, removal is possible (Cowl et al., 2018). The ideal site will vary by species, but examples of those that have been successful have been SQ in the fleshy portion at the base of the ear, inner area of the leg (front or rear), and the umbilical area. Although the animal may be able to lick or scratch these areas, deep placement of the implant at the end of a tunnel created by the trocar can protect it. An area with adequate vascularization should be chosen in order to ensure a sufficient dose is absorbed. Fatty, bony and cartilaginous areas should be avoided in favor of sites with more muscle. An instructional video illustrating implant placement SQ in the inner aspect of the rear leg can be provided on request by contacting contraception@stlzoo.org.

Placement Tips:

1. Identify a location where it is unlikely that the implant will migrate and where the implant can be palpated through the skin.
2. Create a tunnel with the trocar, then slowly withdraw the obturator, leaving the implant in place in the tunnel. The implant should be held steady as the obturator is removed to ensure release of the implant so that it remains in place.
3. Ensure the entire implant is in place by gently palpating, being careful not to crush it, and make note in medical records for future retrieval attempts.
4. At each opportunity, physically palpate the location of the implant to confirm it is in place, again always taking care not to crush the implants, since they become prone to breakage over time.

Tips for removal:

1. Locate implant by palpation, being careful not to crush it.
2. The area should be clipped and cleaned using standard surgical prep techniques.
3. Make a small incision through which the implant can be removed.
4. Grasp implant carefully with forceps and gently remove; even if the implant breaks, attempt to remove all remaining pieces.
5. Confirm that all pieces have been found and removed.
6. Flush area with sterile saline to remove any remaining fragments.
7. Close incision.

Latency to effectiveness

Because the initial effect is to stimulate the reproductive system, it is important to either separate treated animals from opposite sex individuals during the period of enhanced fertility or use another form of contraception. Females treated with deslorelin should be considered fertile for 3 weeks following insertion. Males may remain fertile for up to 2 months, until residual sperm either degenerate or are passed (as following vasectomy).

Suppression of initial estrus/ovulation

Estrus and ovulation that can occur within 2 weeks following implant insertion can be suppressed with supplemental progestin treatment for 2 weeks (7 days prior through 7 days after implant insertion). Megestrol acetate (e.g., Ovaban) tablets are recommended for short-term progestin administration, with the tablet offered as part of a treat. Depo-Provera should not be substituted for megestrol acetate, because its initial high levels and prolonged release can interfere with Suprelorin efficacy. MGA implants can be left in place for 1-2 weeks following Suprelorin implant insertion, but then should be removed to prevent interference with the down-regulation action. Leaving them in place longer may compromise Suprelorin efficacy.

Signs of estrus during treatment

Suprelorin first stimulates then suppresses estrus in females. Thus, signs of estrus may be seen at the beginning of treatment, particularly when alternative contraception such as Ovaban (megestrol acetate) is not used to suppress the stimulation phase. Stimulation of estrus and ovulation can increase chances of uterine pathology, especially in carnivores that have an extended luteal phase with elevated progesterone following induced ovulation (e.g., felids, mustelids, and some bears) and following spontaneous ovulation in canids.

Duration of efficacy and reversibility

The 12-month formulation containing 9.4mg deslorelin is designed to be effective for twice as long as the 4.7mg implants, since the implant matrix releases deslorelin at a slower rate. Thus, the per-kg-body-weight dose for the 9.4mg implants is about twice that of the 4.7mg implants. However, that translates into an equivalent number of implants needed. For example, an animal effectively contracepted for 6 months with two 4.7mg implants will need two 9.4mg implants to achieve contraception for a longer period. That is, one 9.4mg implant will not substitute for two 4.7mg ones.

The minimum duration of efficacy of the 4.7mg implant is 6 months, but the average is about 1 year. For the 9.4mg implants, the minimum duration of efficacy is 12 months but the average is about 2 years. There is considerable variability among species and among individuals, but the response of an individual tends to be consistent. That is, if an individual reverses at 8 months with a 4.7mg implant, it will likely always reverse after about 8 months. If it is not possible to wait for signs of reversal to determine duration of efficacy for the animal, then for continuous contraception the 4.7mg implants should be replaced at 6-month intervals and the 9.4mg ones at 12-month intervals. These implants were developed for and have been used primarily in mammals. Duration of efficacy may differ in other taxa.

Transition phase during reversal

Data from studies of domestic cats and from African lions (Bertchinger et al. 2008) have identified a transition phase of about 6 months during the process of reversal, when follicles grow and produce estrogen sufficient to stimulate recurring signs of estrus and even mating behavior but without ovulation. In addition, information submitted to the RMC suggests that in some individuals there is sustained stimulation of gonadal hormones (e.g., testosterone in males or higher than normal levels of progesterone following ovulation in females) during reversal.

These observations indicate that reversal is a process that may extend for 6 months or more, when abnormal or irregular cycles may be seen in females or a period of increased aggression may be seen in males. It should be possible to hasten or avoid this process by removing the implant(s) (Cowl et al., 2018). The implant(s) may continue to release deslorelin during this time, at levels too low to maintain pituitary down-regulation but high enough to stimulate gonadal steroid production or, in some individuals, to prevent the LH surge required for ovulation.

Use during pregnancy

GnRH agonists should not be used during pregnancy, as they may cause abortion. Even if abortion does not result, deslorelin may interfere with establishment of milk production.

Use during lactation

No known contraindications once lactation has been established.

Use in pre-pubertal animals

Although data on prepubertal use in wildlife species are limited, studies on domestic kittens and puppies have shown successful postponement of puberty with subsequent documentation of reproductive capacity. As in treatment of adults, there was considerable individual difference in duration of effect. Epiphysial closure was delayed, but body size was not affected.

Precautions

In general, the effects on body weight should be similar to those from ovariectomy or castration. Preliminary data indicate that increased appetite will result in weight gain, especially in females, unless food is restricted. In males, muscle loss may result in overall weight loss if not replaced by fat. In sexually dimorphic species, males may become the size (weight) of females. Animals may lose secondary sex characteristics (e.g., lions may lose their manes).

Consideration for seasonal breeders

In females of some taxa, GnRH agonists can induce estrus and ovulation even during the non-breeding season. In males, GnRH agonists can transiently stimulate testosterone production even during the non-breeding season. Treatment should begin more than 2 months prior to the anticipated breeding season to prevent initiation of spermatogenesis, because it appears that suppression of sperm production is more easily accomplished before it has commenced.

Reporting Requirements

All institutions using deslorelin must contribute contraception information for their animals to the AZA Reproductive Management Center's Contraception Database (https://www.zoocontraceptiondata.org) as part of an agreement with Virbac, Australia. The product will not be distributed to any institution that fails to complete the survey.

For questions about the RMC Contraception Database, contact:

Ashley Franklin, Program Analyst
AZA Reproductive Management Center
One Government Drive
Saint Louis, MO 63110
301-956-0171; fax: 314-646-5534
franklin@stlzoo.org

Deslorelin Assay Validation *- The RMC requests that facilities using Suprelorin implants, which contain deslorelin as the active ingredient, collect serum samples any time the animal is in hand after implant placement to help us establish a database of effective deslorelin concentrations and dynamics.*

References:

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Penfold, L. M., Ball, R., Burden, I., Jochle, W., Citino, S. B., Monfort, S. L., Wielebnowski, N. (2002). Case Studies in antelope aggression control using a GnRH agonist. *Zoo Biology*. 21, 435-448.