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Ursids

Please note that these options are not recommendations for a particular taxon, but possible choices that depend on individual circumstances. It is the responsibility of the veterinarian and animal care staff to determine the dosage and best treatment for an individual based short-term and long-term reproductive goals, facility considerations, and logistical concerns.

THE CURRENT OPTIONS FOR FEMALES INCLUDE:

Suprelorin® implants (GnRH agonist) Lupron® injections (GnRH agonist)

Note: Progestins should only be used in special, short-term cases (see cautions below)

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GNRH AGONISTS

Suprelorin® Implants (deslorelin acetate)

- Duration of efficacy: 4.7mg implants are effective a minimum of 6 months, and 9.4mg implants are effective a minimum of 12 months but either formulation may be effective much longer; there is also individual and species variation in duration of efficacy.
- Route of administration: Subcutaneous via trocar in a place where it can be easily detected (e.g., base of the ear, inner thigh, or umbilical region) to facilitate removal when new ones are placed or when a breeding recommendation is received, even if implants are "expired", to reduce duration of efficacy (see <u>Suprelorin Product Page</u>).
- Latency to effectiveness: About 3 weeks for females, 2 months for males; implanted females must be separated from males for 3 weeks or oral megestrol acetate (Ovaban or Megace) must be used for 7 days prior through 7 days after implant placement to prevent the agonist-induced stimulation phase (see Suprelorin Product Page). Implanted males must be separated from females or the females must be treated with an alternative contraceptive for at least 2 months, until residual sperm either degenerate or are passed.
- Dosing: Doses vary by taxon. Dosage guidelines can be obtained by emailing the RMC at contraception@stlzoo.org.
- Estrous cycles during contraceptive treatment: Estrus and ovulation are possible during the 3
 weeks of stimulation, then down-regulation occurs. To prevent the stimulation phase, the oral
 megestrol acetate protocol described above is recommended. Some follicle growth may
 continue, even following down-regulation.
- Use during pregnancy: Not recommended; may cause abortion or if pregnancy progresses, mammary development may be suppressed impairing milk production.
- Use during lactation: No contraindications once lactation is established.
- Use in seasonal breeders: GnRH agonists can induce estrus in females and transiently stimulate testosterone production in males even during the non-breeding season. When used in seasonal

- breeders, implants should be placed in females at least 1 month before and in males at least 2 months before the time of first seasonally anticipated estrus.
- Reversibility: Designed to be reversible, but time to reversal can be quite variable. To decrease time to reversal, implants should be removed.
- Use in prepubertal 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.
- Behavioral effects: In general, the effects should be similar to those from ovariectomy or castration; possible increased appetite can result in weight gain, especially in females, unless food intake is monitored.
- Effects on physical characteristics: In general, the effects should be similar to those from ovariectomy or castration such as suppression of physical secondary sexual characteristics. In males, muscle loss may result in overall weight loss unless replaced by fat. In sexually dimorphic species, males may become the size (weight) of females.
- Other: The RMC is only able to distribute Suprelorin implants to AZA-accredited institutions or
 for animals managed under an SSP or Recovery SAFE Program. Suprelorin F® is commercially
 available in the U.S. through veterinarians, 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, a <u>Suprelorin Registration Form</u>, found on the
 Suprelorin Product Page, must be submitted.
- **Caution:** Depo-Provera should not be substituted for oral megestrol acetate to suppress the Suprelorin stimulation phase because its prolonged initial high levels can interfere with Suprelorin-mediated down-regulation or the reproductive system.

Lupron® Injections (leuprolide acetate)

- **Caution:** Since data for Lupron are limited, most of this information is extrapolated from the use of Suprelorin.
- Duration of efficacy: Available in formulations for human use effective from 1 to 6 months, but duration of efficacy and time to reversal in wildlife species may vary.
- Route of administration: Injectable.
- Latency to effectiveness: About 3 weeks for females, 2 months for males; implanted females
 must be separated from males for 3 weeks or oral megestrol acetate (<u>Ovaban or Megace</u>) must
 be used for 7 days prior through 7 days after implant placement to prevent the agonist-induced
 stimulation phase. Implanted males must be separated from females or the females must be
 treated with an alternative contraceptive for at least 2 months, until residual sperm either
 degenerate or are passed.
- Dosing: Doses vary by taxon. Dosage must be extrapolated from human dosing regimens due to limited use in other wildlife.
- Estrous cycles during contraceptive treatment: As with Suprelorin, estrus and ovulation may occur during the 3 weeks of stimulation, then down-regulation occurs. To prevent the stimulation phase, the oral megestrol acetate protocol described above is recommended.

- Use during pregnancy: Not recommended; may cause abortion or if pregnancy progresses, mammary development may be suppressed impairing milk production.
- Use during lactation: No contraindications once lactation is established.
- Use in seasonal breeders: GnRH agonists can induce estrus in females and transiently stimulate testosterone production in males even during the non-breeding season. When used in seasonal breeders, implants should be placed in females at least 1 month before and in males at least 2 months before the time of first seasonally anticipated estrus.
- Reversibility: Duration of efficacy/time to reversal may vary.
- Use in prepubertal animals: The lack of data on pre-pubertal treatment and potential long-term
 effects on fertility contraindicates recommending contraception before puberty. Also, because
 Lupron suppresses gonadal steroids, its use may delay epiphyseal closure of the long bones,
 resulting in taller individuals, similar to the effects of pre-pubertal spaying and neutering in
 domestic dogs and cats.
- Behavioral effects: In general, the effects should be similar to those from ovariectomy or castration; possible increased appetite can result in weight gain, especially in females, unless food is restricted.
- Effects on physical characteristics: In general, the effects should be similar to those from
 ovariectomy or castration, such as suppression of secondary sexual characteristics. In males,
 muscle loss may result in overall weight loss unless replaced by fat. In sexually dimorphic
 species, males may become the size (weight) of females.
- Other: Lupron, approved for treatment of prostate cancer in men, is expensive but can sometimes be acquired through donation from the manufacturer. In wildlife, it has been used primarily in males to suppress testosterone and sperm production. It has rarely been used in zoo animals since the late 1990s due to cost.

IMMUNOCONTRACEPTION

Porcine Zona Pellucida Vaccine

- Duration of efficacy: Species-dependent; for most species, it is effective 6 months to 1 year. First and second injections should be given no sooner than 2 weeks apart and subsequent boosters administered as needed. For year-round breeders, boosters should be given every 8 months.
- Route of administration: Injectable intramuscular.
- Latency to effectiveness: Effective only after the primer and initial booster injection (typically given at 2-4 week intervals), depending upon species and adjuvant. There must be a minimum 2-week interval after the second dose before the male is placed with the female.
- Dosing: Doses vary by taxon. Dosage guidelines can be obtained from the Science and Conservation Center at https://www.sccpzp.org when ordering this product.
- Estrous cycles during contraceptive treatment: Animals will continue to show signs of breeding behavior even when they are adequately contracepted. The breeding season may extend beyond what is considered typical, resulting in additional estrous cycles. However, with repeated treatment, cycles may become irregular and eventually cease.
- Use during pregnancy: Does not interrupt pregnancy or affect fetal development.
- Use during lactation: No known contraindications based on data from feral horse mares; data deficient in other species.

- Use in prepubertal animals: The lack of data on pre-pubertal treatment contraindicates recommending contraception before puberty.
- Use in seasonal breeders: Because PZP is not effective until after at least 2 injections (typically given 2-4 weeks apart), depending on species and adjuvant, treatment should be initiated at least 2 months before the anticipated onset of the breeding season.
- Reversibility: Is intended to be reversible, but repeated treatment can extend time to reversal. Because reversal becomes less likely with repeated treatment, use should be limited to 3-4 consecutive years or to animals not essential for breeding programs.
- Behavioral effects: Since the vaccine usually doesn't suppress estrous cycles, it has little or no effect on social behavior. In some species the failure to conceive can result in longer than usual breeding season, and in some cases this can result in aggression and social disruption.
- Effects on physical characteristics: Data deficient.
- Other: Contact Kim Frank at the Science and Conservation Center (kfrank@sccpzp.org) for more detailed instructions and to order this product.

PZP-Related Cautions

PZP may not be reversible after long-term use (>3 consecutive years).

OTHER CAUTIONS

Special Progestin-Related Cautions

- Progestins should not be used except for special short-term cases (e.g., if a female will be
 getting a breeding recommendation in <2 years) because progestins have been associated with
 progressive uterine growth, uterine cancer, and/or mammary cancer in other carnivore species
 (e.g., felids and canids).
- Progestins should not be used for more than 2 consecutive years or 2 breeding seasons, preferably followed by pregnancy. Progestins should not be used for more than a total of 4 years during the female's lifetime.
- If a progestin is used, treatment should be initiated before the breeding season begins.
- Pregnant females contracepted with progestins may experience suppression of uterine contractions; thus, treatment should be stopped or implants removed before anticipated parturition.
- Oral megestrol acetate (0.5-1.0 mg/kg body weight daily) or MGA implants are the preferred progestins for short-term use, since administration can be easily stopped or implants can be easily removed; for that reason, Depo-Provera is not recommended due to the potentially very long duration of effect.

Vasectomy-Related Cautions

For carnivore species with induced ovulation (documented for at least some ursid species),
vasectomy of males may not prevent potential adverse effects to females from prolonged
exposure to endogenous progesterone following copulation-induced ovulation that results in
pseudo-pregnancy. Because pregnancy diagnosis in ursids remains challenging, the occurrence
of pseudo-pregnancy in females that copulate and ovulate but do not conceive has not been
confirmed. Castration should eliminate copulation-induced ovulation, preventing possible
pseudo-pregnancies. Endogenous progesterone and progestin contraceptives cause similar side
effects.

For more details on each of these products, please refer the specific product page.

Reporting requirements: Any use of Suprelorin implants in the United States must be reported to the RMC via our online contraception survey website (https://www.zoocontraceptiondata.org), including any and all adverse events associated with product use. Additionally, in order to increase our knowledge of the efficacy and reversibility of other contraception products, it is recommended that all individuals on contraception be added to the RMC's contraception database via our online contraception survey website (https://www.zoocontraceptiondata.org).

Ongoing Studies for which sample collection is encouraged:

- **RHSP Archive** The RMC and the Reproductive Health Surveillance Program (RHSP) request that facilities submit complete reproductive tracts to the RHSP anytime an animal dies or has their reproductive tract removed, to be available for investigations of reproductive health. See the RHSP website (www.stlzoo.org/RHSP) for more specifics.
- **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.

Disclaimer: The RMC strives to provide accurate and current contraception recommendations based on various sources (e.g., publications, AZA RMC/EAZA RMG database records); however, as these are prescription-only medicines, it is the responsibility of the veterinarian and animal managers to determine the dosage and best treatment for an individual.