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of the Saint Louis Inc.

Artiodactyls

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:

MGA implants (progestin)

MGA feed or MGA liquid (progestin)

Depo-Provera® injections (progestin)

Suprelorin® implants (GnRH agonist)

Porcine zona pellucida (PZP) (immunocontraception)

Improvest® (immunocontraception)

Note: MGA feed, MGA liquid, and PZP are not effective in suids

THE CURRENT OPTIONS FOR MALES INCLUDE:

Suprelorin® implants (GnRH agonist)

Improvest® (immunocontraception)

Note: GnRH agonists are not effective in male bovids

PROGESTINS

MGA Implants (melengestrol acetate)

- Duration of efficacy: Effective for at least 2 years, but may be much longer if not removed.
- Route of administration: Surgically inserted after proper sterilization (See <u>MGA Implant Product</u> Page).
- Latency to effectiveness: 1-2 weeks.
- Dosing: Doses vary by taxon. Dosing guidelines can be found on the MGA Implant Product Page.
- Estrous cycles during contraceptive treatment: Unusual but can sometimes occur.
- Use during pregnancy: There is no evidence of problems during early pregnancy; however, not recommended in artiodactyls in late pregnancy, because of the possibility of prolonged gestation or dystocia, although the effect may depend on species and dose.
- Use during lactation: Can be used in lactating females.
- Use in seasonal breeders: Implants should be placed at least 1 month prior to breeding season.
- Reversibility: Generally reliable after implants are removed.
- Use in prepubertal animals: The lack of data on pre-pubertal treatment and potential long-term effects on fertility contraindicates recommending contraception before puberty.
- Behavioral effects: Data deficient.
- Effects on physical characteristics: Data deficient.
- Other: Please note that MGA implants are not available outside the U.S.

MGA Feed and MGA Liquid (melengestrol acetate)

- Duration of efficacy: Not much more than 1 day, so full dose must be consumed daily in order to
 be effective; if a female refuses to consume the dose, she should be separated from males until
 she has consumed the proper dose again for at least one week.
- Route of administration: Given orally; the liquid may be fed directly into mouth or via treat or top-dressing regular diet.
- Latency to effectiveness: 1-2 weeks.
- Dosing: Doses vary by taxon. Dosing guidelines can be found on the <u>MGA Feed</u> and <u>MGA Liquid</u>
 Product Pages.
- Estrous cycles during contraceptive treatment: Unusual but can sometimes occur.
- Use during pregnancy: There is no evidence of problems during early pregnancy; however, not recommended in artiodactyls in late pregnancy because of the possibility of prolonged gestation or dystocia, although the effect may depend on species and dose.
- Use during lactation: Can be used in lactating females.
- Use in seasonal breeders: Start contraception at least 1 month prior to breeding season.
- Reversibility: Predictably reversible; these products clear from the system rapidly once discontinued.
- Use in prepubertal animals: The lack of data on pre-pubertal treatment and potential long-term effects on fertility contraindicates recommending contraception before puberty.
- Behavioral effects: Data deficient.
- Effects on physical characteristics: Antler abnormalities such as malformations, change in annual timing of full shedding of velvet, and occasional aberrant sheeting or breaking of full antlers, have been seen in some cervid species.
- Other: MGA feed obtained from Mazuri and MGA liquid obtained from Wedgewood Pharmacy are not available outside the U.S.; use of these products requires the completion of either the MGA Feed Registration Form or MGA Liquid Registration Form. NOTE: Current FDA regulations restrict sale of MGA feed to only bovids, giraffes, cervids, camelids, and hippos.
- **Cautions:** Protective gloves should be worn when using these products, as MGA can be absorbed through the skin and potentially cause disruption of menstrual cycles and prolongation of pregnancy in humans.

Depo-Provera® Injections (medroxyprogesterone acetate)

- Duration of efficacy: Extremely variable, with reports ranging from 1 to 24 months.
- Route of administration: Injectable.
- Latency to effectiveness: 1-2 weeks.
- Dosing: Doses and injection frequency vary by taxon. Dosing guidelines can be found on the Depo-Provera Product Page.
- Estrous cycles during contraceptive treatment: Unusual but can sometimes occur.
- Use during pregnancy: Depo-Provera is not recommended for females that might be pregnant because its potentially long duration of efficacy may interfere with parturition; females should be confirmed not pregnant before starting treatment.
- Use during lactation: Can be used in lactating females.

- Use in seasonal breeders: First injection should be given at least 1 month prior to breeding season.
- Reversibility: Data from various mammal species have shown that duration of efficacy and latency to conception following last injection can be quite variable across individuals (from 1 month to 2 years); however, individuals do tend to reverse after treatment ends.
- Use in prepubertal animals: The lack of data on pre-pubertal treatment and potential long-term effects on fertility contraindicates recommending contraception before puberty.
- Behavioral effects: While there may be individual and species variation in response, females may show male-like qualities such as increased aggression.
- Effects on physical characteristics: While there may be individual and species variation in response, females may develop male-type secondary sex characteristics.

Progestin-Related Cautions

- Progestins may cause hydrometra, although the condition usually reverses when treatment is stopped.
- Pregnant artiodactyls contracepted with progestins may be especially susceptible to suppression
 of uterine contractions; progestins should only be administered to animals CONFIRMED not
 pregnant.
- Depo-Provera may be a particular problem for parturition in pregnant females; since length of efficacy is so variable (approximate range: 1-24 months), even treatment early in gestation may suppress uterine contractions and prevent or delay parturition.
- Future reproduction was not affected in calves of domestic cows on MGA-treated feed, but no published studies of pre-pubertal treatment with MGA or other progestins have been conducted with other species, so possible long-term effects on fertility are not known.
- MGA has been administered orally to domestic cattle for decades without untoward effects, which suggests that it should be generally safe for ruminants, but there may be species differences.
- MGA feed and MGA liquid are not recommended for suids because the especially high dose required for efficacy has been associated with side-effects.
- Antler abnormalities such as malformations, change in annual timing of full shedding of velvet, and occasional aberrant sheeting or breaking of full antlers, have been seen in some cervid species contracepted with MGA liquid or MGA feed.
- In areas where cleaning is done by hosing (i.e., water under pressure), aerosolization of fecal matter, including excreted steroid hormones from MGA or Depo-Provera, is possible. Proper precautions should be taken.

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 <u>Suprelorin Product Page</u>). 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
 <u>Suprelorin Product Page</u>, 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.

GnRH-Agonist-Related Cautions

• GnRH agonists have been found to be ineffective in male bovids tested; efficacy has not been established in most other male artiodactyls.

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).
- PZP is not effective in suids because it will not elicit an immune response in them.

Improvest® (Anti-GnRH Vaccine)

- Duration of efficacy: The data on duration of efficacy and reversibility for wildlife species are limited.
- Route of administration: Injectable intramuscular or subcutaneous.
- Latency to effectiveness: According to the manufacturer, Improvest becomes effective 1-2
 weeks after the second injection, typically given 1 month after the first, so separation of the
 sexes is recommended until then.
- Dosing: Dosage and frequency of injection information reported to the RMC contraception database are typically based on the manufacturer's instructions. However, species-specific dosing protocols exist for some taxa for which we have more information (e.g., giraffes). See the Improvest Product Page for more details.
- Estrous cycles during contraceptive treatment: Unlike GnRH agonists (e.g., Suprelorin), Improvest should not cause an initial stimulation, or flare, of the reproductive system, but some evidence of a flare has been noted in giraffe. Estrous cycles should cease to occur after the second injection is administered.
- Use during pregnancy: Data deficient.
- Use during lactation: Data deficient.
- 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
 Improvest 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.
- Use in seasonal breeders: For females, both the initial injection and 1-month booster must be completed prior to the anticipated breeding season. For males, both injections must be completed at least 2 months before the anticipated breeding season, since sperm are typically produced in advance of first ovulation.
- Reversibility: Improvest was not designed specifically to be reversible, although reversibility has been demonstrated in some species.
- Behavioral effects: Unknown, but expected to be similar to those following gonadectomy.
- Effects on physical characteristics: In general, the effects should be similar to those from
 ovariectomy or castration. Because appetite may increase food restriction may be needed. 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. Males may lose secondary sex
 characteristics.
- Other: According to the manufacturer, Zoetis, Improvest may cause mild, transient injection-site inflammation. All adverse events should be reported to the AZA Reproductive Management Center and to Zoetis, if requested.

Improvest-Related Cautions

• Improvest may not be reversible after long-term use.

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

Reporting requirements: Any use of Suprelorin implants or MGA feed 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.