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Greater & Lesser Apes

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) Birth control pills (combination and progestin-only) Depo-Provera[®] injections (progestin) Suprelorin[®] implants (GnRH agonist) Lupron[®] injections (GnRH agonist)

THE CURRENT OPTIONS FOR MALES INCLUDE:

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

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> <u>Page</u>).
- 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 late pregnancy because of the possibility of prolonged gestation, 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.

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 <u>Depo-Provera Product Page</u>.
- 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.

Birth Control Pills (Progestin-Only and Combination Estrogen + Progestin)

- Duration of efficacy: Not much more than 1 day, so full dose must be consumed daily in order to be effective; ovulation and conception may occur after missing one progestin-only pill or one or more combination pill following the placebo week. Pills may be crushed and mixed into food or drink to help ensure compliance.
- Route of administration: Given orally.
- Latency to effectiveness: 1-2 weeks.
- Dosing: The dose for apes is one pill daily. Lists of birth-control pill options can be found on the <u>Progestin-Only</u> and <u>Combination Birth Control</u> Product Pages.
- Estrous cycles during contraceptive treatment: For progestin-only pills, estrous cycles are unusual but can sometimes occur; for combination pills, signs of estrus can occur during the placebo week.
- Use during pregnancy: Degree of risk to the fetus is uncertain, and manufacturers recommend discontinuation of combination birth control pills during pregnancy.
- Use during lactation: Combination birth control pills may interfere with milk production or affect the developing infant, so are not recommended; use progestin-only pill instead. Combination pills can be substituted when offspring are weaning, since they have greater efficacy.
- Use in seasonal breeders: Start contraception at least 1 month prior to breeding season.

- Reversibility: Predictably reversible; following cessation of combination pill treatment, conception may occur within the first month for some individuals but not for up to a year for others; conception can be sooner following progestin-only pills.
- 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: Weight gain with combination pills is less likely than with progestin-only treatment, but the estrogen component may cause fluid retention.
- Other: Combination pills are available in different dose formulations with various administration regimes.
- **Cautions:** Because combination pills are more effective, switching from progestin-only to combination pills when offspring are weaning is recommended; while the only antibiotic known to decrease birth-control pill efficacy is Rifampin, some anti-fungal medications (e.g. Griseofulvin and Ketoconazole) and anti-seizure drugs may affect birth-control pill efficacy.

Progestin-Related Cautions

- Progestins may result in weight gain.
- Pregnant females contracepted with progestins may experience suppression of uterine contractions; thus, progestin treatment of pregnant females should be stopped by the third trimester.
- 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.
- Chimpanzee sexual swelling: available data show that females exhibit partial to normal swellings on birth-control pills, especially during the placebo week, and partial to no swellings on MGA implants, with differences likely due to relative doses or pill regimen that includes a placebo week.
- Combination birth control pills are NOT recommended during lactation because the estrogen can suppress milk production.
- Reported birth control pill failures are probably due to failure to consume.
- Depo-Provera is associated with weight gain and possible masculinization of females, e.g., in dichromatic species, females may take on aspects of male coloration.

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 <u>contraception@stlzoo.org</u>.
- 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. Both males and females may lose secondary sex characteristics (e.g., sex skin swelling and coloration).
- 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.

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 (Ovaban or Megace) 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 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. Both males and females may lose secondary sex characteristics (e.g., sex skin swelling and coloration).
- 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.

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

(<u>https://www.zoocontraceptiondata.org</u>), 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 (<u>https://www.zoocontraceptiondata.org</u>).

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.