Fact Sheet Compiled by: Monica McDonald Last Updated: May 7, 2024 Fact Sheet Reviewed by: Cheri Asa





Active Ingredient

Melengestrol acetate

Product Type Progestin

Manufacturer

Wedgewood Pharmacy (formerly compounded by ZooPharm)

Product information

MGA (melengestrol acetate) is a synthetic progestin. MGA implants contain 20% melengestrol acetate by weight in a silastic matrix. MGA implants are effective for a minimum of 2 years, so should be replaced at 2-year intervals. However, efficacy can be much longer in some individuals, so if reversal is desired, the implant should be removed.

Safety to humans

There is no health risk to humans when administered as directed.

Dosing

MGA implant dosages can be calculated using the <u>MGA Implant Dosing Table</u>. Multiply the recommended per kg body weight dose by the animal's body weight in kilograms to generate the appropriate implant weight. Wedgewood Pharmacy offers MGA implants in the following sizes: 0.1g, 0.25g, 0.5g, 1.0g, 3.0g, and 6.0g. These sizes will not necessarily coincide with the dose calculated when using the Table above. There are a few possible options to consider when this happens:

- 1. If the calculated gram dose is close to that of one of the sizes above, round up to the next gram size offered.
- 2. If the calculated dose is not close to one of the sizes, the next larger size can be ordered and cut down (under sterile conditions) to approximately the correct dose.
- 3. If the calculated gram dose is not close to that of one the sizes, but it is possible to purchase more than one implant to get to the desired dose, you can place more than one implant.

We understand that there are benefits and drawbacks to the options above. Contact **Monica McDonald** by email at <u>contraception@stlzoo.org</u> or by phone at **314-646-4595** if an implant is needed for a species not listed in the Dosing Table or to discuss dosing options further.

Implant Sizes

MGA Implants are made by molding the silastic matrix in 1cc, 3cc or 6cc syringe barrels. The 1cc mold will be used to make the 0.1g, 0.25g, 0.5g, and 1.0g implants; the 3cc mold will be used to make the 3.0g implant size; and the 6cc mold will be used to make the 6.0g implant.

Ordering

All orders will be processed through Wedgewood Pharmacy, either by calling **866-823-9314** or by ordering online at <u>https://order.wedgewoodpharmacy.com/login</u>. Wedgewood recommends calling in your first order so they can answer any questions that may arise. Please note that if you decide to place your order online, you may need to write multiple prescriptions to combine implant sizes to achieve your desired dose. Please use the SKU and Lot number for recording the MGA implant information for the animal in the RMC Contraception Database.

The cost of the new MGA implants are as follows:

- 0.10g \$70
- 0.25g \$85
- 0.50g \$115
- 1.0g \$225
- 3.0g \$550
- 6.0g \$600

The lead time required to make the MGA implants manufactured by Wedgewood is approximately 6 weeks (42 days) from the "order-by" date. Please visit <u>https://info.wedgewoodpharmacy.com/mga</u> for the batch schedule to ensure that you meet the necessary ordering deadlines.

PLEASE NOTE: Unfortunately, due to state regulations, Wedgewood is unable to ship MGA Implants to Missouri and California at this time. They expect to be able to ship to those states in the future and will notify the RMC when that occurs.

Storage

The implant should be stored at a controlled room temperature (68° to 77°F) and left inside its sterile pouch until you are ready to place the implant. Implants are labeled with a "Beyond-Use-Date" (BUD), the date beyond which a compounded medication should no longer be used. **The BUD for these implants is currently 45 days from the time the implant is produced**. Wedgewood will continue to invest in the additional sterility and stability testing required by USP to extend the BUD of the MGA implants in the future. They will update you (and the RMC) when they can offer a longer BUD. As it is now, though, it is estimated that the implant will be produced approximately 10 days after the "order-by" date. Wedgewood offers **FREE overnight shipping of implants**. This means the institution will have an estimated **12 days after receipt to place the implant by the BUD**.

Sterilization

MGA implants now come **pre-sterilized through a gamma irradiation process**, eliminating the prep time, inconvenience, and cost incurred applying ethylene oxide sterilization protocols. MGA implants should be inserted using sterile surgical technique.

If, however, if there is a need to re-sterilize an implant for any reason, it is recommended that implants be gas-sterilized with ethylene oxide (EO) followed by de-gassing at room temperature for a minimum of 2 weeks prior to use. Because the implants are porous, they must be de-gassed longer than metal instruments. Inadequate de-gassing may result in residual gas that may evoke a tissue reaction. An alternative is the low temperature hydrogen peroxide gas sterilization (STERRAD). A lab test found no difference in MGA release rates after implant sterilization with the STERRAD system, but long-term efficacy of these implants has not yet been evaluated. If neither of these options are available, the implant may be rinsed with alcohol and dried with sterile gauze prior to placement. Do not soak in alcohol, which will leach the MGA steroid hormone from the implant. Sterilization with a cold-soak solution is not recommended, because the chemicals can be absorbed and/or, as will alcohol, MGA may be leached from the implant. Because heat may change the structure of the MGA and of the silastic matrix, implants should not be autoclaved.

Insertion/Administration

Implants should be inserted through a small incision between the scapulae intra-muscularly (IM) if possible, but, if subcutaneous (SQ) is necessary, place implant in a "tunnel" created by blunt dissection of fascia away from the incision. Migration may be controlled by suturing the implant in place at the time of insertion.

Implant loss can be reduced by separating the animal from conspecifics during the period of healing. (NOTE: in some primate taxa, stainless steel sutures placed away from the implant site have been successful in diverting grooming attention and preventing over-grooming and implant removal by conspecifics, thereby avoiding the need to separate animals). The implant's presence and location should be confirmed whenever the animal is handled.

Implant Placement and/or Removal Tips

Identification transponder microchips inserted in MGA implants can be used to confirm presence and location. Implants cannot be supplied with transponders already in place. Using sterile procedure, puncture implant longitudinally with needle containing transponder chip (it comes sterile) and insert into implant as you would under the skin. Insert implant into animal using standard surgical technique as outlined above. Alternatively, stainless steel suture or orthopedic wires/pins or comparable material may be incorporated into the implant prior to sterilization to make it visible on radiographs. For cases needing more than a single implant for a single animal, connecting the implants together will facilitate later removal. Using stainless steel suture to string them together will also make them visible on X-ray. As with single implants, they can be sutured in place to prevent migration.

Latency to effectiveness

Although individuals vary, threshold levels of the hormone should be reached in the blood within 1 to 3 days following IM insertion and within 1 week after SQ insertion. However, pre-ovulatory follicles are difficult to suppress, so, if cycle stage is not known, extra time must be allowed. Therefore, separation or alternative contraception should be used for at least 1 week (if IM) or 2 weeks (if SQ) following insertion.

Signs of estrus during treatment

Synthetic progestins may achieve contraception by blocking ovulation, causing thickening of cervical mucus, slowing ovum transport, and/or interfering with fertilization or implantation. However, follicle growth may continue and sometimes be accompanied by estrogen production sufficient to cause estrous behavior. Ovulation may occur even though pregnancy does not ensue. Higher progestin doses may be preferred so that estrous behavior is prevented, but may not be effective in completely suppressing follicle growth and all estrogen production.

Duration of efficacy and reversibility

MGA Implants are effective for at least 2 years, but in most individuals, reproduction will be suppressed much longer. In some cases, they were effective for as much as 5 years when left in place. This means that implants should be replaced every 2 years to ensure contraception, but should be removed when pregnancy is desired. For this reason too, old implants should be removed when a new one is placed to avoid administering a higher than intended dose. Once the implant is removed, the circulating MGA clears very rapidly, so that ovulation and conception may occur within days, although actual latency is usually longer and will depend on the individual.

Use during pregnancy

Progestins are not recommended in late pregnancy because of the possibility of prolonged gestation, although the effect may depend on species and dose.

Use during lactation

Progestins are sometimes prescribed for lactating women and are considered generally safe for nursing infants.

Use in pre-pubertal animals

Lack of data on pre-pubertal treatment and potential long-term effects on fertility contraindicates recommending contraception before puberty. 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.

Precautions

Progestins may cause weight gain in all species. Possible deleterious effects on uterine and mammary tissues vary greatly by species; see cautions for each taxon.

Consideration for seasonal breeders

Treatment should begin at least 1 month before the anticipated onset of the breeding season. However, in canids, treatment should begin more than 2 months before the time of anticipated estrus, because proestrus increases in estradiol can begin as much as 2 months before estrus, and it is known that this endogenous estradiol can exacerbate deleterious effects of progestins on the uterus and mammary glands. This synergy of estradiol and progestins may also occur in other carnivores, such as mustelids and ursids.

Contraception must continue for the full breeding season, which may be longer than anticipated for females that are not conceiving.

Reporting Requirements

All institutions using this product are asked to contribute contraception information for their animals to the AZA Reproductive Management Center's Contraception Database (<u>https://www.zoocontraceptiondata.org</u>). It is essential that accurate records of doses and treatment intervals be maintained, and results reported, to contribute to dosage development.

NOTE: Part of the RMC's mission is to provide the AZA community with optimal contraception advice. Since these are new implants, and institutions will need to come up with creative solutions to deal with differences between the pre-2024 versus post-2024 MGA implants, we highly encourage our database users to add specifics to our contraception database via the "Add/Edit Comment" box about how you reached your desired dose. This feedback will be critical for us in providing optimal contraceptive advice in the future.

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 <u>franklin@stlzoo.org</u>