Zeuterin: The Non-Surgical Alternative to Neutering

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Introduction

Zeuterin™ is a non-surgical sterilant for male dogs delivered via intratesticular injection. The active ingredient is zinc gluconate neutralized with arginine. The formulation causes permanent sterility in one treatment. The process of neutering with Zeuterin is also known as "zinc neutering."

History

This formulation of the chemical compound of zinc gluconate neutralized with arginine was developed to chemically sterilize male dogs. The formulation was initially developed by Pet Healthcare International; it received approval from the United States Food & Drug Administration (FDA) in 2003 and was distributed in the U.S. under the name Neutersol® until early 2005. Ark Sciences, Inc., subsequently acquired rights to the technology and registered it under the name EsterilSol™ in Mexico, Colombia, Bolivia, Panama, and Turkey. On February 17, 2014, Ark Sciences launched Zeuterin™ in the United States. It is presently approved for male dogs between three and ten months of age in the U.S., and for male dogs over three months of age in the other countries. Ark Sciences is currently working to modify the label in the US to include male dogs three months and older.

Mechanism of Action

The exact mechanism of action of Zeuterin is not known. The product is administered as an intratesticular injection into the center of the testicle via the dorsal cranial portion of testicle, parallel to the longitudinal axis. After injection, the compound diffuses in all directions from the center of the testis. In the concentration used, zinc gluconate acts as a spermicide and destroys spermatozoa in all stages of development and maturation. Zinc gluconate is absorbed and metabolized by the body within 72 hours after the injection. As the dog's body increases blood flow and creates inflammation to heal, it results in permanent and irreversible fibrosis in the seminiferous tubules, rete testis, and epididymis. This process results in permanent sterilization, and the endocrine feedback system remains intact. Following injection, the testicles atrophy over a period of time ranging from weeks to months, resulting in a reduction in testicular size and changes in shape or texture. These changes may or may not be symmetrical.

Use and Effectiveness

Injection technique is critical to preventing adverse reactions. Because of this, Ark Sciences requires veterinarians to be certified in its administration. Zeuterin is administered via an injection to each testicle with either a 28 gauge, ¾-inch or a 30 gauge, ½-inch needle, depending on testicle size. Dosage is determined by measuring each testicle with a caliper provided by Ark Sciences. The correct dose is indicated on the caliper and is based on the maximum width of each testicle. Zeuterin is labeled for use in dogs with an individual testicular width of 10.0 to 27.0 mm, although the product has been used in dogs with testicular widths of up to 31.0 mm.

Anesthesia is not necessary for the zinc neutering procedure. Ark Sciences recommends light sedation to ensure that the dog holds still during the injection; reversible sedation is commonly used so that dogs are awake and alert in as little as 15-20 minutes after the injection.

Concerns about possible pain of an intratesticular injection are not uncommonly expressed by pet owners or by practitioners who are not experienced with this technology. In studies reviewed and accepted by the FDA (in which 76% of dogs were not sedated), only 2.5% of dogs showed discomfort by moving or vocalizing. The other 97.5% did not show any reaction to the injection. Scrotal pain was the most common local reaction observed in the FDA-reviewed study, reported in 6.3% of dogs. To prevent discomfort caused by post-injection swelling, Ark Sciences recommends concurrent use of a nonsteroidal anti-inflammatory drug (NSAID).

Testosterone, Behavior, and Health

One study submitted for FDA approval measured the effect of Zeuterin on male beagles (aged 6 months at the start of the study) in a clinical setting. At two years post-treatment, mean serum testosterone levels for dogs who received varying quantities of zinc gluconate neutralized with arginine were between 41.0 and 52.0% lower than mean serum testosterone levels of dogs in the control group.

The effect of maintaining higher levels of testosterone on hormone-dependent behaviors and diseases has not been established. Some persons seek behavioral changes commonly associated with surgical castration, and thus view a lesser impact on testosterone production as a drawback. Other pet owners cite health and behavior benefits from retaining some level of circulating testosterone. In short, although more is known about the non-reproductive (behavior and health) effects of surgical castration than sterilization with Zeuterin, further study on both methods is merited.

Expected Reactions and Complications

Proper injection technique is critical to prevent adverse reactions. Normal reactions include:

Generally non-painful swelling for 24-48 hours
Listlessness for the first 24 hours
May or may not vomit during the first 24 hours
Should return to normalcy within 24 hours

According to Ark Sciences, only 1.1% of the 270 dogs in FDA Clinical Trial needed any follow up medical attention. The most common complications, and their recommended treatment, include:

Scrotal Irritation: Apply anti-inflammatory/antibiotic ointment, possible E-collar, 2-3 days
Scrotal Ulceration: Antibiotics, Saline soaks, E-collar, 1-2 weeks
Testicle abscess/infection: Antibiotics, E-collar, 1-2 weeks
Scrotal ablation may be necessary in the event of severe ulceration

Conclusions

Zeuterin is a safe, effective method for sterilizing male dogs without surgery. Though sedation is recommended and administration protocol requires precision and care, this method may offer savings in cost, time, and facility requirements, thus helping animal welfare organizations sterilize more animals and/or redirect resources to other lifesaving projects. It also presents an option for pet owners who would prefer to sterilize their dog without surgery, or whose pets cannot safely undergo anesthesia.

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