REGUMATE- altrenogest solution
Merck Sharp & Dohme Corp.

Regu-Mate® (altrenogest)

2.2 mg altrenogest per mL (0.22%)

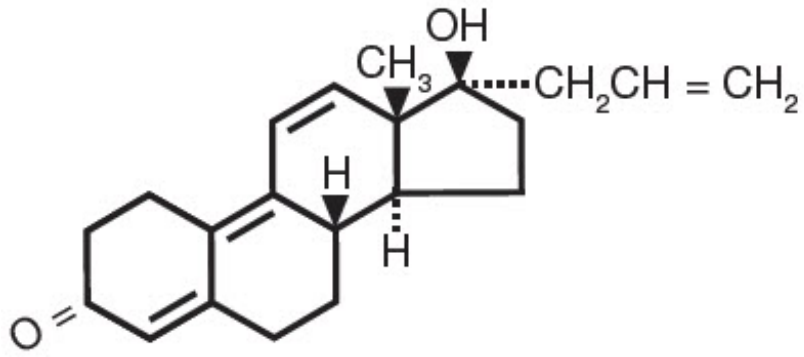
Oral Solution for Horses

CAUTION:

Federal law restricts this drug to use by or on the order of a licensed veterinarian.

DESCRIPTION:

Regu-Mate® (altrenogest) contains the active synthetic progestin, altrenogest. The chemical name is 17a-allyl-17b-hydroxyestra-4,9,11-trien-3-one. The CAS Registry Number is 850-52-2. The chemical structure is:



Each mL of Regu-Mate® (altrenogest) contains 2.2 mg of altrenogest in an oil solution.

Regu-Mate® (altrenogest) produces a progestational effect in mares.

INDICATIONS:

For suppression of estrus in mares. Suppression of estrus allows for a predictable occurrence of estrus following drug withdrawal. This facilitates the attainment of regular cyclicity during the transition from winter anestrus to the physiological breeding season. Suppression of estrus will also facilitate management of prolonged estrus conditions. Suppression of estrus may be used to facilitate scheduled breeding during the physiological breeding season.

DOSAGE AND ADMINISTRATION:

Administer solution orally at the rate of 1 mL per 110 pounds body weight (0.044 mg/kg) once daily for 15 consecutive days. Administer solution directly on the base of the mare's tongue or on the mare's usual grain ration.

Dosage Chart

Approximate Weight	Dose in

(Pounds)	mL
770	7
880	8
990	9
1100	10
1210	11
1320	12

When handling Regu-Mate® product, the dosing device, or syringes, **always use vinyl, neoprene, or nitrile gloves. Latex gloves are not protective.** The product may be dosed using Regu-Mate® Equine Dosing Device or a luer lock syringe. Use of the Regu-Mate® Equine Dosing Device is recommended to reduce the risk of human exposure. Follow all instructions when using the dosing device. **Do not use any dosing device other than the Regu-Mate® Equine Dosing Device.**

For use with Regu-Mate® Equine Dosing Device, first assemble the device according to directions supplied with the Regu-Mate Equine Dosing Device. Remove the shipping cap and seal on Regu-Mate (altrenogest) bottle. Store the cap in a clean and dry location. Apply downward force and fasten the quick connect cap with dip tube onto the product bottle. The flexible dip tube will contact the bottom of the product bottle and bend slightly. Turn the dose selection dial to 15. Hold the dosing device vertically with the nozzle on the top. Direct the opening of the nozzle away from any person and cover it with absorbent material. Slowly squeeze and release handle until air in the barrel is expelled and product starts to come out. Prime the device by expelling two (2) doses of 15 mL of product into a waste container or absorbent material. (Re-prime the dosing device by expelling two (2) doses if air is observed inside the barrel after switching to a fresh bottle or during dosing period). Set the dose according to DOSAGE CHART provided herein by turning the dose selection dial. The dosing device is ready for use. Refer to the Regu-Mate® Equine Dosing Device label for equipment cleaning instructions.

For use with a luer lock syringe, remove shipping cap and seal; replace with enclosed plastic dispensing cap. Remove cover from bottle dispensing tip and connect luer lock syringe (without needle). Draw out appropriate volume of Regu-Mate® solution and return bottle to upright position before detaching syringe. (Note: Do not remove syringe while bottle is inverted as spillage may result.) Replace cover on bottle dispensing tip to prevent leakage. Syringes used for administration should be replaced frequently and disposed of in a secure manner to prevent exposure to the product.

Which mares will respond to Regu-Mate® (altrenogest):

Extensive clinical trials have demonstrated that estrus will be suppressed in approximately 95% of the mares within three days; however, the post-treatment response depended on the level of ovarian activity when treatment was initiated. Estrus in mares exhibiting regular estrus cycles during the breeding season will be suppressed during treatment; these mares return to estrus four to five days following treatment and continue to cycle normally. Mares in winter anestrus with small follicles continued in anestrus and failed to exhibit normal estrus following withdrawal.

Response in mares in the transition phase between winter anestrus and the summer breeding season depended on the degree of follicular activity. Mares with inactive ovaries and small follicles failed to respond with normal cycles post-treatment, whereas a higher

proportion of mares with ovarian follicles 20 mm or greater in diameter exhibited normal estrus cycles post-treatment. Regu-Mate® (altrenogest) was very effective for suppressing the prolonged estrus behavior frequently observed in mares during the transition period (February, March, and April). In addition, a high proportion of these mares responded with regular estrus cycles post-treatment.

Specific Uses for Regu-Mate®:

1. Suppression of estrus to facilitate attainment of regular cycles during the transition period from winter anestrus to the physiological breeding season. To facilitate attainment of regular cycles during the transition phase, mares should be examined to determine the degree of ovarian activity. Estrus in mares with inactive ovaries (no follicles greater than 20 mm in diameter) will be suppressed, but these mares may not begin regular cycles following treatment. However, mares with active ovaries (follicles greater than 20 mm in diameter) frequently respond with regular post-treatment estrus cycles.
2. Suppression of estrus to facilitate management of the mare exhibiting prolonged estrus during the transition period. Estrus will be suppressed in mares exhibiting prolonged behavioral estrus either early or late during the transition period. Again, the post-treatment response depends on the level of ovarian activity. The mares with greater ovarian activity initiate regular cycles and conceive sooner than the inactive mares. Regu-Mate® (altrenogest) may be administered early in the transition period to suppress estrus in mares with inactive ovaries to aid in the management of these mares or to mares later in the transition period with active ovaries to prepare and schedule the mare, for breeding.
3. Suppression of estrus to permit scheduled breeding of mares during the physiological breeding season. To permit scheduled breeding, mares which are regularly cycling or which have active ovarian function should be given Regu-Mate® (altrenogest) daily for 15 consecutive days beginning 20 days before the date of the planned estrus. Ovulation will occur 5 to 7 days following the onset of estrus as expected for non-treated mares. Breeding should follow usual procedures for mares in estrus. Mares may be regulated and scheduled either individually or in groups.

CONTRAINDICATIONS:

Do not use Regu-Mate® (altrenogest) in mares having a previous or current history of uterine inflammation (e.g., acute, subacute, or chronic endometritis). Natural or synthetic gestagen therapy may exacerbate existing low-grade or "smoldering" uterine inflammation into a fulminating uterine infection in some instances.

WARNINGS AND PRECAUTIONS:

User Safety Warnings:

Not for use in humans. Keep out of reach of children. Avoid skin contact. Regu-Mate® is absorbed through unbroken skin, and exposure may result in serious side effects to both women and men. **Wear vinyl, neoprene, or nitrile gloves when handling or administering Regu-Mate®, or when touching contaminated surfaces or equipment. Latex gloves are not protective.**

PREGNANT WOMEN OR WOMEN WHO MAY BE PREGNANT SHOULD NOT HANDLE REGU-MATE®. WOMEN OF CHILDBEARING AGE SHOULD EXERCISE EXTREME CAUTION WHEN HANDLING THIS PRODUCT.

Accidental absorption, such as via direct contact with the skin, could lead to a disruption of the menstrual cycle or prolongation of pregnancy. Immediately wash off accidental spillage on the skin with soap and water. Any equipment or surfaces that come in contact with Regu-Mate® should be adequately cleaned and decontaminated to prevent human exposure (see *Reported HUMAN Effects from Exposure*).

Potential Effects of Human Exposure

There has been no human use of this specific product. The information contained in this section is extrapolated from data available on other products of the same pharmacological class that have been used in humans. Effects anticipated are due to the progestational activity of altrenogest.

Acute effects after a single exposure are possible; however, continued daily exposure has the potential for more untoward effects such as disruption of the menstrual cycle, uterine or abdominal cramping, increased or decreased uterine bleeding, prolongation of pregnancy, and headaches. The oil base may also cause complications if swallowed.

The list of people who should not handle this product (see below) is based upon the known effects of progestins used in humans on a chronic basis.

PEOPLE WHO SHOULD NOT HANDLE REGU-MATE®:

1. Women who are or may be pregnant.
2. Anyone with blood clots or clotting disorders, or with a history of these events.
3. Anyone with a history of heart disease or stroke.
4. Women with known or suspected breast cancer.
5. People with known or suspected estrogen-dependent cancer.
6. Women with vaginal bleeding of unknown cause.
7. People with tumors which developed during the use of oral contraceptives or other estrogen-containing products.
8. Anyone with liver dysfunction or disease.

ACCIDENTAL EXPOSURE:

Regu-Mate® is readily absorbed through the skin. In addition, this oil-based product can penetrate latex or other types of porous gloves. **Always wear vinyl, neoprene, or nitrile gloves when handling Regu-Mate®. Latex gloves are not protective.** If Regu-Mate® gets inside gloves by damage or spilling, the covered skin may absorb more of the drug.

IN CASE OF ACCIDENTAL EXPOSURE:

Skin Exposure and/or clothing contamination: Wash skin immediately with soap and water, and launder clothing with detergent.

Eye Exposure: Immediately flush with plenty of water for 15 minutes. Get medical attention. If wearing contact lenses, flush eyes immediately with water before removing lenses.

If Swallowed: Do not induce vomiting. Seek medical attention immediately. Regu-Mate® contains an oil. Vomiting should be supervised by a physician because of possible pulmonary damage via aspiration of the oil base. If possible, bring the labeling to the physician.

Reported HUMAN Effects from Exposure:

These symptoms have been reported in women and men following accidental exposure to altrenogest products, including Regu-Mate®, either through handling of the product or contact with contaminated surfaces:

- Adverse reproductive effects reported in women included abnormal or absent menstrual cycles.
- Adverse reproductive effects reported in men included decreased libido.
- Other adverse effects reported in women and men included headaches, fever, abdominal pain, nausea, diarrhea, vomiting, and rashes.

ANIMAL SAFETY WARNINGS AND PRECAUTIONS:

Keep Regu-Mate® in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Various synthetic progestins, including altrenogest, when administered to rats during the embryogenic stage of pregnancy at doses manyfold greater than the recommended equine dose, caused fetal anomalies, specifically masculinization of the female genitalia.

OTHER WARNINGS:

Do not use in horses intended for human consumption.

CONTACT INFORMATION:

- To report suspected adverse events, contact Merck at 1-866-349-3497, or www.merck-animal-health-usa.com
- To obtain product information, including safety data sheet (SDS), call 1-800-441-8272.
- For additional information about reporting adverse drug experiences for animal drugs, contact FDA at 1-888-FDA-VETS or www.fda.gov/reportanimalae

REPRODUCTIVE SAFETY STUDY:

A 3-year well-controlled reproductive safety study was conducted in 27 pregnant mares, and compared with 24 untreated control mares. Treated mares received 2 mL Regu-Mate® (altrenogest) /110 lb body weight (2 x dosage recommended for estrus suppression) from day 20 to day 325 of gestation. This study provided the following data:

1. In filly offspring (all ages) of treated mares, clitoral size was increased.
2. Filly offspring from treated mares had shorter interval from Feb. 1 to first ovulation than fillies from their untreated mare counterparts.
3. There were no significant differences in reproductive performance between treated and untreated animals (mares & their respective offspring) measuring the following parameters:
    - interval from Feb. 1 to first ovulation, in mares only.
    - mean interovulatory interval from first to second cycle and second to third cycle, mares only.
    - follicle size, mares only.
    - at 50 days gestation, pregnancy rate in treated mares was 81.8% (9/11) and untreated mares was 100% (4/4).
    - after 3 cycles, 11/12 treated mares were pregnant (91.7 %) and 4/4 untreated mares were pregnant (100%).
    - colt offspring of treated and control mares reached puberty at approximately the

same age (82 & 84 weeks respectively).
- stallion offspring from treated and control mares showed no differences in seminal volume, spermatozoal concentration, spermatozoal motility, and total sperm per ejaculate.
- stallion offspring from treated and control mares showed no difference in sexual behavior.
- testicular characteristics (scrotal width, testis weight, parenchymal weight, epididymal weight and height, testicular height, width, & length) were the same between stallion offspring of treated and control mares.

References:

Shoemaker, C.F., E.L. Squires, and R.K. Shideler. 1989. Safety of Altrenogest in Pregnant Mares and on Health and Development of Offspring. Eq. Vet. Sci. (9); No. 2: 69-72.

Squires, E.L., R.K. Shideler, and A.O. McKinnon. 1989. Reproductive Performance of Offspring from Mares Administered Altrenogest During Gestation. Eq. Vet. Sci. (9); No. 2: 73-76.

HOW SUPPLIED:

Regu-Mate® (altrenogest) contains 2.2 mg/mL in an oil solution.

Product supplied in 1,000 mL plastic bottles.

Regu-Mate® Equine Dosing Device supplied separately.

STORAGE, HANDLING, AND DISPOSAL:

Store Regu-Mate® solution bottle and Dosing Device when loaded with solution for continued use at or below room temperature, 77°F (25°C). Close tightly. **Refer to the Regu-Mate ® Equine Dosing Device label for equipment cleaning instructions.** Place empty drug containers, waste from rinsing the Dosing Device, protective gloves, or other articles that contact this product in a leak-resistant container for disposal in accordance with applicable Federal, state, and local regulations.

Approved by FDA under NADA # 131-310

Restricted Drug (California) - use only as directed.

Manufactured for:
Intervet Inc. (d/b/a Merck Animal Health), Madison, NJ 07940

Rev. 10/2022

MERCK
Animal Health

PRINCIPAL DISPLAY PANEL - 1,000 mL Bottle Label

MERCK
Animal Health

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(altrenogest)

Oral Solution for Horses

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Synthetic Progestin

CAUTION: Federal law restricts this drug to use by
or on the order of a licensed veterinarian.

INDICATIONS FOR USE:
For suppression of estrus in mares.

Suppression of estrus allows for a predictable occurrence of estrus following drug withdrawal in mares with ovarian follicles 20 mm or greater. Suppression of estrus will facilitate:

- Attainment of regular cyclicity during the transition from winter anestrus to the physiological breeding season.
- Management of prolonged estrus conditions.
- Scheduled breeding during the physiological breeding season.

Net Contents 1,000 mL

Approved by FDA under NADA # 131-310

MERCK Animal Health

Regu-Mate®

(altrenogest)

Oral Solution for Horses

2.2 mg altrenogest per mL (0.22%)
Synthetic Progestin

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Net Contents 1,000 mL

Approved by FDA under NADA # 131-310

MERCK Animal Health

Regu-Mate®

(altrenogest)

Before using this drug, read package insert for full prescribing information.

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Manufactured for: Intervet Inc.
(d/b/a Merck Animal Health),
Madison, NJ 07940
Made in France.

MERCK Animal Health

0 21784 42247 5

354664 R10

Lot number

expiration date:

Imprint area

REGUMATE
altrenogest solution

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:57926-100
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
ALTRENOGEST (UNII: 2U0X0JA2NB) (ALTRENOGEST - UNII:2U0X0JA2NB)	ALTRENOGEST	2.2 mg in 1 mL

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:57926-100-70	1000 mL in 1 BOTTLE		

Marketing Information			
Marketing Category	**Application Number or Monograph Citation**	**Marketing Start Date**	**Marketing End Date**
NADA	NADA131310	09/12/1983	

Labeler - Merck Sharp & Dohme Corp. (001317601)

Revised: 10/2024 Merck Sharp & Dohme Corp.