

Date of Approval: DEC 3 2004

## FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-343

HEIFERMAX 500  
(melengestrol acetate)  
Liquid Premix

Type A Medicated Article

For Increased Rate of Weight Gain, Improved Feed Efficiency and  
Suppression of Estrus in Heifers

Sponsored by:  
Ivy Laboratories,  
Division of Ivy Animal Health, Inc.

## FREEDOM OF INFORMATION SUMMARY

### 1. GENERAL INFORMATION:

- a. File Number: ANADA 200-343
- b. Sponsor: Ivy Laboratories,  
Div. of Ivy Animal Health, Inc.  
8857 Bond Street  
Overland Park, KS 66214
- Drug Labeler Code: 021641
- c. Established Name: Melengestrol acetate
- d. Proprietary Name: HEIFERMAX 500 Liquid Premix
- e. Dosage Form: Type A Medicated Article
- f. How Supplied: 40 pound (18 kg) (4.627 gal [17.5 L]) containers
- g. How Dispensed: OTC
- h. Amount of Active Ingredients: 500 mg melengestrol acetate per pound
- i. Route of Administration: Oral
- j. Species/Class: Cattle/Heifers
- k. Recommended Dosage: **Heifers Fed in Confinement for Slaughter:**  
HEIFERMAX 500 Liquid Premix should be thoroughly mixed in liquid Type C medicated feed which must be fed at 0.5 to 2.0 pounds per head daily to provide 0.25 to 0.5 mg of melengestrol acetate per head per day. Average daily intakes approximating the middle of this range provide the most optimal and economical improvements in rate of weight gain and feed utilization. Constant daily intakes of 0.35 to 0.50 mg per head per day give a high degree of estrus suppression. Levels of 0.25 to 0.35 mg provided a lower but still effective degree of estrus suppression.

Withdrawal periods of three to five days or more should be avoided to prevent the possibility that the heifers may come into estrus (heat) at loading time.

**Heifers Intended for Breeding:**

HEIFERMAX 500 Liquid Premix should be thoroughly mixed in the supplement to provide 0.50 mg of melengestrol acetate per head per day.

Do not exceed 24 days of feeding of melengestrol acetate to heifers intended for breeding. A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

- l. Pharmacological Category: Hormone
- m. Indications: Heifers Fed in Confinement for Slaughter: For increased rate of weight gain, improved feed efficiency and suppression of estrus (Heat). Heifers Intended for Breeding: For suppression of estrus (Heat).
- n. Pioneer Product: MGA 500; melengestrol acetate; NADA 039-402; Pharmacia & Upjohn Co.

**2. TARGET ANIMAL SAFETY AND DRUG EFFECTIVENESS:**

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act (GADPTRA) of 1988, an Abbreviated New Animal Drug Application (ANADA) may be submitted for a generic version of an approved new animal drug (pioneer product). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor shows the generic product is bioequivalent to the pioneer, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guidance, revised October 9, 2002).

Based on the formulation characteristics of the generic product, Ivy Laboratories, Div. of Ivy Animal Health, Inc. was granted a waiver from the requirement of an *in vivo* bioequivalence study for HEIFERMAX 500 (melengestrol acetate) Liquid Premix. The generic product is marketed as a Type A Medicated Article, contains the same active ingredient in the same concentration and dosage form as the pioneer product, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient. The pioneer product MGA 500

(melengestrol acetate), the subject of Pharmacia & Upjohn Co. NADA 039-402, was approved on May 22, 1968.

### 3. **HUMAN SAFETY:**

- **Tolerances for Residues:**

The tolerances established for the pioneer product apply to the generic product. A tolerance of 25 parts per billion is established for residues of the parent compound, melengestrol acetate, in fat of cattle under 21 CFR 556.380.

- **Withdrawal Times:**

Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

A withdrawal time is not required for the use of melengestrol acetate in heifers.

- **Regulatory Method for Residues:**

The analytical method for the determination of melengestrol acetate in tissues uses a gas chromatographic assay procedure. This method is found in *Official Methods of Analysis of AOAC International*, 16th edition.

### 4. **AGENCY CONCLUSIONS:**

This ANADA filed under section 512(b) of the Federal Food, Drug, and Cosmetic Act satisfies the requirements of section 512(n) of the Act and demonstrates that HEIFERMAX 500 Liquid Premix, when used under its proposed conditions of use, is safe and effective for its labeled indications.

### 5. **ATTACHMENTS:**

Facsimile generic labeling and currently approved pioneer labeling are attached as indicated below:

Generic Labeling for ANADA 200-343:

HEIFERMAX 500 (melengestrol acetate) Liquid Premix

1 – Type A Medicated Article container label (front and back); 1 – Type C Medicated Feed blue bird label

Pioneer Labeling for NADA 039-402:

MGA 500 (melengestrol acetate) Liquid Premix

1 – Type A Medicated Article container label (onsert); 1 – Type C Medicated Feed blue bird label

Liquid Premix

# Heifermax<sup>TM</sup> 500

Melengestrol Acetate

*Liquid Premix*  
**(Type A Medicated Article)**

**HEIFERS FED IN CONFINEMENT FOR SLAUGHTER:**

**For Increased Rate of Weight Gain, Improved Feed Efficiency, and Suppression of Estrus (Heat).**

**HEIFERS INTENDED FOR BREEDING:**

**For Suppression of Estrus (Heat).**

---

**Each Pound Contains:**

**Active Drug Ingredient:**

Melengestrol Acetate ..... 500 mg  
(as melengestrol acetate and its propylene glycol ketal)

**Inactive Ingredient:**

Propylene Glycol, U.S.P. .... 99.89%

**Caution:** For manufacturing, processing, or repacking. To be mixed with feed prior to animal use. Use only as directed. Excessive contact with skin should be avoided. Destroy empty container. Do not reuse.

**Store at room temperature**

ANADA 200-343, Approved by FDA

Ivy Animal Health, Inc. • Overland Park, KS 66214, USA

01 30 16 00

**Net Weight 40 Pounds (18 kg) (4.627 gal [17.5 L])**



6 13562 03108 7

# Heifermax<sup>TM</sup> 500

Melengestrol Acetate

## Liquid Premix (Type A Medicated Article)

**Heifers Fed in Confinement for Slaughter: For Increased Rate of Weight Gain, Improved Feed Efficiency, and Suppression of Estrus (Heat).**

**Heifers Intended for Breeding: For Suppression of Estrus (Heat).**

### Directions for Use:

#### Heifers Fed in Confinement for Slaughter:

HEIFERMAX<sup>TM</sup> 500 Liquid Premix (Type A Medicated Article) should be thoroughly mixed in liquid Type C medicated feed which must be fed at 0.5 to 2.0 pounds per head daily to provide 0.25 to 0.5 mg of melengestrol acetate per head per day. Average daily intakes approximating the middle of this range provide the most optimal and economical improvements in rate of weight gain and feed utilization. Constant daily intakes of 0.35 to 0.50 mg per head per day give a high degree of estrus suppression. Levels of 0.25 to 0.35 mg provide a lower but still effective degree of estrus suppression.

#### Heifers Intended for Breeding:

HEIFERMAX 500 Liquid Premix (Type A Medicated Article) should be thoroughly mixed in the supplement to provide 0.5 mg of melengestrol acetate per head per day.

**Not for human use. Restricted Drug — Use only as Directed (California)  
CAUTION: Not effective in steers or spayed heifers.**

#### Heifers Fed in Confinement for Slaughter:

Withdrawal periods of three to five days or more should be avoided to prevent the possibility that the heifers may come into estrus (heat) at loading time.

#### Heifers Intended for Breeding:

Do not exceed 24 days of feeding of melengestrol acetate to heifers intended for breeding. A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

#### Mixing Directions:

Liquid Type B and C medicated feeds containing melengestrol acetate must have a pH of 4.0 to 8.0 and their labels must bear appropriate mixing directions. Mixing directions for liquid Type B or C feeds stored in recirculation tank systems are: "Recirculate immediately prior to use for no less than 10 minutes, moving not less than 1 percent of the tank contents from the bottom of the tank to the top. Recirculate daily, as directed in this paragraph even when the Type B (or C) feed is not used." Mixing directions for liquid Type B and C feeds stored in mechanical, air or other agitation-type tank systems are: "Agitate immediately prior to use for not less than 10 minutes, creating a turbulence at the bottom of the tank that is visible at the top. Agitate daily, as directed in this paragraph, even when the Type B (or C) feed is not used."

Intermediate premixes should not be made from HEIFERMAX 500 Liquid Premix (Type A Medicated Article) except as a part of a continuous mixing operation to make a complete liquid Type B or C medicated feed.

Thoroughly mix 0.5 to 4 pounds of HEIFERMAX 500 Liquid Premix (Type A Medicated Article) per ton of a non-medicated feed to prepare a Type C medicated feed containing 0.25 to 2.0 grams of melengestrol acetate per ton. The following table may be used as a guide in determining the amount of HEIFERMAX 500 Liquid Premix (Type A Medicated Article) to be added to prepare a ton of Type C medicated feed.

Amount of Type C Feed Fed (lb/head/day)	Melengestrol Acetate (mg/head/day)	HEIFERMAX 500 Liquid Premix Per Ton of Type C Feed	
		When Added by Weight (lb)	When Added by Volume (mL)
0.5	0.25	2.00	876
0.5	0.30	2.40	1051
0.5	0.35	2.80	1226
0.5	0.40	3.20	1402
0.5	0.45	3.60	1577
0.5	0.50	4.00	1752
1.0	0.25	1.00	438
1.0	0.30	1.20	526
1.0	0.35	1.40	613
1.0	0.40	1.60	701
1.0	0.45	1.80	788
1.0	0.50	2.00	876
1.5	0.25	0.66	289
1.5	0.30	0.80	350
1.5	0.35	0.93	407
1.5	0.40	1.07	469
1.5	0.45	1.20	526
1.5	0.50	1.33	582
2.0	0.25	0.50	219
2.0	0.30	0.60	263
2.0	0.35	0.70	307
2.0	0.40	0.80	350
2.0	0.45	0.90	394
2.0	0.50	1.00	438

Type B medicated feed containing 4 to 10 grams melengestrol acetate per ton may be manufactured by thoroughly mixing 8 to 20 lbs of HEIFERMAX 500 Liquid Premix with 1992 to 1980 lbs of non-medicated feed. Labeling for such Type B feed shall contain directions for manufacturing Type C medicated feeds containing 0.25 to 2.0 grams melengestrol acetate per ton (0.125 to 1.0 mg/lb). The Type C medicated feed, containing melengestrol acetate, must be top dressed on grain or roughage or mixed with a complete ration at the rate of 0.5 to 2.0 pounds per head per day.

Good manufacturing practice regulations must be adhered to in manufacturing feeds containing HEIFERMAX 500.

Ivy Animal Health, Inc. • Overland Park, KS 66214, USA

Heifermax and VetLife® are trademarks of Ivy Animal Health, Inc.



**BULK ONLY**  
**LIQUID HEIFER SUPPLEMENT**  
 Medicated  
 (Type C Medicated Feed)

**INDICATIONS**

Heifers Fed in Confinement for Slaughter: For Increased Rate of Weight Gain, Improved Feed Efficiency and Suppression of Estrus (Heat).

Heifers Intended for Reproduction: For Suppression of Estrus (Heat).

**ACTIVE DRUG INGREDIENTS**

Melengestrol acetate (0.0000276-0.00022%)  
 Each pound contains (0.125-1.0) mg melengestrol acetate.

**GUARANTEED ANALYSIS**

Crude Protein, not less than	_____ %
Crude Fat, not less than	_____ %
Crude Fiber, not more than	_____ %

**INGREDIENTS**

Each ingredient will be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions adopted by the AAFCO. Include also ingredients of the trace mineral and vitamin premixes. Collective terms may be used in accordance with 21 CFR § 501.110.

**DIRECTIONS FOR USE**

Must be top dressed on grain or silage or mixed with a complete ration.

Heifers Fed in Confinement for Slaughter: Feed at the rate of 0.5-2.0 pound(s) per head per day (specify one level) to provide 0.25-0.5 mg melengestrol acetate per head per day (specify one level). Continue feeding throughout the time the heifers are being grown and finished for slaughter.

Heifers Intended for Reproduction: Feed at the rate of 0.5-2.0 pound(s) per head per day (specify one level) to provide 0.5 mg melengestrol acetate per head per day.

**AGITATE OR RECIRCULATE THOROUGHLY BEFORE USING TO INSURE PROPER MIXING OF THE INGREDIENTS**

**IMPORTANT:** Not effective in steers and spayed heifers.

**CAUTION:** Heifers Fed in Confinement for Slaughter: Withdrawal periods of three to five days should be avoided to prevent the possibility that the heifers may come into estrus (heat) at the time of loading.

Heifers Intended for Reproduction:  
 Do not exceed 24 days of feeding.

A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

**MANUFACTURED BY**  
**Blue Bird Feed Company**  
 Robin, Indiana 11111

**EXP:**

**July 2002**

NDC 0009-0547-01

Net Weight 40 Pounds (18 kg)  
(4.627gal [17.5 L])

# MGA<sup>®</sup> 500

Liquid Premix

**(Type A Medicated Article)**

**Heifers Fed in Confinement for Slaughter:  
For Increased Rate of Weight Gain, Improved Feed Efficiency  
and Suppression of Estrus (Heat).**

**Heifers Intended for Breeding: For Suppression of Estrus (Heat).**

**Each Pound Contains:**

**Active Drug Ingredient:**

Melengestrol Acetate ..... 500 mg  
(as melengestrol acetate and its propylene glycol ketal)

**Inactive Ingredient:**

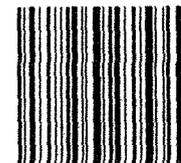
Propylene Glycol, U.S.P. .... 99.89%

**Caution:** For manufacturing, processing, or repacking. To be mixed with feed prior to animal use. Use only as directed. Excessive contact with skin should be avoided. Destroy empty container. Do not reuse.

**Store at room temperature**

NADA #39-402, Approved by FDA

Pharmacia  
& Upjohn



**DIRECTIONS FOR USE:****Heifers Fed in Confinement for Slaughter:**

MGA 500 Liquid Premix (Type A Medicated Article) should be thoroughly mixed in liquid Type C medicated feed which must be fed at 0.5 to 2.0 pounds per head daily to provide 0.25 to 0.5 mg of melengestrol acetate per head per day. Average daily intakes approximating the middle of this range provide the most optimal and economical improvements in rate of gain and feed utilization. Constant daily intakes of 0.35 to 0.50 mg per head per day give a high degree of estrus suppression. Levels of 0.25 to 0.35 mg provide a lower but still effective degree of estrus suppression.

**Heifers Intended for Breeding:**

MGA 500 Liquid Premix (Type A Medicated Article) should be thoroughly mixed in the supplement to provide 0.5 mg of melengestrol acetate per head per day.

**Not for human use. Restricted Drug—Use Only As Directed (California)**

**CAUTION: Not effective in steers and spayed heifers.**

**Heifers Fed in Confinement for Slaughter:**

Withdrawal periods of three to five days or more should be avoided to prevent the possibility that the heifers may come into estrus (heat) at loading time.

**Heifers Intended for Breeding:**

Do not exceed 24 days of feeding of melengestrol acetate to heifers intended for breeding. A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

**MIXING DIRECTIONS:**

Liquid Type B and C medicated feeds containing melengestrol acetate must have a pH of 4.0 to 8.0 and their labels must bear appropriate mixing directions. Mixing directions for liquid Type B or C feeds stored in recirculation tank systems are: "Recirculate immediately prior to use for no less than 10 minutes, moving not less than 1 percent of the tank contents from the bottom of the tank to the top. Recirculate daily, as directed in this paragraph even when the Type B (or C) feed is not used." Mixing directions for liquid Type B and C feeds stored in mechanical, air or other agitation-type tank systems are: "Agitate immediately prior to use for not less than 10 minutes, creating a turbulence at the bottom of the tank that is visible at the top. Agitate daily, as directed in this paragraph, even when the Type B (or C) feed is not used."

Intermediate premixes should not be made from MGA 500 Liquid Premix (Type A Medicated Article) except as a part of a continuous mixing operation to make a complete liquid Type B or Type C medicated feed. Thoroughly mix 0.5 to 4 pounds of MGA 500 Liquid Premix (Type A Medicated Article) per ton of a non-medicated feed to prepare a Type C medicated feed containing 0.25 to 2.0 grams of melengestrol acetate per ton. The following Table may be used as a guide in determining the amount of MGA 500 Liquid Premix (Type A Medicated Article) to be added to prepare a ton of Type C medicated feed.

Amount of Type C Feed Fed (lb/head/day)	Melengestrol Acetate (mg/head/day)	MGA 500 Liquid Premix Per Ton of Type C Feed		Amount of Type C Feed Fed (lb/head/day)	Melengestrol Acetate (mg/head/day)	MGA 500 Liquid Premix Per Ton of Type C Feed	
		When Added by Weight (lb)	When Added by Volume (mL)			When Added by Weight (lb)	When Added by Volume (mL)
0.5	0.25	2.00	876	1.5	0.25	0.66	289
0.5	0.30	2.40	1051	1.5	0.30	0.80	350
0.5	0.35	2.80	1226	1.5	0.35	0.93	407
0.5	0.40	3.20	1402	1.5	0.40	1.07	469
0.5	0.45	3.60	1577	1.5	0.45	1.20	526
0.5	0.50	4.00	1752	1.5	0.50	1.33	582
1.0	0.25	1.00	438	2.0	0.25	0.50	219
1.0	0.30	1.20	526	2.0	0.30	0.60	263
1.0	0.35	1.40	613	2.0	0.35	0.70	307
1.0	0.40	1.60	701	2.0	0.40	0.80	350
1.0	0.45	1.80	788	2.0	0.45	0.90	394
1.0	0.50	2.00	876	2.0	0.50	1.00	438

Type B medicated feed containing 4 to 10 grams melengestrol acetate per ton may be manufactured by thoroughly mixing 8 to 20 lbs of MGA 500 Liquid Premix with 1992 to 1980 lbs of non-medicated feed. Labeling for such Type B feed shall contain directions for manufacturing Type C medicated feeds containing 0.25 to 2.0 grams melengestrol acetate per ton (0.125 to 1.0 mg/lb). The Type C medicated feed, containing melengestrol acetate, must be top dressed on grain or roughage or mixed with a complete ration at the rate of 0.5 to 2.0 pounds per head per day. Good manufacturing practice regulations must be adhered to in manufacturing feeds containing MGA 500.

813 931 308

Pharmacia & Upjohn Company  
Kalamazoo, MI 49001, USA

**BULK ONLY**

**LIQUID HEIFER SUPPLEMENT**  
**Medicated**  
**(Type C Medicated Feed)**

**INDICATIONS**

Heifers Fed in Confinement for Slaughter: For Increased Rate of Weight Gain, Improved Feed Efficiency and Suppression of Estrus (Heat).

Heifers Intended for Reproduction. For Suppression of Estrus (Heat).

**ACTIVE DRUG INGREDIENTS**

Melengestrol acetate (0 0000276-0.00022%)  
 Each pound contains (0.125-1.0) mg melengestrol acetate

**GUARANTEED ANALYSIS**

Crude Protein, not less than	_____ %
Crude Fat, not less than	_____ %
Crude Fiber, not more than	_____ %

**INGREDIENTS**

Each ingredient will be specifically named (unless stated as such in the guaranteed analysis listing) in accordance with the names and definitions adopted by the AAFCO. Include also ingredients of the trace mineral and vitamin premixes. Collective terms may be used in accordance with 21 CFR § 501.110.

**DIRECTIONS FOR USE**

Must be top dressed on grain or silage or mixed with a complete ration.

Heifers Fed in Confinement for Slaughter: Feed at the rate of 0.5-2.0 pound(s) per head per day (specify one level) to provide 0.25-0.5 mg melengestrol acetate per head per day (specify one level). Continue feeding throughout the time the heifers are being grown and finished for slaughter.

Heifers Intended for Reproduction: Feed at the rate of 0.5-2.0 pound(s) per head per day (specify one level) to provide 0.5 mg melengestrol acetate per head per day.

**AGITATE OR RECIRCULATE THOROUGHLY BEFORE USING TO INSURE PROPER  
 MIXING OF THE INGREDIENTS**

**IMPORTANT:** Not effective in steers and spayed heifers.

**CAUTION:** Heifers Fed in Confinement for Slaughter: Withdrawal periods of three to five days should be avoided to prevent the possibility that the heifers may come into estrus (heat) at the time of loading.

Heifers Intended for Reproduction:  
 Do not exceed 24 days of feeding.  
 A reduced conception rate can be expected if heifers are bred at estruses observed within 1 to 12 days after withdrawal of melengestrol acetate, whereas heifers bred at subsequent observed estruses are expected to have normal conception rates.

**MANUFACTURED BY**  
**Blue Bird Feed Company**  
 Robin, Indiana 11111

EXP: