

Environmental Assessment for SYNOVEX® ONE Grower Implants for Feedlot Beef Steers and Heifers

Active Ingredients: Trenbolone Acetate, Estradiol Benzoate

21 July 2021

Approved

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SUMMARY

SYNOVEX® ONE Grower is an extended release implant that is compositionally identical to SYNOVEX ONE Grass and administered as a subcutaneous ear implant. SYNOVEX ONE Grower contains the active ingredients trenbolone acetate and estradiol benzoate (150 mg and 21 mg per implant, respectively). The proposed action of this supplemental approval for SYNOVEX ONE (NADA 141-348) is to allow the use of SYNOVEX ONE Grower for increased rate of weight gain for up to 200 days in steers and heifers fed in confinement for slaughter.

The potential risk of adverse effects on the environment from the use of SYNOVEX ONE Grower was assessed following guidance from the Center for Veterinary Medicine (CVM). The environmental assessment (EA) for SYNOVEX ONE Grower was developed based on the information and data contained in the EA for SYNOVEX ONE.

This EA demonstrates that trenbolone acetate and estradiol benzoate metabolites excreted in manure from cattle administered this product do not pose a significant risk to terrestrial or aquatic environments on individual farms, landscapes, and watersheds.

1. INTRODUCTION

In accordance with the Code of Federal Regulations 21 CFR 25.15(a), all applications or petitions requesting agency action require the submission of an EA or a claim of categorical exclusion (CE) to evaluate whether the approval of the product will cause significant impacts to the environment. In some cases, supplemental actions on products that are already approved may be granted a CE from the need to prepare an EA under 21 CFR 25.33(a)(1), i.e., actions that do not increase the use of a drug such as an animal drug to be marketed under the same conditions of approval as a previously approved animal drug.

As described under 21 CFR 25.5(b)(4), increased use of a drug may occur if the drug will be administered at higher dosage levels, for longer duration, or for different indications that were previously in effect. This definition has been extended to include additional species or subclasses of species and increased frequency of use of a drug. Addition of cattle fed in confinement for slaughter, even at the lower dosage of SYNOVEX ONE Grower, is considered to be an additional subclass of a species that would not have otherwise received the drug product. Accordingly, the FDA has determined that an EA is required.

2. PURPOSE AND NEED

This EA is provided to support approval of a supplemental New Animal Drug Application for the use of SYNOVEX ONE Grower. SYNOVEX ONE Grower delivers 21 mg estradiol benzoate and 150 mg trenbolone acetate over 200 days via an ear implant and is proposed for increased rate of weight gain in beef steers and heifers fed in confinement for slaughter. SYNOVEX ONE Grower is intended to meet the market need for quickly and safely producing beef cattle meat for consumption. SYNOVEX ONE Grower contains 75% of the total dose of SYNOVEX ONE Feedlot, thus providing producers with the ability to use a lower-dose extended release SYNOVEX ONE implant in cattle fed in confinement.

3. DESCRIPTION OF PROPOSED ACTION

The proposed action of this supplemental approval of SYNOVEX ONE (NADA 141-348) is to allow the use of SYNOVEX ONE Grower for increased rate of weight gain for up to 200 days in steers and heifers fed in confinement for slaughter.

4. IDENTIFICATION OF SUBSTANCES

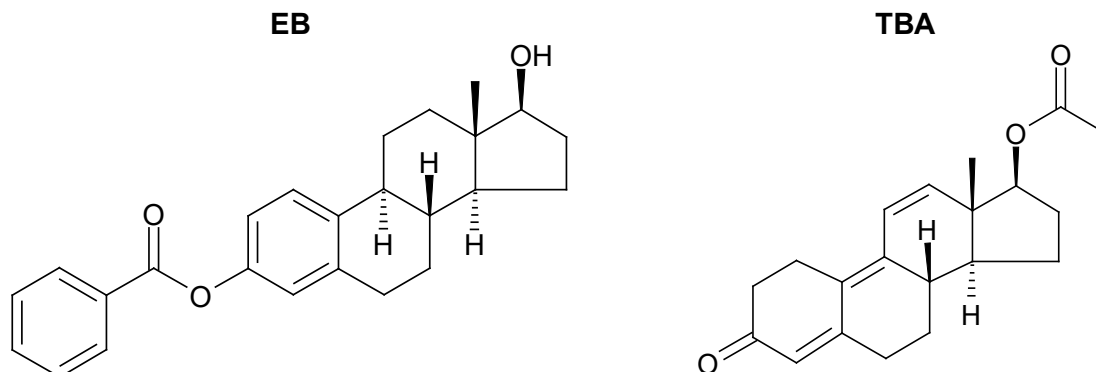
4.1. Active Components

Estradiol benzoate (EB) - The IUPAC name for estradiol benzoate (CAS 50-50-0) is: [(8R,9S,13S,14S,17S)-17-hydroxy-13-methyl-6,7,8,9,11,12,14,15,16, 17-decahydrocyclopenta[a]-phenanthren-3-yl] benzoate. Molecular weight = 376.5 g/mol

Trenbolone acetate (TBA) - The IUPAC name for trenbolone acetate (CAS 10161-34-9) is: [(8S,13S,14S,17S)-13-methyl-3-oxo-2,6,7,8,14,15,16, 17-octahydro-1H-cyclopenta[a]-phenanthren-17-yl] acetate. Molecular weight = 312.4 g/mol

The chemical structures of EB and TBA are shown in Figure 1.

Figure 1. Chemical Structures of Estradiol Benzoate (EB) and Trenbolone Acetate (TBA)



4.2. Formulation and Dose

SYNOVEX ONE Grower consists of a series of precisely formulated pellets each containing 3.5 mg EB and 25 mg TBA. Six pellets are implanted in the ear of cattle as a single subcutaneous injection. Each pellet is coated with a porous polymer film that results in a steady release of the active components *in vivo*, effectively providing 200 days of release. The compositions of each pellet and the pellet film coating are provided in Table 1 and Table 2, respectively.

Table 1. SYNOVEX ONE Core Pellet Ingredients

Ingredient	Function
Trenbolone acetate	Active ingredient
Estradiol benzoate	Active ingredient
Povidone (K-90), USP	Binder
Polyethylene glycol 8000, NF	Binder
Magnesium stearate, NF	Lubricant
Purified water, USP	---

Table 2. SYNOVEX One Pellet Coating Ingredients

Ingredient	Function
Ethylcellulose aqueous dispersion, NF	Film coating
Dibutyl sebacate, NF	Plasticizer
Polyethylene glycol 8000, NF	Pore former
Purified water, USP	---

The implant pellets are manufactured in strict accordance with the procedures approved under NADA 141-348. The pellets are placed in molded low density polyethylene (LDPE) resin cartridges that are intended for use with a specially designed implant gun. Each of the ten channels in the cartridge contains six implant pellets. Ten cartridges are placed on a specially designed plastic tray. The tray with the ten cartridges is sealed in a laminated foil pouch. Although the pellets are contained in a cartridge in the implant gun, they are implanted in the ear as individual pellets.

4.3. Label Indications for Use

SYNOVEX ONE Grower is a pelleted implant indicated for increased rate of weight gain for up to 200 days in steers and heifers fed in confinement for slaughter.

4.4. Annual Frequency of Use

Each feedlot animal will be implanted once.

4.5. Disposal of Synovex One Implants

MSDS: "Avoid release to the environment. Do not discharge into drains, water courses or onto the ground. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater. Dispose of contents/container in accordance with local/regional/national/international regulations."

Label: "SYNOVEX ONE Grower waste materials should be disposed of according to prescribed Federal, State, and Local guidelines."

5. RISK CHARACTERIZATION

A comprehensive EA was written to assess the environmental safety of SYNOVEX ONE Feedlot and SYNOVEX ONE Grass for beef steers and heifers under NADA 141-348 [1]. The potential for environmental impact from the runoff of estradiol and trenbolone was adequately evaluated for a higher dosage under the previous EA, and it was determined that no significant impacts were expected. Because SYNOVEX ONE Grower contains lower doses of trenbolone acetate and estradiol benzoate, no significant impacts are expected from use of SYNOVEX ONE Grower.

6. ALTERNATIVES TO THE PROPOSED ACTION

The only alternative to the proposed action is the "no action" alternative, which would be the failure to approve the NADA for SYNOVEX ONE Grower. However, based on our analysis in

the environmental assessment, we do not believe that significant environmental impacts will occur from this action; therefore, the “no action” alternative was eliminated from consideration.

7. AGENCIES AND PERSONS CONSULTED

This EA was prepared with input and assistance from members of the Environmental Safety Team in the Office of New Animal Drug Evaluation in FDA’s Center for Veterinary Medicine.

8. REFERENCES

1. Environmental Assessment for Synovex One (Estradiol Benzoate and Trenbolone Acetate Extended Release Implant) Feedlot and Grass for Beef Steers and Heifers, May 29, 2014.

9. PREPARER / APPROVAL

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Electronic Signature for Zoetis Document Number ZRD-STU-092562 (2.0)
Synovex One Grower Environmental Assessment - Amended

Dawn Merritt Approver	21-Jul-2021 13:08:06 GMT+0000
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