

Date of Approval: September 14, 2026

FREEDOM OF INFORMATION (FOI) SUMMARY

ORIGINAL NEW ANIMAL DRUG APPLICATION (NADA)

NADA 141-633

MULTIMIN[®] SELENIUM FREE

(zinc, copper, and manganese injection)

Injectable solution

Cattle. Not for use in pregnant cows and heifers during their first trimester because reproductive safety testing has not been done in these animals. Do not use in beef calves less than 2 months of age, dairy calves, and veal calves because safety has not been established.

To provide a supplemental source of zinc, copper, and manganese in cattle. Not for use in pregnant cows and heifers during their first trimester because reproductive safety testing has not been done in these animals. Do not use in beef calves less than 2 months of age, dairy calves, and veal calves because safety has not been established.

Sponsored by:

Warburton Technology Ltd.

Executive Summary

MULTIMIN[®] SELENIUM FREE (zinc, copper, and manganese injection) is approved as a supplemental source of zinc, copper, and manganese in cattle. The drug is an injectable solution of the three minerals and administered subcutaneously. MULTIMIN[®] SELENIUM FREE is not for use in pregnant cows and heifers during their first trimester, beef calves less than 2 months of age, dairy calves, and veal calves.

Safety and Effectiveness

Each of the three minerals in MULTIMIN[®] SELENIUM FREE contributes to the drug's effectiveness because individual sources of zinc, copper, and manganese are necessary to increase the blood concentrations of zinc, copper, and manganese. The Food and Drug Administration (FDA) did not require effectiveness studies for this approval, as the effectiveness data supporting MULTIMIN[®] 90 (zinc, copper, manganese, and selenium injection) (NADA 141-582, approval date April 26, 2024) was extrapolated to support effectiveness for MULTIMIN[®] SELENIUM FREE. The sponsor provided a white paper argument based on scientific literature demonstrating that the removal of selenium from the formulation is not expected to impact the bioavailability of zinc, copper, and manganese after subcutaneous injection or their oral absorption from the diet.

The effectiveness for MULTIMIN[®] 90 was demonstrated through a multi-site clinical field study in Holstein replacement dairy heifers. Animals were administered either saline or MULTIMIN[®] 90 by subcutaneous injection at the labeled dose, with blood samples collected at multiple timepoints post-injection. Compared with the control group, cattle in the treatment group had higher mean plasma concentrations of all four minerals, as calculated by the area under the curve from the time of injection (time zero) to 8 hours post-injection.

FDA did not require target animal safety studies for this approval, as the safety data supporting MULTIMIN[®] 90 was extrapolated to support target animal safety for MULTIMIN[®] SELENIUM FREE. The sponsor provided a white paper argument based on scientific literature demonstrating that selenium removal from the formulation does not impact the safety profile of the remaining minerals. The safety evaluation for MULTIMIN[®] 90 included a margin of safety study and injection site irritation study in young, healthy beef cattle.

The margin of safety study demonstrated that MULTIMIN[®] 90 was well-tolerated at 1X and 3X the labeled dose. Cattle in all treatment groups experienced injection site swelling and inflammation. At higher doses (3X and 5X), cattle showed decreased feed consumption and decreased serum cholesterol compared with controls. The 5X group also experienced hepatic centrilobular necrosis and associated serum chemistry changes caused by copper toxicity, indicating that if administered in excess or used with other sources of copper, cattle may show clinical signs associated with copper toxicity.

The injection site irritation study showed that MULTIMIN[®] 90 caused injection site reactions including pain during injection, injection site swelling, and injection site induration (thickening and hardening of the skin). Injection site lesions ranged from mild to severe on necropsy examination, with abnormal microscopic findings consistent with a marked local irritant effect. These reactions may result in trim loss of edible tissue at slaughter.

The sponsor evaluated reproductive safety of MULTIMIN[®] 90 using scientific literature and pharmacovigilance reports. However, due to a lack of studies evaluating administration during the first trimester of pregnancy, the Agency concluded that reproductive safety was demonstrated in both male and female cattle except in pregnant cows and heifers during their first trimester.

Human Food Safety

FDA did not require new human food safety information for this approval. The human food safety for MULTIMIN[®] SELENIUM FREE is supported by the human food safety assessment conducted for the approval of NADA 141-582 for MULTIMIN[®] 90. The FOI Summary for the original approval of NADA 141-582 dated April 26, 2024, contains summaries of studies and information used to assess human food safety for MULTIMIN[®] 90. A 14-day withdrawal period and zero-day milk discard time are assigned for the approved use of MULTIMIN[®] SELENIUM FREE in cattle. A withdrawal period has not been established for this product in pre-ruminating calves.

User Safety

Due to the high mineral concentrations in MULTIMIN[®] SELENIUM FREE, there is a potential risk of zinc, copper, and manganese toxicity in people who handle or are exposed to the drug. Symptoms of toxicity in people include aches, chills, nausea, vomiting, diarrhea, epigastric pain, tremors, and irritability.

Conclusions

Based on the data submitted by the sponsor for the approval of MULTIMIN[®] SELENIUM FREE, FDA determined that the drug is safe and effective when used according to the labeling.

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I. GENERAL INFORMATION

A. File Number

NADA 141-633

B. Sponsor

Warburton Technology Ltd.
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Drug Labeler Code: 066679

U.S. Agent Name and Address:

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C. Proprietary Name

MULTIMIN® SELENIUM FREE

D. Drug Product Established Name

zinc, copper, and manganese injection

E. Pharmacological Category

Minerals

F. Dosage Form

Injectable solution

G. Amount of Active Ingredient

zinc (60 mg/mL) as zinc oxide
copper (15 mg/mL) as copper carbonate
manganese (10 mg/mL) as manganese carbonate

H. How Supplied

100 mL and 500 mL vials

I. Dispensing Status

Prescription (Rx)

J. Dosage Regimen

Cattle up to 1 year, 1 mL/100 lb bodyweight
Cattle from 1-2 years, 1 mL/150 lb bodyweight
Cattle over 2 years, 1 mL/200 lb bodyweight

To be administered as a single dose. The maximum volume per injection site is 7 mL. Allow a minimum of 30 days before considering repeat dosing.

K. Route of Administration

Subcutaneous injection

L. Species/Classes

Cattle. Not for use in pregnant cows and heifers during their first trimester because reproductive safety testing has not been done in these animals. Do not use in beef calves less than 2 months of age, dairy calves, and veal calves because safety has not been established.

M. Indication

To provide a supplemental source of zinc, copper, and manganese in cattle. Not for use in pregnant cows and heifers during their first trimester because reproductive safety testing has not been done in these animals. Do not use in beef calves less than 2 months of age, dairy calves, and veal calves because safety has not been established.

II. EFFECTIVENESS

FDA did not require effectiveness studies for this approval. Each of the three active ingredients in MULTIMIN[®] SELENIUM FREE (zinc, copper, and manganese injection) contributes to the drug's effectiveness because individual sources of zinc, copper, and manganese are necessary to increase the blood concentrations of zinc, copper, and manganese. The sponsor provided a white paper argument based on scientific literature to justify that the removal of selenium from the MULTIMIN[®] 90 (zinc, copper, manganese, and selenium injection) formulation is not expected to impact the bioavailability of zinc, copper, and manganese after subcutaneous injection of MULTIMIN[®] SELENIUM FREE or their oral absorption from the diet. The data supporting effectiveness for MULTIMIN[®] 90 was extrapolated to support effectiveness for MULTIMIN[®] SELENIUM FREE. The FOI Summary for the original approval of NADA 141-582 dated April 26, 2024, contains a summary of effectiveness studies for cattle for MULTIMIN[®] 90.

The sponsor conducted a multi-site clinical field study to demonstrate that a single injection of MULTIMIN[®] 90 is effective to provide a supplemental source of zinc, copper, manganese, and selenium in cattle. Holstein replacement dairy heifers sourced from commercial dairy herds were enrolled in the study. The heifers were administered either saline or MULTIMIN[®] 90 by subcutaneous injection at the labeled dose, and blood samples were collected at multiple timepoints post-injection. Compared with the control group, cattle in the treatment group had higher mean plasma concentrations of all four minerals, as calculated by the area under the curve from the time of injection (time zero) to 8 hours post-injection (AUC₀₋₈).

III. TARGET ANIMAL SAFETY

FDA did not require target animal safety studies for this approval. The sponsor provided a white paper argument based on scientific literature to justify that the removal of selenium from the MULTIMIN[®] 90 formulation is not expected to impact the bioavailability of zinc, copper, and manganese after subcutaneous injection of MULTIMIN[®] SELENIUM FREE or their oral absorption from the diet. The data supporting target animal safety for MULTIMIN[®] 90 was extrapolated to support target animal safety for MULTIMIN[®] SELENIUM FREE. The FOI Summary for the original approval of NADA 141-582 dated April 26, 2024, contains a summary of target animal safety studies for cattle for MULTIMIN[®] 90.

As summarized in the NADA 141-582 approval, the sponsor conducted a margin of safety study and an injection site study and evaluated the reproductive safety of MULTIMIN[®] 90 using scientific literature and pharmacovigilance reports.

The margin of safety study was conducted using young, healthy, purebred and crossbred beef cattle. Both non-pregnant females and intact males were enrolled. Each animal was injected at three administration sites with MULTIMIN[®] 90 subcutaneously at 0X, 1X, 3X, or 5X the labeled dose for 3 consecutive days (three times the labeled duration). The 0X group received saline at the 5X dose volume. The drug was well-tolerated in the 1X and 3X groups. Cattle in all treatment groups had injection site swelling and inflammation. Cattle in the 3X and 5X groups had decreased feed consumption and decreased serum cholesterol compared with the 0X group. The 5X group also had hepatic centrilobular necrosis and associated serum chemistry changes caused by copper toxicity. If administered in excess or used with other sources of copper, cattle may show clinical signs associated with copper toxicity.

The injection site irritation study was conducted using young, healthy, purebred and crossbred beef cattle of both sexes. Each animal was administered both MULTIMIN[®] 90 and saline on different sides of the neck. MULTIMIN[®] 90 caused injection site reactions including pain during the injection, injection site swelling, and injection site induration (thickening and hardening of the skin). Injection site lesions were seen grossly on necropsy and ranged from mild to severe. Abnormal microscopic findings were consistent with a marked local irritant effect. These reactions may result in trim loss of edible tissue at slaughter.

The reproductive safety of MULTIMIN[®] 90 in male and female cattle was evaluated in a weight of evidence approach using scientific literature and pharmacovigilance reports. However, there is a lack of studies that evaluated the administration of MULTIMIN[®] 90 during the first trimester. Therefore, the Agency concluded that the sponsor demonstrated reproductive safety in both male and female cattle except in pregnant cows and heifers during their first trimester.

IV. HUMAN FOOD SAFETY

A. Microbial Food Safety

The Agency previously determined that the conditions of use for MULTIMIN[®] 90 in cattle (NADA 141-582) were compatible with the Agency's risk management

strategies for a drug with an estimated low risk to human health. The currently proposed use of the same product less selenium, poses no added microbial food safety risk and the Agency's conclusion remains unchanged.

B. Toxicology

The Agency previously summarized the toxicology evaluation for the use of MULTIMIN® 90 in cattle in the FOI Summary for the original approval of NADA 141-582, dated April 26, 2024. The tolerable upper intake levels (ULs) of the components (in adults) are as follows: copper 10 mg/day, manganese 11 mg/day, and zinc 40 mg/day. The Agency concluded that there are sufficient margins between the referenced values and human exposure to residues to ensure the safety of humans consuming edible tissues from treated cattle.

The only difference between this product and MULTIMIN® 90 is the lack of selenium. Removal of selenium will not change the toxicity profiles of the remaining components (zinc, copper, and manganese). The Agency's conclusion remains the same.

C. Residue Chemistry

1. Summary of Residue Chemistry Studies

The residue chemistry study used to support this approval is described in the FOI Summary for MULTIMIN® 90 (NADA 141-582, approval date April 26, 2024). The study is entitled, "Residue Depletion Study of Multimin Solution for Injection for Cattle (Copper Carbonate/Benzyl Alcohol Formulation)" (Study No. V8167).

2. Target Tissue and Marker Residue

A target tissue is not identified. Residues of zinc, copper, and manganese do not accumulate above the ULs in edible tissues after treatment.

3. Tolerances

Tolerances for manganese, copper, and zinc are not assigned because the tissue residues are evaluated in reference to the ULs for manganese, zinc and copper.

4. Withdrawal Period and Milk Discard Time

A 14-day withdrawal period accommodates variation in depletion of residues across all edible tissues, including injection site muscle, prior to slaughter of the treated animal. A zero-day milk discard time is assigned because residues are not anticipated to increase in milk from treated cattle. A withdrawal period has not been established for this product in pre-ruminating calves.

D. Analytical Method for Residues

An official method is not needed because tolerances are not being assigned.

V. USER SAFETY

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to MULTIMIN® SELENIUM FREE:

Not for use in humans. Keep out of reach of children. Do not allow children access to used or empty syringes. Wash hands after use.

This product is highly concentrated in zinc, copper, and manganese. Due to a potential risk of zinc, copper, and manganese toxicity, care should be taken when handling the product to avoid accidental self-injection. Symptoms of exposure to zinc, copper, and manganese include aches, chills, nausea, vomiting, diarrhea, epigastric pain, tremors, and irritability.

In case of accidental self-injection or ingestion, SEEK IMMEDIATE MEDICAL ATTENTION and take the vial with you.

VI. AGENCY CONCLUSIONS

The data submitted in support of this NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR part 514. The data demonstrate that MULTIMIN® SELENIUM FREE, when used according to the label, is safe and effective for the conditions of use in the General Information Section above. Additionally, data demonstrate that residues in food products derived from species treated with MULTIMIN® SELENIUM FREE will not represent a public health concern when the product is used according to the label.

A. Marketing Status

This product may be dispensed only by or on the order of a licensed veterinarian (Rx marketing status). Adequate directions for lay use cannot be written because professional expertise is required to monitor the safe use of the product, including treatment of any adverse reactions.

B. Exclusivity

MULTIMIN® SELENIUM FREE, as approved in our approval letter, qualifies for THREE years of marketing exclusivity beginning as of the date of our approval letter. This drug qualifies for exclusivity under section 512(c)(2)(F)(ii) of the FD&C Act because the sponsor submitted an original NADA that contains new studies that demonstrate the safety and effectiveness of MULTIMIN® SELENIUM FREE.

C. Patent Information

For current information on patents, see the Green Book Reports in the Animal Drugs @ FDA database.