

Date of Approval: NOV 13 2008

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 013-076

TYLAN Soluble

Tylosin tartrate
Soluble powder
Swine

For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by TYLAN Type A medicated article in feed.

For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by TYLAN Type A medicated article in feed.

Sponsored by:

Elanco Animal Health

2008-013-076

FDA 2008-N-0039

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TABLE OF CONTENTS

I. GENERAL INFORMATION:..... 1

II. EFFECTIVENESS:..... 2

 A. Dosage Characterization: 2

 B. Substantial Evidence:..... 2

III. TARGET ANIMAL SAFETY:..... 9

IV. HUMAN FOOD SAFETY: 9

 A. Toxicology: 9

 B. Residue Chemistry:..... 9

 C. Microbial Food Safety: 9

 D. Analytical Method for Residues: 10

V. USER SAFETY: 10

VI. AGENCY CONCLUSIONS:..... 10

 A. Marketing Status: 10

 B. Exclusivity: 10

 C. Supplemental Applications: 11

 D. Patent Information: 11

VII. ATTACHMENTS:..... 11

I. GENERAL INFORMATION:

- A. File Number:** NADA 013-076
- B. Sponsor:** Elanco Animal Health
A Division of Eli Lilly & Co.
Lilly Corporate Center
Indianapolis, IN 46285
- Drug Labeler Code: 000986
- C. Proprietary Names:** TYLAN Soluble
- D. Established Name:** Tylosin tartrate
- E. Pharmacological Category:** Antimicrobial
- F. Dosage Forms:** Water soluble powder
- G. Amount of Active Ingredient:** 100 grams tylosin base per jar
- H. How Supplied:** Jars containing tylosin tartrate equivalent to 100 grams tylosin base
- I. How Dispensed:** OTC
- J. Dosage:** 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g tylosin per ton of complete feed (Type C medicated feed manufactured from TYLAN Type A medicated article) for 2 to 6 weeks.
- K. Routes of Administration:** Oral in water
- L. Species/Class:** Swine
- M. Indications:** For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by TYLAN Type A medicated article in feed.
- For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by TYLAN

Type A medicated article in feed.

N. Effect of Supplement:

This supplement provides for the approval of TYLAN Soluble (tylosin tartrate) followed by TYLAN Type A medicated article (tylosin phosphate) for the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* in swine and the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* in swine.

II. EFFECTIVENESS:

A. Dosage Characterization:

The dosage regimen tested for the control of porcine proliferative enteropathies (PPE, ileitis) was the currently approved dosage regimen for the use of tylosin in drinking water followed by tylosin in feed for the treatment and control of swine dysentery. This dosage regimen was selected because, while PPE and swine dysentery are caused by different pathogens, the two diseases share some clinical signs and are diagnosed under similar conditions. The effectiveness of tylosin in drinking water at 250 mg/gallon for 3 to 10 days followed by tylosin in feed at 40 to 100 grams per ton for 2 to 6 weeks for the treatment and control of swine dysentery was demonstrated for the approval of NADA 012-491 (TYLAN Type A medicated article) dated October 6, 1965 [30 FR 12730].

B. Substantial Evidence:

1. CVM did not require effectiveness studies for the supplemental approval of the indication for the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* (when treatment with TYLAN Soluble is followed immediately by TYLAN Type A medicated article in feed). The supplemental approval of NADA 012-491 (TYLAN Type A medicated article) dated October 6, 1965 [30 FR 12730], contains a summary of studies that demonstrate effectiveness of this dosage regimen for the treatment and control of swine dysentery in pigs.

2. Type of Study: Dose Confirmation Model Study

1) Title: "An Efficacy Dose Confirmation Study with TYLAN Soluble Powder Followed by TYLAN Premix for the Control of Porcine Proliferative Enteropathy (ileitis) in Swine." Study # T1XAM0501. January 2007 to March 2007.

2) Investigators and Locations:

Terry TerHune, DVM, PhD, HMS, Veterinary Development Inc.,
Tulare, CA

Kelly Lechtenberg, DVM, PhD, Midwest Veterinary Services, Inc.,
Oakland, NE

3) Study Design:

- a) *Objective:* To confirm the clinical effectiveness of tylosin tartrate administered in drinking water followed by tylosin phosphate, administered in a Type C medicated feed for the control of porcine proliferative enteropathies (PPE, ileitis) in swine. This study was conducted in accordance with CVM Guidance for Industry 85, "Good Clinical Practice" (VICH GL9) May 9, 2001.
- b) *Test Animals:* A total of 480 healthy, four to five week-old barrows and gilts were enrolled in this study. Pigs were obtained from separate swine sources for each study site. Animals weighed 11.4 to 28.6 pounds at enrollment, and originated from herds demonstrated to be free of *Lawsonia intracellularis* by polymerase chain reaction testing of random fecal samples prior to purchase.
- c) *Experimental Design:* The study was conducted at two independent sites. A randomized complete block design was used at each site. The pen was the experimental unit. Treatment and control animals were not commingled in pens. Pens contained six pigs at the beginning of the study and there were 20 pens enrolled at each site.

On Day 0, all pigs were challenged with intestinal mucosal homogenate prepared from sections of affected pig intestine which were obtained from a recent, North American case of PPE. Pigs were dosed by gastric gavage to inoculate each pig with approximately 10^9 *Lawsonia intracellularis* organisms.

- d) *Treatment Groups:* On Day -7, animals were ranked by descending weight within gender and randomly assigned to pens. Pens were then randomly assigned to treatment group (Table 1).

Table 1. Treatment Groups

Group	Test Article	Dose/Route	Frequency/Duration
Treated	Tylosin tartrate	250 mg tylosin/gallon of drinking water	<i>Ad libitum</i> for three days
	Followed by: Tylosin phosphate	40 g tylosin/ton in feed	<i>Ad libitum</i> for 14 days
Negative Control	Non-medicated water	0	<i>Ad libitum</i> for three days
	Followed by: Non-medicated feed	0	<i>Ad libitum</i> for 14 days

- e) *Test Article Administration:* Tylosin as the tartrate salt (TYLAN Soluble) was administered in the drinking water at 250 mg tylosin/gallon (65.8 ppm) for three days followed by tylosin as the phosphate salt (TYLAN Type A medicated article) administered in feed containing 40 g tylosin/ton for 14 days. Day X was defined as the day that 15% of the total population of study pigs at the study site were observed to be clinically affected with PPE in a single day. A pig was considered clinically affected when it had a diarrhea score of 2 or 3 (see score definitions below). Tylosin was administered in the drinking water from Day X + 1 through Day X + 3 and tylosin was administered in the feed from Day X + 4 through Day X + 17. Control pigs received no medication in water or feed for the duration of the study.

On Day X, four clinically affected pigs at each site were randomly selected for necropsy and areas of affected intestine were tested for *L. intracellularis* by immunohistochemical (IHC) stain to confirm the presence of PPE in study animals. Not more than one pig was removed from an individual pen for this test.

- f) *Measurements and Observations:* Pigs were observed twice daily. Animal health observations included observations for survival, general condition, and any abnormal clinical signs.

The primary variables were the percent abnormal pig days for each clinical score (diarrhea, abdominal gut fill, and pig attitude), mortality, lesion index, and average daily gain (ADG).

Clinical scores were evaluated daily from Day X + 1 through Day X + 17.

Diarrhea was described using the following clinical scoring scale.

- 1 = Normal, no diarrhea – Feces are formed with no evidence of abnormal consistency.

- 2 = Semi-loose – Feces are soft: examples include “oatmeal” or “cow-pie” consistency. Fecal material will “pile or puddle” on the pen floor.
- 3 = Watery diarrhea – Feces are watery, containing primarily fluid versus solid material, readily running off the slatted floor.

Abdominal gut fill was described using the following clinical scoring scale.

- 1 = Normal – Flank is full and rounded.
- 2 = Moderately gaunt – Flank is flat.
- 3 = Severely gaunt – Flank is very hollow.

Pig attitude was described using the following clinical scoring scale.

- 1 = Normal – Animal is bright, alert, and active, responding to stimuli.
- 2 = Slightly to moderately depressed or listless – Animal slowly responds to stimuli, but may keep head/ears lowered.
- 3 = Severely depressed or recumbent – Animal may slowly respond to stimuli briefly, but prefers to lie back down quickly. Remains isolated from group.

The percent abnormal pig days for each clinical score was calculated for each pen by summing the total number of days with an abnormal score (Score = 2 or Score = 3) for all pigs in a pen and dividing this numerator by the sum of all study days for which each pig was alive, across all pigs in each pen.

Pigs that died or were euthanized from Day X + 1 through Day X+17 were weighed, necropsied, and considered “mortalities associated with PPE” if they had intestinal lesions consistent with PPE at necropsy (see scoring scale below).

On Day X + 18, all remaining pigs were weighed, euthanized, necropsied, and scored for PPE lesions according to the following criteria:

- 1 = Normal; no gross lesions
- 2 = Mild mesoserosal edema and hyperemia; a mild PPE lesion
- 3 = Edema, hyperemia, reticulated serosa and thickened mucosa; a moderate PPE lesion

4 = Edema, hyperemia, reticulated serosa and mucosa, very gross thickening of the mucosa, blood or fibrin; a severe PPE lesion and/or necrotic enteritis

The lesion index was defined as the sum of the lesion score multiplied by the associated lesion length:

$$\text{Lesion Index} = \sum (i \times l_i),$$

where $i = 2, 3, 4$ (lesion score)
and $l_i =$ length (cm) associated with lesion score i .

Individual pig body weights (BW) by pen were recorded on Days -7, Day X, and X + 18. ADG was calculated for each pen by averaging the individual pigs' average daily gains within the pen. ADG for each individual pig was calculated by subtracting the study animal's weight on Day X from that same weight on Day X + 18 and dividing the result by 18.

At least one of the following sets of criteria had to be met in order to demonstrate effectiveness:

- At least two of the three clinical parameters were statistically significantly improved ($p \leq 0.05$) in the treated group compared to the control group – AND – Mortality was not statistically significantly higher ($p \leq 0.05$) in the treated group compared to the control group.

OR

- The lesion index was statistically significantly improved ($p \leq 0.05$) in the treated group compared to the control group – AND – Average daily gain (ADG) was numerically higher in the treated group compared to the control group – AND – Mortality was not statistically significantly higher ($p \leq 0.05$) in the treated group compared to the control group.

g) *Statistical Analysis:* The criteria for substantial evidence of effectiveness required demonstration of effectiveness at each site, analyzed separately. For each of the clinical parameters (diarrhea score, abdominal gut fill score, pig attitude score) arcsine square root transformed percent of pig-days with abnormal scores (Score = 2 or Score = 3) was analyzed using a mixed effect linear model with treatment as a fixed effect and with block and residual as random effects. A one-sided comparison of tylosin versus negative control was conducted at the 0.05 significance level, with lower percent abnormal among treated groups considered favorable.

Percent mortality was compared between the two treatment groups using Fisher's Exact Test at the 0.05 level of significance.

- 4) **Results:** A total of 470 pigs completed the study.
- a) *Clinical Scores:* At Site 1, abnormal pig days for gut fill was significantly improved in the treated group compared to the control group ($p = 0.0034$), and abnormal pig days for diarrhea was significantly improved in the treated group compared to the control group ($p = 0.0017$). Similarly, at Site 2, abnormal pig days for gut fill was significantly improved in the treated group compared to the control group ($p < 0.0001$), and abnormal pig days for diarrhea was significantly improved in the treated group compared to the control group ($p = 0.0001$). Significant differences in percent abnormal pig days for attitude were seen between control and treated groups at Site 1 ($p = 0.0011$) but not at Site 2 ($p = 0.2067$).

Table 2. Percent Abnormal Pig-Days for Clinical Parameters¹

Site	Treatment Group	Diarrhea ² (%)	Pig Attitude ² (%)	Gut Fill ² (%)
1	Tylosin	77.9 ^a	8.1 ^a	12.9 ^a
	Control	90.7 ^b	17.8 ^b	20.5 ^b
2	Tylosin	40.0 ^a	2.3 ^a	47.2 ^a
	Control	56.7 ^b	3.3 ^a	69.3 ^b

¹ Within each column at a given site, values with different superscripts indicate statistically significant differences between treatment and control groups ($p \leq 0.05$).

² Values are back-transformed from LSMeans.

- b) *Mortality:* At each site, no significant increase in mortality was observed in the tylosin-treated group. At Site 1, percent mortality was 10.3% for control animals and 3.3% for tylosin-treated animals. At Site 2, percent mortality was 0% for both control and tylosin-treated animals.
- c) *Lesion Index:* The lesion index for each pig was calculated as the sum of the lesion score multiplied by the associated lesion length. The average pen lesion index was then computed. Examination of the standard errors versus the means justified the use of the LOG+1 transformation. The lesion index differed significantly between control and tylosin-treated animals at Site 1 ($p < 0.0001$) but not at Site 2 ($p = 0.0549$). At Site 1, the back-transformed mean lesion index was numerically less in tylosin-treated animals (73) than in control animals (237). At Site 2, however, the back-transformed mean lesion index was numerically greater in tylosin-treated animals (180) than in control animals (122).

- d) *ADG*: ADG was computed for each individual pig, and averaged across all pigs within a pen. At Site 1, ADG differed significantly ($p = 0.0007$) between tylosin-treated pens (0.25 kg/day) and control pens (0.19 kg/day). At Site 2, ADG was not significantly different ($p = 0.5156$) in the tylosin-treated pens (0.35 kg/day) compared to the control pens (0.33 kg/day).
- e) *Secondary Variables*: Mean average daily feed intake (ADFI), mean feed to gain ratio (F/G), and mean pen total BW gain were examined at each site (Table 3). At Site 1, ADFI did not significantly change ($p = 0.1497$) in the tylosin-treated pens (0.59 kg feed/day) compared to the control pens (0.57 kg feed/day), F/G significantly decreased ($p = 0.0002$) in the tylosin-treated pens (2.46) compared to the control pens (3.43), and pen total BW gain significantly increased ($p < 0.0001$) in the tylosin-treated pens (27.3 kg) compared to the control pens (18.9 kg). At Site 2, ADFI did not significantly increase ($p = 0.4334$) in the tylosin-treated pens (0.64 kg/day) compared to the control pens (0.65 kg/day), F/G did not significantly decrease ($p = 0.1145$) in the tylosin-treated pens (1.89) compared to the control pens (1.97), and pen total BW gain did not significantly increase ($p = 0.4948$) in the tylosin-treated pens (35.8 kg) compared to the control pens (35.8 kg).

Table 3. Secondary Variables¹

Site	Treatment Group	Average Daily Feed Intake (kg/day) ²	Feed/Gain ²	Pen Total Weight Gain (kg) ²
1	Tylosin	0.59 ^a	2.46 ^a	27.3 ^a
	Control	0.57 ^a	3.43 ^b	18.9 ^b
2	Tylosin	0.64 ^a	1.89 ^a	35.8 ^a
	Control	0.65 ^a	1.97 ^a	35.8 ^a

¹Values with different superscripts within each column are statistically significant ($p \leq 0.05$).

²Values are LSM means.

- 5) Adverse Reactions: No adverse reactions attributable to the test article were reported at either site.
- 6) Conclusions: Treated animals had statistically significant improvement in two of the three clinical parameters (abnormal pig days for gut fill and abnormal pig days for diarrhea) and mortality was not statistically significantly higher in the treated group compared to the control group. This study demonstrated that the use of tylosin tartrate, administered in drinking water at 250 mg tylosin/gallon (65.8 ppm) for three days followed by tylosin phosphate administered at 40 g tylosin/ton in feed for two weeks, was effective for the control of PPE (ileitis) in swine.

III. TARGET ANIMAL SAFETY:

CVM did not require target animal safety studies for this supplemental approval. Target animal safety for the use of TYLAN Soluble in swine at 250 mg tylosin per gallon of drinking water for 3 to 10 days was demonstrated for the approval of NADA 013-076 dated April 5, 1962.

IV. HUMAN FOOD SAFETY:

A. Toxicology:

CVM did not require toxicology studies for this supplemental approval. The original approval of NADA 012-491 as published in the FEDERAL REGISTER [26 FR 4369] on May 19, 1961, contains summaries of all toxicology studies.

B. Residue Chemistry:

1. Summary of Residue Chemistry Studies

CVM did not require residue chemistry studies for this supplemental approval. The original approval of NADA 012-491 as published in the FEDERAL REGISTER [26 FR 4369] on May 19, 1961, contains a summary of residue chemistry studies for swine.

2. Target Tissue and Marker Residue Assignment

No marker residue or target tissue is specified for tylosin.

3. Tolerance Assignments

As described in CFR 556.740, a tolerance of 0.2 parts per million (negligible residue) is established for residues of tylosin in the uncooked edible tissues of swine.

4. Withdrawal Time

The product qualifies for a zero-day withdrawal period.

C. Microbial Food Safety:

The Agency carefully considered the additional label indications, "for treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*," and "for control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis*," for tylosin administered at 250 mg/gal in drinking water for 3 to 10 days, followed by 40 to 100 g/ton tylosin in feed for 2 to 6 weeks in swine. The Agency determined that the additional indications should not significantly impact

public health, and therefore an evaluation of microbial food safety was not necessary at this time.

D. Analytical Method for Residues:

The original approval of NADA 012-491 as published in the FEDERAL REGISTER [26 FR 4369] on May 19, 1961, contains the analytical method summaries for tylosin in swine.

V. USER SAFETY:

The product labeling contains the following information regarding safety to humans handling, administering, or exposed to TYLAN Soluble:

When directed to mix the product with water, always add the water to the powder. Do not pour the powder into the water. Prepare a fresh TYLAN Solution every three days. When mixing and handling tylosin, use protective clothing and impervious gloves.

Avoid contact with human skin. Exposure to tylosin may cause a rash.

Not for human use.

To report adverse effects, access medical information, or obtain additional product information, call 1-800-428-4441.

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 and 21 CFR part 514. The data demonstrate that TYLAN Soluble, when used according to the label, is safe and effective for the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* and for the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* in swine when followed immediately by TYLAN Type A medicated article in feed. Additionally, data demonstrate that residues in food products derived from swine treated with TYLAN Soluble will not represent a public health concern when the product is used according to the label.

A. Marketing Status:

This product can be marketed over-the-counter (OTC) because the approved labeling contains adequate directions for use by laypersons and the conditions of use prescribed on the label are reasonably certain to be followed in practice.

B. Exclusivity:

Under section 512(c)(2)(F)(iii) of the Federal Food, Drug, and Cosmetic Act, this

approval qualifies for THREE years of marketing exclusivity beginning on the date of the approval. The three years of marketing exclusivity applies only to the new claim for the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by TYLAN Type A medicated article in feed for which this supplement is approved.

C. Supplemental Applications:

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(1)).

D. Patent Information:

The sponsor did not submit any patent information with this application.

VII. ATTACHMENTS:

Facsimile Labeling:

TYLAN Soluble – 100 g jar; English-only jar label

TYLAN Soluble – 100 g jar; English/Spanish jar label



Indications

Chickens: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of CRD associated with *Mycoplasma gallisepticum* sensitive to tylosin at the time of vaccination or other stress in chickens. For the control of CRD associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens.

Turkeys: For maintaining weight gain and feed efficiency in the presence of infectious ariallitis associated with *Mycoplasma gallisepticum* sensitive to tylosin.

Swine: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*. For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by TYLAN Type A medicated article in feed. For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by TYLAN Type A medicated article in feed.

Honey Bees: For the control of American foulbrood (*Praenibacillus larvae*).

Ingredients

Tylosin (as tylosin tartrate) 100 g

Mixing Directions

Chickens and Turkeys: To assure thorough dissolution, place the Tyilan (contents of this jar) in a mixing container and add one gallon of water (3780 mL) to the material. Mix this concentrated solution with water to make 50 gallons (189 liters) of treated drinking water.

Swine: To assure thorough dissolution, place the Tyilan (contents of this jar) in a mixing container and add one gallon of water (3780 mL) to the material. Mix this concentrated solution with water to make 400 gallons of treated drinking water resulting in 250 mg/gallon.

Honey Bees: Mix 200 mg tylosin in 20 g confectioners/powdered sugar. Use immediately.

When directed to mix the product with water, always add the water to the powder. Do not pour the powder into the water. Prepare a fresh Tyilan solution every three days. When mixing and handling tylosin, use protective clothing and impervious gloves.

Directions for Use

Chickens should be treated for three days; however, treatment may be administered for one to five days depending upon severity of infection. Treated chickens must consume enough medicated water to provide 50 mg per pound of body weight per day. Only medicated water should be available to the birds.

Turkeys should be treated for three days; however, treatment may be administered for two to five days depending upon severity of infection. Treated turkeys must consume enough medicated water to provide 50 mg per pound of body weight per day. Only medicated water should be available to the birds.

Swine For the treatment and control of swine dysentery medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, depending upon severity of infection. Alternatively, medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g tylosin per ton of complete feed (Type C medicated feed manufactured from TYLAN Type A medicated article) for 2 to 6 weeks. For control of porcine proliferative enteropathies (PPE, ileitis) medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g of tylosin per ton of complete feed (Type C medicated feed manufactured from TYLAN Type A medicated article) for 2 to 6 weeks. Swine must consume enough medicated water to provide a therapeutic dose. Only medicated water (250 mg tylosin per gallon) should be available while medicating with TYLAN Soluble.

Honey Bee colonies should receive three treatments administered as a dust in confectioners/powdered sugar. The 200 mg dose is applied (dusted) over the top bars of the brood chamber once weekly for 3 weeks.

Ileitis: Organisms vary in their degree of susceptibility to any chemotherapeutic. If no improvement is observed after recommended treatment, diagnosis and susceptibility should be reconfirmed.

NOT FOR HUMAN USE

RESIDUE WARNING: Chickens must not be slaughtered for food within 24 hours after treatment. Turkeys must not be slaughtered for food within five days after treatment. Swine must not be slaughtered for food within 48 hours after treatment. Do not use in layers producing eggs for human consumption. Honey Bees: The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins, to avoid contamination of production honey. Complete treatments at least 4 weeks prior to main honey flow.

Avoid contact with human skin. Exposure to tylosin may cause a rash.

Manufactured For: Elanco Animal Health, A Division of Eli Lilly and Company, Indianapolis, IN 46285, USA
 Store at Room Temperature, 25°C (77°F). (Excursions Permitted to 40°C). Avoid Moisture.
 Restricted Drug (California) - Use Only as Directed.
 To report adverse effects, access medical information, or obtain additional product information, call 1-800-428-4441.

*Elanco, Tyilan and the diagonal color bar are trademarks of Eli Lilly and Company. Lot/Exp. date 083965USMOCKUP (AUG-2008)

FRONT LABEL

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ELANCO AF1300-67X

Tylan

Equivalent to 100 g tylosin base
An Antibiotic

NADA #13-076, Approved by FDA
Indications

Chickens: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of CRD associated with *Mycoplasma gallisepticum* sensitive to tylosin at the time of vaccination or other stress in chickens. For the control of CRD associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens.

Turkeys: For maintaining weight gain and feed efficiency in the presence of infectious sinusitis associated with *Mycoplasma gallisepticum* sensitive to tylosin.

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Swine: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*.

For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by TYLAN Type A medicated article in feed.

For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by TYLAN Type A medicated article in feed.

Honey Bees: For the control of American Foulbrood (*Paenibacillus larvae*).

Manufactured For:
Elanco Animal Health
A Division of Eli Lilly and Company
Indianapolis, IN 46226, USA


7 27804 30030 2

Lot / Lot#
Exp. date / Fecha de venc.

DOTTED LINES INDICATE
OVERPRINT AREA AND
ARE NOT FOR PRINTING.

SUBMISSION ARTWORK	
PRODUCT NAME: TYLAN SOLUBLE	
COMPONENT: LABEL PACKAGING INSERT	
COUNTRY: AMERICA	
PRODUCT CODE: AF1300	
ITEM CODE: 081400USMOCKUP_P2	
TEXT APPROVAL CODE: JUN-2008	
PACK SIZE: 100g	
PHARMA CODE: POSITIONAL	
EAN 13: N/A	
BARCODE (UPC-A): 727804300302	
ARTWORK DIMENSIONS: 85mm x 78mm	
FILE TYPE: Quark XPress 6.5	
CREATED BY: INTOUCH / MB	
DATE: 17-JUN-2008	
	
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SUBMISSION ARTWORK	

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 PROCESS
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 BLACK

150 mm Rule Bar

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REVERSE OF FRONT LABEL

ELANCO AF1300-87X

Tylan

Equivalente a 100 g de
tiosina base

Un antibiótico

NADA n.º 13-076, aprobado por la FDA

Indicaciones

Pollos: Como ayuda en el tratamiento para enfermedades respiratorias crónicas (CRD) relacionadas con *Mycoplasma gallisepticum* sensible a la tiosina en pollos de engorde y de reemplazo. Para el control de CRD relacionadas con *Mycoplasma gallisepticum* sensible a la tiosina al momento de la vacunación o de otra causa de estrés en pollos. Para el control de CRD relacionadas con *Mycoplasma synoviae* sensible a la tiosina en pollos de engorde.

Pavos: Para mantener el aumento de peso y la eficiencia del alimento en presencia de sinusitis infecciosa relacionada con *Mycoplasma gallisepticum* sensible a la tiosina.

Cerdos: Para el tratamiento y el control de la disentería porcina relacionada con *Brachyspira hyodysenteriae*.

Para el tratamiento y el control de la disentería porcina relacionada con *Brachyspira hyodysenteriae* cuando es tratada inmediatamente con TYLAN®, artículo medicado tipo A, administrado en el alimento.

Para el control de la enteropatia proliferativa porcina (EPP o íatila) relacionada con *Lawsonia intracellularis*, cuando es tratada inmediatamente con TYLAN®, artículo medicado tipo A, administrado en el alimento.

Abejas: Para el control de Loque americana (*Fraenobacillus larvae*).

Fabricado por:
Elanco Animal Health
Una división de Eli Lilly and Company
Indianapolis, IN 46285, USA

081400USMOCKUP (JUN-2008)

AVISO DE RESIDUOS: Los pollos no deben faenarse para consumo dentro de las 24 horas posteriores al tratamiento. Los pavos no deben faenarse para consumo dentro de los cinco días siguientes al tratamiento. Los cerdos no deben faenarse para consumo dentro de las 48 horas posteriores al tratamiento. No debe usarse en gallinas ponedoras que producen huevos para el consumo humano.
Abejas: El fármaco debe suministrarse a principios de la primavera o del otoño para que las abejas lo consuman antes de que comience el principal flujo de miel, a fin de evitar la contaminación de la producción. Finalizar los tratamientos como mínimo 4 semanas antes del flujo principal de miel.

Evitar el contacto con la piel humana.
 La exposición a la tiosina puede provocar sarpullido.

Fabricado por:
 Elanco Animal Health
 Una división de Eli Lilly and Company
 Indianapolis, IN 46285, USA
 Almacenar a temperatura ambiente; 25 °C (77 °F).
 (Temperatura máxima permitida 40°C).
 Evitar la exposición a la humedad.
 Medicamento restringido (California) -
 Usar únicamente según las instrucciones.
 NADA n.º 13-076, aprobado por la FDA
 Para informar efectos adversos, obtener información médica o
 información adicional sobre el producto, llame al 1-800-428-4441.
 *Elanco®, Tylan® y la barra diagonal de color son marcas registradas de
 Eli Lilly and Company.

8

AF1300-67X
 ELANCO

Tylan® Soluble

Tylosin Tartrate

For Use in Chickens, Turkeys, Swine and Honey Bees Only
 Equivalent to 100 g tylosin base

An Antibiotic

Indications

Chickens: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of CRD associated with *Mycoplasma gallisepticum* sensitive to tylosin at the time of vaccination or other stress in chickens. For the control of CRD associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens.

Turkeys: For maintaining weight gain and feed efficiency in the presence of infectious ailments associated with *Mycoplasma gallisepticum* sensitive to tylosin.

Swine: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*.

For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by TYLAN Type A medicated article in feed.

For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by TYLAN Type A medicated article in feed.

1

PAGE 2

PAGE 7

Honey Bees: For the control of American Foulbrood (*Paenibacillus larvae*).

Ingredients

Tylosin (as tylosin tartrate) 100 g

Mixing Directions

Chickens and Turkeys: To assure thorough dissolution, place the Tylen (contents of this jar) in a mixing container and add one gallon of water (3780 mL) to the material. Mix this concentrated solution with water to make 50 gallons (189 liters) of treated drinking water.

Swine: To assure thorough dissolution, place the Tylen (contents of this jar) in a mixing container and add one gallon of water (3780 mL) to the material. Mix this concentrated solution with water to make 400 gallons of treated drinking water resulting in 250 mg/gallon.

Honey Bees: Mix 200 mg tylosin in 20 g confectioners/powdered sugar. Use immediately.

When directed to mix the product with water, always add the water to the powder. Do not pour the powder into the water. Prepare a fresh Tylen solution every three days. When mixing and handling tylosin, use protective clothing and impervious gloves.

Directions for Use

Chickens should be treated for three days; however, treatment may be administered for one to five days depending upon severity of infection. Treated chickens must consume enough medicated water to provide 50 mg per pound of body weight per day. Only medicated water should be available to the birds.

Los pavos deben tratarse durante tres días; sin embargo, el tratamiento puede administrarse de dos a cinco días, según la gravedad de la infección. Los pavos tratados deben consumir suficiente agua con medicamento para lograr una dosis de 60 mg por libra de peso corporal por día. Las aves deben beber únicamente agua con medicamento.

Cerdos: Para el tratamiento y control de disentería porcina, medicar con 250 mg de tilosina por galón en el agua para beber entre 3 y 10 días, según la gravedad de la infección. Como alternativa, medicar con 250 mg de tilosina por galón en agua para beber entre 3 y 10 días, y luego entre 40 y 100 g de tilosina por tonelada de alimento completo (alimento medicado tipo C elaborado por Tylen, artículo medicado tipo A) entre 2 y 8 semanas.

Para el control de la enteropatía proliferativa porcina (EPP o ileitis), medicar con 250 mg de tilosina por galón en agua para beber entre 3 y 10 días, y luego entre 40 y 100 g de tilosina por tonelada de alimento integral (alimento medicado tipo C elaborado por Tylen, artículo medicado tipo A) entre 2 y 8 semanas.

Los cerdos deben consumir suficiente agua con medicamento para lograr una dosis terapéutica. Deben beber únicamente agua con medicamento (250 mg de tilosina por galón) mientras se utiliza TYLAN Soluble.

Las colonias de abejas deben recibir tres tratamientos administrados en forma de polvo en azúcar en polvo/azúcar glass. La dosis de 200 mg se aplica (espolvoreada) sobre las barras superiores de la cámara de cría una vez por semana, durante 3 semanas.

Importante: El grado de sensibilidad a cualquier quimioterapia varía en los organismos. Si no se observara ninguna mejoría después del tratamiento recomendado, se deberá confirmar nuevamente el diagnóstico y la sensibilidad.

NO APTO PARA USO EN SERES HUMANOS

PAGE 6

PAGE 3

Abejas: Para el control de Loque americana (*Paenibacillus larvae*).
Ingredientes

Tilosina (como extracto de tilosina) 100 g

Instrucciones de mezcla

Pollos y pavos: Para asegurar su completa disolución, colocar Tylan (el contenido de este frasco) en un recipiente para mezclar y agregar un galón de agua (3790 ml). Mezclar esta solución concentrada con agua para obtener 50 galones (189 litros) de agua tratada para beber.

Cerdos: Para asegurar su completa disolución, colocar Tylan (el contenido de este frasco) en un recipiente para mezclar y agregar un galón de agua (3790 ml). Mezclar esta solución concentrada con agua para obtener 400 galones de agua tratada para beber lo que dará como resultado 250 mg/galón.

Abejas: Mezclar 200 mg de tilosina en 20 g de azúcar en polvo/azúcar glass. Utilizar de inmediato.

Quando se mezcle el producto con el agua, agregar siempre el agua al polvo. No verter el polvo en el agua. Preparar una nueva solución de Tylan cada tres días. Cuando se mezcle y manipule tilosina, usar ropa de protección y guantes impermeables.

Instrucciones de uso

Los pollos deben tratarse durante tres días; sin embargo, el tratamiento puede administrarse de uno a cinco días, según la gravedad de la infección. Los pollos tratados deben consumir suficiente agua con medicamento para lograr una dosis de 50 mg por libra de peso corporal por día. Las aves deben beber únicamente agua con medicamento.

Turkeys should be treated for three days; however, treatment may be administered for two to five days depending upon severity of infection. Treated turkeys must consume enough medicated water to provide 60 mg per pound of body weight per day. Only medicated water should be available to the birds.

Swine For the treatment and control of swine dysentery medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, depending upon severity of infection. Alternatively, medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g tylosin per ton of complete feed (Type C medicated feed manufactured from TYLAN Type A medicated article) for 2 to 6 weeks.

For control of porcine proliferative enteropathies (PPE, ileitis) medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g of tylosin per ton of complete feed (Type C medicated feed manufactured from TYLAN Type A medicated article) for 2 to 6 weeks.

Swine must consume enough medicated water to provide a therapeutic dose. Only medicated water (250 mg tylosin per gallon) should be available while medicating with TYLAN Soluble.

Honey Bee colonies should receive three treatments administered as a dust in confectioners/powdered sugar. The 200 mg dose is applied (dusted) over the top-bars of the brood chamber once weekly for 3 weeks.

Notice: Organisms vary in their degree of susceptibility to any chemotherapeutic. If no improvement is observed after recommended treatment, diagnosis and susceptibility should be reconfirmed.

NOT FOR HUMAN USE

RESIDUE WARNING: Chickens must not be slaughtered for food within 24 hours after treatment. Turkeys must not be slaughtered for food within five days after treatment. Swine must not be slaughtered for food within 48 hours after treatment. Do not use in layers producing eggs for human consumption. Honey Bees: The drug should be fed early in the spring or fall and consumed by the bees before the main honey flow begins, to avoid contamination of production honey. Complete treatments at least 4 weeks prior to main honey flow.

Avoid contact with human skin. Exposure to tylosin may cause a rash.

Manufactured For:
Elanco Animal Health
A Division of Eli Lilly and Company
Indianapolis, IN 46285, USA
Store at Room Temperature, 25°C (77°F).
(Excursions Permitted to 40°C).
Avoid Moisture.

Restricted Drug (California) - Use Only as Directed.
NADA # 13-076, Approved by FDA

To report adverse effects, access medical information, or obtain additional product information, call 1-800-428-4441.

*Elanco®, Tylan® and the diagonal color bar are trademarks of Eli Lilly and Company.

AF1300-67X
EJANCO*

Tylan® Soluble

Tartrato de tilosina

Para uso exclusivo en pollos, pavos, cerdos y abejas

Equivalente a 100 g de tilosina base

Un antibiótico

Indicaciones

Pollos: Como ayuda en el tratamiento para enfermedades respiratorias crónicas (CRD) relacionadas con *Mycoplasma gallisepticum* sensible a la tilosina en pollos de engorde y de reemplazo. Para el control de CRD relacionadas con *Mycoplasma gallisepticum* sensible a la tilosina al momento de la vacunación o de otra causa de estrés en pollos. Para el control de CRD relacionadas con *Mycoplasma synoviae* sensible a la tilosina en pollos de engorde.

Pavos: Para mantener el aumento de peso y la eficiencia del alimento en presencia de sinusitis infecciosa relacionada con *Mycoplasma gallisepticum* sensible a la tilosina.

Cerdos: Para el tratamiento y el control de la disentería porcina relacionada con *Brachyspira hyodysenteriae*.

Para el tratamiento y el control de la disentería porcina relacionada con *Brachyspira hyodysenteriae* cuando es tratada inmediatamente con TYLAN®, artículo medicado tipo A, administrado en el alimento.

Para el control de la enteropatía proliferativa porcina (EPP o ileítis) relacionada con *Lawsonia intracellularis*, cuando es tratada inmediatamente con TYLAN®, artículo medicado tipo A, administrado en el alimento.

BASE LABEL

ELANCO® AF1300



Equivalent to 100 g tylosin base
An Antibiotic

NADA #13-076, Approved by FDA
Indications

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