SUROLAN- miconazole nitrate, polymyxin b sulfate, and prednisolone acetate suspension/ drops
Vetoquinol USA Inc

Surolan®

otic suspension
(miconazole nitrate, polymyxin B sulfate, prednisolone acetate)

Rx

Antifungal, antibacterial and anti-inflammatory
For otic use in dogs only

CAUTION

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

DESCRIPTION

SUROLAN contains 23 mg/mL miconazole nitrate, 0.5293 mg/mL polymyxin B sulfate and 5 mg/mL prednisolone acetate. Inactive ingredients are colloidal silicon dioxide and liquid paraffin.

INDICATIONS

SUROLAN is indicated for the treatment of canine otitis externa associated with susceptible strains of yeast (*Malassezia pachydermatis)* and bacteria (*Staphylococcus pseudintermedius*).

DOSAGE AND ADMINISTRATION

Shake well before use.

The external ear should be thoroughly cleaned and dried before the initiation of treatment. Verify that the eardrum is intact. Instill 5 drops of SUROLAN in the ear canal twice daily and massage the ear. Therapy should continue for 7 consecutive days.

CONTRAINDICATIONS

SUROLAN is contraindicated in dogs with suspected or known hypersensitivity to miconazole nitrate, polymyxin B sulfate, or prednisolone acetate.

Do not use in dogs with known perforated tympanum. Do not use with drugs known to induce ototoxicity.

WARNINGS

Not for use in humans. Keep this and all drugs out of reach of children.

ANIMAL WARNINGS

Do not administer orally.

For otic use only.

PRECAUTIONS

Before instilling any medication into the ear, examine the external ear canal thoroughly to be certain the tympanic membranes are not ruptured.

If overgrowth of non-susceptible bacteria or fungi occurs, treatment should be discontinued and appropriate therapy instituted.

Long-term use of topical otic corticosteroids has been associated with adrenocortical suppression and iatrogenic hypoadrenalcorticism in dogs.

The safe use of SUROLAN in dogs used for breeding purposes, during pregnancy, or in lactating bitches, has not been evaluated.

ADVERSE REACTIONS

In the field study, 161 dogs treated with SUROLAN were included in the safety database. Two dogs experienced reduced hearing at the end of treatment; on follow-up one dog had normal hearing capacity while the other case was lost for follow-up. The owner of another dog reported that on day 4 of treatment, build-up of the medication decreased the dog's hearing. At the end of treatment, this dog had normal hearing as assessed by the investigator. Residue build-up was reported in 1 dog and pain upon drug application in another dog.

A total of 161 dogs treated with the active control was included in the safety database and adverse reactions were reported in 8 dogs treated with the active control. One dog experienced reduced hearing at the end of treatment. Residue build-up was noted in 1 dog. Four dogs vomited during treatment, 1 dog showed red pustules on the pinna and head shaking was observed in another dog.

Foreign market experience: the following adverse events were reported voluntarily during post-approval use of the product in foreign markets: deafness, reduced hearing, topical hypersensitivity reactions and red blisters on pinna.

For a copy of the Material Safety Data Sheet (MSDS), for technical assistance or to report adverse reactions call Vétoquinol USA Inc. at 1-800-835-9496.

PHARMACOLOGY

By virtue of its 3 active ingredients, SUROLAN has antibacterial, antifungal, and anti-inflammatory activity. **Polymyxin B sulfate** is a broad-spectrum polypeptide antibiotic with activity against both Gram-positive and Gram-negative species. **Miconazole nitrate** is a synthetic imidazole derivative with antifungal activity and antibacterial activity against Gram-positive bacteria. Moreover, synergistic effects between miconazole nitrate and polymyxin B sulfate have been demonstrated in an *in vitro* study[(1)]. **Prednisolone acetate** is a glucocorticoid with anti-inflammatory activity. A study performed using an experimentally-induced model of ear inflammation in mice demonstrated the effectiveness of prednisolone acetate in treating ear inflammation either alone or in combination with the other active ingredients of SUROLAN[(2)].

MICROBIOLOGY

The compatibility and additive effect of each of the components in SUROLAN was demonstrated in a component effectiveness and non-interference study. An *in vitro* study of organisms collected from clinical cases of otitis externa at a veterinary teaching hospital and from dogs enrolled in the clinical effectiveness study for SUROLAN determined that polymyxin B sulfate and miconazole nitrate inhibit the growth of bacteria and yeast commonly associated with canine otitis externa. Furthermore, a synergistic effect of the two antimicrobials was demonstrated. The addition of prednisolone acetate to the combination did not impair antimicrobial activity to any clinically-significant extent.

ANIMAL SAFETY

The following adverse reactions were reported in a study when SUROLAN was administered at 1X, 3X and 5X for 42 consecutive days (6 times the recommended treatment duration) in laboratory Beagles: hypersensitivity reactions which included mild erythema and hyperemia, painful and sensitive ear canals on examination, changes in hematology, clinical chemistry and urinalysis values consistent with the systemic absorption of topical corticosteroids, and veterinary observations of pale ear canals.

EFFECTIVENESS

Of 337 dogs enrolled in the field study, 176 dogs were included in the effectiveness database; 91 were treated with SUROLAN and 85 were treated with an FDA-approved active control. Clinical evaluations of otitis externa included pain/discomfort, swelling, redness, and exudate. A non-inferiority evaluation was used to compare SUROLAN with the active control with respect to each clinical sign of otitis externa and overall clinical improvement. SUROLAN was determined to be non-inferior to treatment with the active control for otitis externa. *Malassezia pachydermatis* and *Staphylococcus pseudintermedius* were identified pre-treatment in at least 10 cases that were clinically responsive to SUROLAN.

Table 1. Mean Percentage of Improvement in Clinical Signs of Otitis Externa

Clinical sign	SUROLAN N=91	Active control N=85
Pain/discomfort	94.4%	91.7%
Swelling	89.1%	90.5%
Redness	91.2%	86.1%
Exudate	83.1%	82.1%
Overall	96.7%	95.2%

HOW SUPPLIED

SUROLAN is available in 15 mL and 30 mL plastic dispensing bottles with applicator tip for otic use.

STORAGE AND HANDLING

Store at or below 25 °C (77 °F).

NADA 141-298, Approved by FDA.

Manufactured for Vétoquinol USA Inc. by:
Janssen Pharmaceutica NV
Turnhoutseweg 30
B-2340 Beerse
Belgium

Date of most recent labeling revision: 09/2009

US - 973772

REFERENCES

1. Pietschmann S. et al. (2009)
Synergistic effects of miconazole and polymyxin B on microbial pathogens.

Veterinary Research Communications 33(6), 489-505
2. Bolinder A. et al. (2006)
In vivo efficacy study of the anti-inflammatory properties of Surolan
The Canadian Journal of Veterinary Research 70, 234-236

PRINCIPAL DISPLAY PANEL - 15 mL Box

NDC 17030-947-15

Surolan®

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(miconazole nitrate,
polymyxin B sulfate,
prednisolone acetate)

15mL

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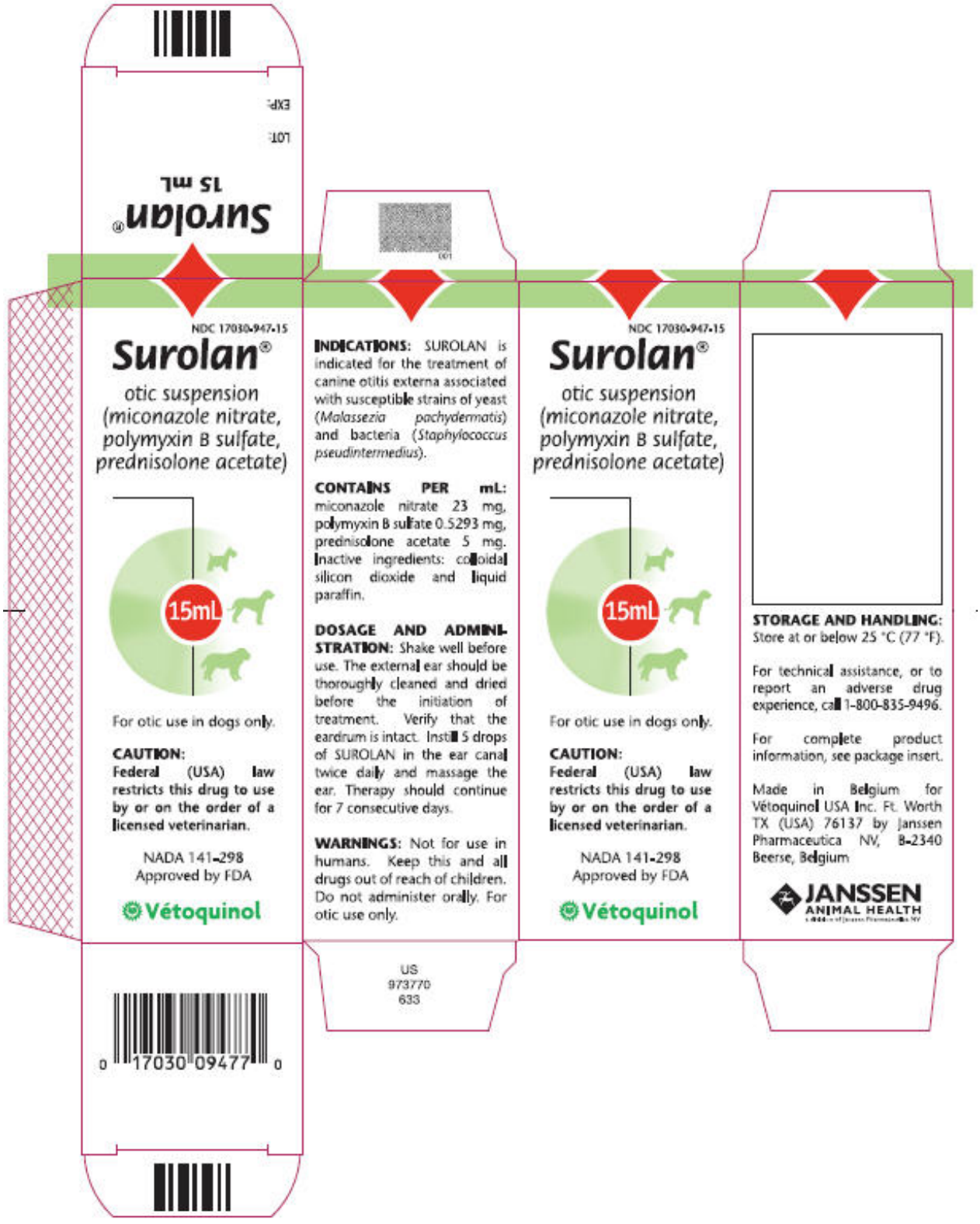
NADA 141-298
Approved by FDA

Vétoquinol



SUROLAN

miconazole nitrate, polymyxin b sulfate, and prednisolone acetate suspension/ drops

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:17030-947
Route of Administration	AURICULAR (OTIC)		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
miconazole nitrate (UNII: VW4H1CYW1K) (miconazole - UNII:7NNO0D7S5M)	miconazole nitrate	23 mg in 1 mL
polymyxin B sulfate (UNII: 19371312D4) (polymyxin B - UNII:J2VZ07J96K)	polymyxin B sulfate	0.5293 mg in 1 mL
prednisolone acetate (UNII: 8B2807733D) (prednisolone - UNII:9PHQ9Y1OLM)	prednisolone acetate	5 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
paraffin (UNII: I9O0E3H2ZE)	

Product Characteristics			
Color	WHITE (opaque)	**Score**	
Shape		**Size**	
Flavor		**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:17030-947-15	1 in 1 BOX		
1		15 mL in 1 BOTTLE, WITH APPLICATOR		
2	NDC:17030-947-30	1 in 1 BOX		
2		30 mL in 1 BOTTLE, WITH APPLICATOR		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141298	12/30/2009	

Labeler - Vetoquinol USA Inc (106824209)

Establishment

Name	Address	ID/FEI	Business Operations
Jansen Pharmaceutica NV		370005019	MANUFACTURE

Revised: 12/2009 Vetoquinol USA Inc