SUPPLEMENTAL FREEDOM OF INFORMATION
SUMMARY

TASK® TABS
(DICHLORVOS)

NADA 048-271

Boehringer Ingelheim Vetmedica, Inc.
15th and Oak
P.O. Box 338
Elwood, KS 66024
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SUPPLEMENTAL
FREEDOM OF INFORMATION SUMMARY

1. GENERAL INFORMATION

A. NADA Number: 048-271

B. Sponsor: Boehringer Ingelheim Vetmedica, Inc. 15th & Oak PO Box 339 Elwood, Kansas 66024

C. Generic Name: Dichlorvos

D. Trade Name: TASK® Tabs 2, TASK® Tabs 5, TASK® Tabs 10 and TASK® Tabs 20

E. Marketing Status: A prescription (Rx) drug that includes the caution statement as follows:

Federal Law restricts this drug to use by or on the order of a licensed veterinarian.

F. Effect of Supplement: 1) To provide for the use of Task® Tabs in kittens not less than three months of age and in adult dogs.

2) To add two additional tablet sizes, TASK® Tabs 10 and TASK® Tabs 20.

2. INDICATIONS FOR USE

TASK Tabs (dichlorvos) is an anthelmintic product recommended for the removal and control of the roundworms (Toxocara canis, Toxocara cati, Toxascaris leonina) and hookworms (Ancylostoma caninum, Ancylostoma tubaeforme, Uncinaria stenocephala) occurring in the intestinal tract of dogs, puppies, cats and kittens. The drug is vermicide.

3. DOSAGE FORM, ROUTE OF ADMINISTRATION, RECOMMENDED DOSE

Dosage Form: Tablet
Route of Administration: Oral

Recommended Dosage: TASK® Tabs are administered as a single dose to provide 5 mg dichlorvos per pound body weight to dogs, puppies, cats, and kittens.

4. AND 5. EFFECTIVENESS AND SAFETY

The original NADA was approved May 30, 1973 Federal Register (38 FR 14166), prior to the requirement for preparation of a Freedom of Information Summary.

The data in the original approval were reevaluated to determine the safety and effectiveness of TASK® Tabs in kittens three to five months of age and adult dogs.

Clinical Study 1 in Dogs:

Investigator:

Dr. M. L. Sharp
Sharp Veterinary Research Hospital
Vernon, Texas

General Design:

(1) Purpose of Study: The purpose of this study was to make an assessment of the effectiveness and safety of Task® Tabs at the doses of 5 and 10 mg/lb of body weight in adult dogs (one to seven years old) and geriatric dogs (over seven years old).

(2) Test Animals: This study included 15 dogs over 60 pounds. Five geriatric dogs (over 7 years of age) were included in the study. Ten adult dogs (between 1 and 7 years of age) were included in the study. Two dogs in this study had roundworms. All of the dogs had hookworms.

Ten of the dogs were administered 250 mg once. This dose approximated 1X. Three of the dogs were administered two doses of 250 mg (given morning and evening). This dose approximated 2X. Two of the dogs were administered 500 mg once. This dose approximated 5X.

(3) Results:

The drug was 100 % effective in removing both nematodes. Effectiveness was based on reductions in egg per gram (epg) counts. There were no adverse reactions in noted in this study.
Conclusions:

The study demonstrated the effectiveness and safety of Task® Tabs in adult and geriatric dogs when administered at doses up to 5X.

Clinical Study 2 in Dogs:

Investigators: The fourteen investigators listed below generated data in adult dogs up to 50 lbs.

Dr. R. Billings  
Michigan Road Animal Hospital  
7720 Michigan Road  
Indianapolis, Indiana 46368

Dr. D. G. Carlson  
Carson Pet Hospital  
311 West Sunshine  
Springfield, Missouri 65804

Dr. C. Cullen  
730 S. Front Street  
Mankato, Minnesota 56001

Dr. E. P. Davis  
515 Clifton Terrace  
Carrolton, Georgia 30117

Dr. R. H. De Motte  
Oden Veterinary Clinic  
Highway 58 West  
Oden, Kansas 47562

Dr. R. J. Dogue  
429 North Maize Road  
Wichita, Kansas 67212

Dr. J. S. Elder  
Belmont Veterinary Clinic  
2900 Belmont Avenue  
Youngstown, Ohio 44505
Dr. K. S. Grady  
9211 Winston Road  
Cincinnati, Ohio 45231

Dr. A. D. Kaplan  
Arlington Veterinary Medical Center  
71 Massachusetts Avenue  
Arlington, Massachusetts 02174

Dr. Kipper  
Bloomington Veterinary Hospital  
P.O. Box 1480  
Bloomington, Indiana

Dr. C. B. Legget  
2921 South West Parkway  
Wichita Falls, Texas

Dr. L. E. Martin 111  
1411 North Olive Avenue  
Turlock, California 95380

Dr. S. L. Suarvari  
1701 Guintoli Lane  
Arcata, California 95521

Dr. J. W. Walson  
5816 Highway 15 South  
Southhaven, Mississippi 38671

General Design:

(1) Purpose of Study: The purpose of this study was to make an assessment of the effectiveness and safety of TASK® Tabs at the dose of 5 mg per pound body weight in adult dogs.

(2) Test Animals: The study included 171 dogs of various ages, sex, sizes and breeds. The majority of the dogs in the study were adult dogs (between 1 and 7 years old), weighing up to 50 pounds.
Measurements and Observations: To evaluate effectiveness, eggs per gram (epg) reduction rates and parasite clearance rates were determined. The parasite clearance rate was based upon the number of dogs actually cleared of parasites (egg counts to zero). Fecal counts were conducted both pre-treatment and post-treatment.

Results:

In this study, 171 dogs were treated for roundworm infections and 124 dogs were treated for hookworm infections.

**SUMMARY OF CANINE FIELD STUDY - ROUNDWORMS AND HOOKWORMS**

<table>
<thead>
<tr>
<th>Parasite</th>
<th>Clearance Rate</th>
<th>EPG Reduction Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roundworms (ascarids)</td>
<td>157/171 (91.2%)</td>
<td>549 to 17 (96.9%)</td>
</tr>
<tr>
<td>Hookworms</td>
<td>114/124 (91.9%)</td>
<td>348 to 16 (95.4%)</td>
</tr>
</tbody>
</table>

The adverse reactions recorded in the clinical trial were related to the cholinergic effects of the drug. The most common adverse reactions recorded were vomiting, excessive salivation, pupillary contraction, dyspnea, watery diarrhea, muscle fasciculations, abdominal pain, ataxia, and general weakness.

Conclusions:

The clinical field study demonstrated the effectiveness and safety of Task® Tabs in adult dogs when administered at a dose of 5 mg/lb of body weight.

**Critical Study in Dogs:**

Investigator:

D. K. Hass
Shell Chemical Company
San Ramon, California

General Design:

1. Purpose of Study: A critical test was conducted to evaluate the effectiveness of TASK® Tabs at the dose of 5 mg per pound body weight in young adult dogs.

2. Test Animals: The study included 25 young adult Beagle dogs.
Measurements and Observations: To evaluate effectiveness, feces were collected for 3 days after treatment and on the fourth day, the dogs were killed and a necropsy conducted for the purpose of collecting any remaining parasites in the gastrointestinal tract. The necropsy collections and fecal washings were then inspected for the recovery of all parasite populations, and the parasites were identified, counted and tabulated.

Results:

ROUNDWORMS AND HOOKWORMS EXPELLED

<table>
<thead>
<tr>
<th>Parasite</th>
<th>Number Expelled</th>
<th>% Expelled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxocara canis</td>
<td>141/141</td>
<td>100%</td>
</tr>
<tr>
<td>Toxascaris leonina</td>
<td>213/292</td>
<td>73%0</td>
</tr>
<tr>
<td>Ancylostoma caninun</td>
<td>147/151</td>
<td>97.4%</td>
</tr>
</tbody>
</table>

Conclusions:

The study demonstrated the effectiveness of TASK® Tabs for removal and control of roundworms and hookworms in adult dogs.

Clinical Study in Kittens (three to five months of age)

Investigators: Twelve clinical investigators participated in the clinical study.

The investigators were:

Dr. R. E. Billings  
Michigan Road Animal Hospital  
7720 North Michigan Road  
Indianapolis, Indiana 46368

Dr. D. G. Carlson  
Carson Pet Hospital  
311 West Sunshine  
Springfield, Missouri 65804

Dr. C. Cullen  
730 S. Front Street  
Mankato, Minnesota 56001
Dr. R. J. Dogue  
429 North Maize Road  
Wichita, Kansas 67212

Dr. J. S. Elder  
Belmont Veterinary Clinic  
2900 Belmont Avenue  
Youngstown, Ohio 44505

Dr. K. S. Grady  
9211 Winston Road  
Cincinnati, Ohio 45231

Dr. A. D. Kaplan  
Arlington Veterinary Medical Center  
71 Massachusetts Avenue  
Arlington, Massachusetts 02174

Dr. Kipper  
Bloomington Veterinary Hospital  
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Dr. C. B. Legget  
2921 South West Parkway  
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Dr. L. E. Martin 111  
1411 North Olive Avenue  
Turlock, California 95380

Dr. S. L. Suarvari  
1701 Guintoli Lane  
Arcata, California 95521

Dr. J. W. Walson  
5816 Highway 15 South  
Southhaven, Mississippi 38671
General Design:

(1) Purpose of the study: The purpose of the study was to make an assessment of the effectiveness and safety of Task® Tabs at the dose of 5 mg/lb of body weight in kittens.

(2) Test Animals: Forty-three kittens 3 to 5 months of age.

(3) Measurements and Observations: To evaluate the effectiveness, egg per gram (epg) reduction rates and parasite clearance rates were determined. The parasite clearance rate was based on the number of kittens actually cleared of parasites (egg counts to zero). Fecal counts were done both pre-treatment and post-treatment.

Results:

**SUMMARY OF FIELD STUDY IN KITTENS-ROUNDWORMS AND HOOKWORMS**

<table>
<thead>
<tr>
<th>Parasite</th>
<th>Clearance Rate</th>
<th>EPG Reduction Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roundworms (ascarids)</td>
<td>91%</td>
<td>95%</td>
</tr>
<tr>
<td>Hookworms</td>
<td>91%</td>
<td>94%</td>
</tr>
</tbody>
</table>

Typical signs of cholinesterase inhibition were observed in the study, but all the kittens recovered with no additional treatment.

Conclusions:

The study demonstrated the effectiveness and safety of Task® Tabs in kittens three to five months of age when administered at a dose of 5 mg/lb.

6. HUMAN FOOD SAFETY

Data on human safety pertaining to consumption of drug residues were not required for this supplemental NADA. The drug is to be labeled for use in dogs, puppies, cats and kittens, which are non-food animals.

7. AGENCY CONCLUSIONS

No new safety or effectiveness data were required to support this supplemental NADA. The data in the original approval were adequate to satisfy the requirements of Section 512 of the Act and Section 514 of the Implementing Regulations. The data demonstrate that Task® Tabs, when used under the labeled conditions of use, are safe and effective.
According to the Center’s supplemental approval policy (21 CFR 514.106), this is a Category 11 change. This supplement provides for additional tablet sizes and additional claims. Therefore, safety and effectiveness data from the original approval were reevaluated.

Task® Tabs are restricted to use by or on the order of a licensed veterinarian because professional expertise, especially the determination of the specific species of nematodes present, is required to make an accurate diagnosis. In addition, a veterinarian’s professional expertise is needed to determine if retreatment is necessary and to determine the importance of any adverse effects.

Attachments:

- Labeling:
- Package insert
- Immediate container label
Each tablet contains 100 mg dichlorvos.

Dosage: 1 tablet for each 20 lbs of body weight. Weigh each animal prior to dosing. Do not use Task Tabs (dichlorvos) in puppies under 10 days of age or under 1 lb of body weight or in kittens less than 3 months of age.

Warning: Keep out of reach of children. Between lab let withdrawal keep bottle tightly capped. This drug is a tranquilizer in birds, Atropine and 2-PAM are antidotal.

Caution: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

NADA 048-271. Approved by FDA.

Net Contents: 50 Tablets

Boehringer Ingelheim Vetmedica, Inc.
St. Joseph, MO 64506 U.S.A.

Code 617825
Pharmacology and Physiology Dosage Limitations with Task Tabs (dichlorvos), while as it is known, are due to the drug's action on the nervous system, whereas it depresses the enzyme acetylcholinesterase. This allows for an accumulation of the neurotransmitter acetylcholine at the neuronal junctions, with resultant overstimulation of the motor and parasympathetic fibers. The severity of this effect is directly related to the dose.

Study animals have shown no detectable drop in circulating (blood) cholinesterase activities when administered the recommended dosage of Task Tabs. Normal values are regained within five to ten days. Fifty ppm of undiluted dichlorvos in the ration of dogs for 40 consecutive days were required to effect a significant drop in red blood cell and plasma cholinesterase activities. Sixty days of 15 and 25 ppm continuous feeding of undiluted dichlorvos were required to cause comparable cholinesterase depressions. These drug levels did not produce visible signs of toxicity, and weight gains were not reduced.

The exact significance of plasma, red blood cells, and/or plasma cholinesterase depression is not known since animals have been observed to survive long periods of time in chronic toxicological studies with near normal levels of detectable circulating cholinesterase activity. Such measurements serve only to indicate that very small amounts of the intact drug are absorbed from the digestive tract.

Reproduction: Single or repeated recommended dosages of dichlorvos have been administered to bitches and queens in various stages of pregnancy, indicating no interference with gestation, parturition, or the subsequent performance of their offspring. Adult dogs have had chronic feeding of the drug for two years or more, through one or more generations, with no adverse effects on the overall reproductive scheme.

Task Tabs have been administered twice weekly to 15 strains of rats continuing throughout their gestation. Again, there was no apparent interference with gestation, parturition, or the health of the kittens.**

Pathology: The administration of varying dosages of dichlorvos for varying periods of time to dogs and cats produced minimal or no evidence histopathological changes in the organ or tissues. Occasionally large single dosages of the active ingredients in dogs and cats have caused hyperemia and congestion of the intestinal mucosa.

Postmortem examination of dogs and cats succumbing to lethal doses of Task Tabs have shown minimal gross pathology. Typical of the lesions seen are engorgement of intestinal vessels, inflammation and congestion of the intestinal mucosa with occasional hemorrhage, and congestion of the liver and lungs.

Recommended Dosage: Task Tabs (dichlorvos) are available in five tablet sizes, containing 10, 25, 50 and 100 mg dichlorvos respectively. The dose in dogs, puppies, cats, and kittens is 5 mg/dichlorvos per pound body weight. The product is designed for use in dogs, puppies, cats, and kittens according to the following table:

<table>
<thead>
<tr>
<th>Weight (lb)</th>
<th>Dosage Tablet Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10, 25, 50 mg</td>
</tr>
<tr>
<td>2</td>
<td>10, 25 mg</td>
</tr>
<tr>
<td>3</td>
<td>10, 25 mg</td>
</tr>
<tr>
<td>4</td>
<td>10, 25 mg</td>
</tr>
<tr>
<td>5</td>
<td>10, 25 mg</td>
</tr>
<tr>
<td>6</td>
<td>10, 25 mg</td>
</tr>
<tr>
<td>8</td>
<td>10, 25 mg</td>
</tr>
<tr>
<td>10</td>
<td>10, 25 mg</td>
</tr>
</tbody>
</table>

*Weight Erich Animal Prior to Dosing: The small tablet is scored. Accordingly, one-half of this tablet will treat 1 lb of body weight. Task Tabs should not be used in puppies under 10 days of age or under 1 lb body weight or in kittens less than 3 months of age. Pretreatment fasting is not necessary, although feeding simultaneously with the tablet dose may tend to hold the drug in the animal and reduce its effectiveness down the tract. Since the drug is not active against migrating tissue-phase larvae, a second treatment two to three weeks after the first is advisable.

Occasionally a dog, puppy, or kitten may show signs of emesis within 30 to 90 minutes after dosing. This initial vomiting should not be induced; the product's effectiveness against roundworms and hookworms is usually not altered. These subjects that do not show a negative fecal egg count within a few days, because of emesis or any other reason, may then be retreated with the drug. In clinical trials undetermined vomiting reported in up to 23% of the treated animals.

Dogs, puppies, cats, and kittens known to be maintained in high hookworm exposure environments are best treated with Task Tabs in advance of their clinical signs. Once hookworm disease has progressed to the clinical stage, then supportive therapy (Molybdenum) should precede withholding of the animal's usual food. If there is a chance for survival, the cause of accidental overdoses, atropine and 2-PAM are indicated.

Contraindications: Do not administer other anthelminthics concurrently with Task Tabs. Do not administer to dogs, puppies, cats, or kittens showing signs of constipation, mechanical blockage of the intestinal tract, impaired liver function, or to animals recently exposed to or showing signs of infectious disease. Do not use the product for animals simultaneously or within a few days before or after treatment with or exposure to cholinesterase-inhibiting drugs, pesticides, or cholinesterase inhibitors. Do not use in animals infected with O. circumcincta. Task Tabs are not recommended for use in animals other than dogs and cats.

Attention: Task Tabs (dichlorvos) used in the control of gastrointestinal nematodes of dogs, puppies, cats, or kittens are not a substitute for good sanitary practices, but rather should be used in conjunction with such practices. Treatment schedules with Task Tabs are at the discretion of the veterinarian. Dogs, puppies, cats, or kittens which are returned to parasite-contaminated areas will become reinfected. The rate of reinfection will be related to the life cycle of the parasite and the exposure level.

Warning: Keep out of reach of children. Between tablet withdrawal, keep bottle tightly capped. Store under refrigeration. This drug is a cholinesterase inhibitor and atropine and 2-PAM are indicated.

How Supplied: 10 mg dichlorvos/tablet and 25 mg dichlorvos/tablet, 100 tablets/bottle, 50 mg dichlorvos/tablet and 100 mg dichlorvos/tablet, 50 tablets/bottle.

Store under refrigeration (40°F). Between tablet withdrawal, the bottle must be tightly capped. Observe expiration dates.

References:
**Task Tabs**
(dichlorvos)
Antihelminthic for Dogs, Puppies, Cats and Kittens

For use in animals only.

Caution: Federal (U.S.A.) law restricts this drug to use by or on the order of a licensed veterinarian.

**Indications:** Task Tabs (dichlorvos) is an antihelminthic product recommended for the removal and control of roundworms (Toxocara canis, Toxascaris leonina), hookworms (Ancylostoma caninum, Ancylostoma braziliense) and hookworms (Uncinaria stenocephala) occurring in the intestinal tract of dogs, puppies, cats and kittens. The drug is vermifugal.

Rapidity of Action: Task Tabs have demonstrated extremely rapid vermifugal properties in two-month-old puppies. Death, unattached hookworms have been found in the small intestine within one hour following dosage. Parasite expulsion from cats and dogs generally begins within six hours and all practical purposes is complete within 48 hours following treatment.

**Toxicology:** The minimum lethal dosages for dogs and cats have been determined to be 45 mg/lb (IX) and 75 mg/lb (IX), respectively.

Profuse vomiting in multi-dose amounts of formulated drug which cannot be administered in acute toxicity studies.

The cardinal signs of toxicity from dichlorvos overdose in dogs and puppies are excessive salivation, pupillary constriction, dyspnea, retching, emesis, watery diarrhea, muscular fasciculations, evidence of abdominal pain, anorexia, and general weakness progressing toward paralysis. Puppies and kittens high dosages of the drug will cause apprehension and convulsive muscular activity in addition to the other cholinergic signs. Task Tabs were evaluated in a clinical field trial in three to five-month-old kittens. The kittens were administered a single dose of 0.5 mg/kg body weight (IX) and typical signs of cholinesterase inhibition were observed, but all signs were reversible. All kittens survived the study without medical intervention.

This formulation provides every rapid release of the active ingredient; when the tablets are given at elevated multi-dose amounts of toxicity general signs regress without incident therapy in two to four hours.

Task Tabs were administered to 10 puppies at three times the therapeutic dose, twice weekly from three weeks of age through six weeks of age, in another group of 10 puppies given three times a week. Emesis was common (23%) but when compared to control and placebo-treated groups, there were no detrimental effects noted on survival, growth, or on the hematology and serum chemistry measured. After six weeks of continuous therapy, average RBC acetylcholinesterase activity was depressed 30% below the controls, whereas plasma cholinesterase activity in some puppies had rebounded to twice that of the controls. In another treatment group, one of seven puppies succumbed after six continuous weeks of six times the therapeutic dosage, given twice weekly. The incidence of emesis and the reduction in cholinesterase activity literature dogs were comparable to puppies.

Task Tabs were administered to young adult cats at three times the recommended therapeutic dose twice weekly for three weeks. Adverse reactions were minimal (<5% headache) and when compared to control cats, there were no detrimental effects noted on general clinical condition, or on the hematology and serum chemistry measured. At the conclusion of the test average whole blood cholinesterase activity was depressed 15 to 20% below the control values. Some of these test cats became pregnant, and the Task Tabs treatments were continued throughout their gestation; no reproductive problems were encountered. in = 4-6

Single or repeated (weekly) recommended dosages of Task Tabs to puppies and cats have not produced abnormal changes in the erythrocyte count, leukocyte count, leukocyte differential, hemoglobin, hematoctrit, blood glucose, blood urea nitrogen, alkaline phosphatase, aspartate dehydrogenase, serum glutamic oxalacetic transaminase, serum cholesterol, serum urea acid, serum calcium, phosphorus, magnesium, phosphorus, urine total protein.

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