REBALANCE ANTIPROTOZOAL- sulfadiazine and pyrimethamine suspension
Pegasus Laboratories, Inc

ReBalance Antiprotozoal Oral Suspension

Approved by FDA under NADA # 141-240

ReBalance® Antiprotozoal Oral Suspension (sulfadiazine and pyrimethamine)

CAUTION:

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

DESCRIPTION:

ReBalance Antiprotozoal Oral Suspension is supplied in 946.4 mL (1 quart) bottles. Each mL of ReBalance Antiprotozoal Oral Suspension contains 250 mg sulfadiazine (as the sodium salt) and 12.5 mg of pyrimethamine.

INDICATIONS:

ReBalance Antiprotozoal Oral Suspension is indicated for the treatment of horses with equine protozoal myeloencephalitis (EPM) caused by *Sarcocystis neurona*.

DOSAGE AND ADMINISTRATION:

ReBalance Antiprotozoal Oral Suspension is to be administered at a dose of 20 mg/kg sulfadiazine and 1 mg/kg pyrimethamine daily or 4 mL of ReBalance Antiprotozoal Oral Suspension per 110 lb. (50 kg) of body weight once per day. The duration of treatment is dependent upon clinical response, but the usual treatment regimen ranges from 90 to 270 days.

Administer orally by suitable dosing syringe at least one hour prior to feeding with hay or grain. Insert nozzle of syringe through the interdental space and deposit the dose on the back of the tongue by depressing the plunger. Shake well before use.

CONTRAINDICATIONS:

The use of ReBalance Antiprotozoal Oral Suspension in contraindicated in horses with known hypersensitivity to sulfonamide drugs or pyrimethamine.

WARNINGS:

For use in horses only. Do not use in horses intended for human consumption. Not for human use. Keep out of the reach of children.

PRECAUTIONS:

Prior to treatment with ReBalance Antiprotozoal Oral Suspension, EPM should be distinguished from the diseases that may cause ataxia in horses. injuries or lameness may also complicate the evaluation of an animal with EPM. In most instances, ataxia due to EPM is asymmetrical and affects the front and/or the hind limbs.

Treatment may cause generalized bone marrow suppression, anemia, leukopenia, neutropenia and thrombocytopenia. A complete blood count (CBC) should be performed monthly to monitor horses for development of these conditions. The administration of the drug may need to be discontinued and/or treatments for bone marrow suppression initiated.

Worsened neurologic deficits (treatment crisis) may be observed during a period beginning with the first few days of treatment with ReBalance Antiprotozoal Oral Suspension and ranging out to 5 weeks. This neurologic deficit exacerbation may be the result of an inflammatory reaction to the dying parasites in the CNS tissue.

The safe use of ReBalance Antiprotozoal Oral Suspension in horses used for breeding purposes during pregnancy, or in lactating mares has not been evaluated. The safety of ReBalance Antiprotozoal Oral Suspension with concomitant therapies in horses has not been evaluated.

ADVERSE REACTIONS:

Seventy-five horses (37 horses in the 1X group, 38 horses in the 2X group) that were treated with test article for at least 90 days were evaluated for adverse reaction.

Bone marrow suppression: Anemia: ReBalance Antiprotozoal Oral Suspension administration caused overall anemia (classification of anemia based on HBC, Hgb, and PCV/HCT values in 12% of the observations in the 1X group and 21% of the 2X group. In the 1X group, anemia was noted in in 22%, leukopenia in 19%, neutropenia in 5% and thrombocytopenia in 3% of the cases. In the 2X group, anemia was noted in 58%, leukopenia in 55%, neutropenia in 29% and thrombocytopenia in 5% of the cases. The incidence of bone marrow suppression in the 2X treatment group was two or more times that of the 1X group and the degree of suppression was more serious (mild to severe vs. mild to moderate). because of these blood dyscrasias, test article was interrupted over four times more often in horses treated at the 2X dosage than those treated 1X, Although both groups were off treatment for about the same amount of time (approximately 20% of the treatment period). In some instances of bone marrow suppression, diet was supplemented with folinic acid.

GI: Anorexia was observed in two horses in the 1X group and one hose in the 2X group. One horse in the 1X group and one horse in the 2X group were observed to be off feed. Observation of Anorexia and decreased appetite occurred predominately during the first 90 days of the treatment period. Observation of anorexia/decreased appetite in two of the above-referenced cases were due to unrelated illnesses. Loose stools were observed in three horses in the 1X group and five in the 2X group. The majority of these observations occurred in the first thirty days of treatment .

Diarrhea was observed in one horse in the 2X group on Day 4 of the study. The appearance of loose stool/diarrhea observations were self-limiting and resolved without treatment or discontinuation of test article. Brief, mild colic was observed in the three

cases (one in the 1X group and two in the 2X group). colic was treated conservatively or not at all and resolved without sequelae.

Integument: Urticaria was observed in one horse in the 1X group and two horses in the 2X group. One horse was treated topically, two were untreated. All cases resolved without sequelae.

Treatment crisis: (marked worsening of the neurological condition) was reported in one horse in the 1X treatment group.

Depression/lethargy was observed infrequently occurred during the early part of the study in both groups and was primarily associated with the EPM syndrome. In one case, depression was associated with acute onset of a liver disorder.

Seizure: One horse in the 1X treatment group suffered from seizures. Seizure activity may be associated CNS damage from EPM.

CLINICAL PHARMACOLOGY:

Sulfonamides (a specific group of antimicrobial agents) and pyrimethamine are two different antimicrobial agents which inhibit folic acid synthesis at two different sites, in the same synthetic pathway. The combination of a sulfonamide and pyrimethamine is synergistic with the drug combination having an antiprotozoal effect.

EFFECTIVENESS SUMMARY:

A field effectiveness study was conducted at eight sites with eight investigators across the the United States. The study was conducted using historical controls. In the study each animal's response to treatment was compared to its pre-treatment values. The following standardized overall neurological dysfunction (OND) scale was used to grade the horses:

0 = Clinically normal. No detectable dysfunction.

1 = Slightly deficit. Dysfunction barely perceptible.

2 = Moderate deficit. Dysfunction easily detectable.

3 = Marked deficit. Dysfunction strikingly conspicuous.

4 = Severe deficit. profound dysfunction.5 = Recumbent.

ninety-seven horses were randomly assigned one of two treatment groups and administered a daily oral dose of ReBalance Antiprotozoal Oral Suspension for a minimum of 90 days. The two treatment groups were as follows:

(1) 1X labeled dose, 20 mg/kg sulfadiazine and 1 mg/kg pyrimethamine (48 horses); or

(2) 2X dose, twice the labeled dose, 40 mg/kg sulfadiazine and 2 mg/kg pyrimethamine (40 horses).

A physical examination and neurological evaluation and complete blood profile were conducted at the end of each 30-day treatment period for the first 90 days of treatment.

At the end of the 90-day treatment period, a videotape recording of the neurological

condition and CSF and serum sample immunoblot and protein electrophoresis analysis were made. Based on the degree of clinical improvement and results of the CSF immunoblot analysis on test day 90 treatment in 30 day increments up to a period of 180 days was continued. In fourteen cases, the treatment was extended beyond 180 days (up to 270 days). A 30 day follow-up evaluation was made following cessation of treatment.

Treatment success was defined as: (1) horse that became CSF Western Blot Test negative with or without clinical improvement; and (2) a horse that remained CSF Western Blot Positive but demonstrated marked clinical improvement (two or more grade improvement from baseline OND score).

Only the 1X dose was evaluated for effectiveness due to the toxicity (bone marrow suppression) seen in the 2X dose. of the forty eight horses assigned to the 1X group, 26 horses completed the study. Based on the improvement in the OND scores and/or a negative CSF immunoblot, 16 out of the 26 horses (61.5%) were considered successes. Five of the 26 horses (19.2%) , had a negative CSF immunoblot by day 150 of the study. Three of these five horses were also clinically successes based on the improvement in OND scores. Fourteen of the 26 horses (53.8%) were corroborated as successes by masked expert evaluation and videotapes.

ANIMAL SAFETY:

ReBalance Antiprotozoal Oral Suspension was administered to ten horses (5 males and 5 females) ata dosage of 8 mL/50kg (110 lbs) a day (2X the labeled dose) for 92 days. Four horses (2 males and 2 females) were untreated controls.

Complete physical examinations, CBCs and serum chemistry values were determined on test days (TD) minus 14, TD minus 7, TD 0, biweekly throughout the 92 day treatment period and 14 and 29 days following the end of treatment.

Declines in RBC, HCT, Hgb and PCV were greater in the treated group and reached statistical significance. Twenty-nine days after cessation of treatment, blood parameter values returned to baseline levels. No clinical signals of anemia were observed in either group.

Most serum chemistry values remained within normal limits throughout the study in both groups. Alkaline phosphatase (ALP) values were evaluated (slightly above the upper end of the normal range) in three treated horses on study day 84 and 105.

Loose stool, along with infrequent diarrhea, were noted in the treatment group. The conditions were transient and required no medical intervention.

A depressed appetite of 1 to 2 days duration occurred infrequently in all but one of the treated horses. One horse became anorexic and required a change in diet.

ReBalance Antiprotozoal Oral Suspension administered at 2X the recommended label for 92 days resulted in clinical signs of toxicity including transient anemia and loose stools; however, medical intervention was not necessary,

STORAGE:

Store at 20°C-25°C (68°F-77°F), excursions permitted between 15°C-30°C (59°F-86°F).

Protect from freezing.

HOW SUPPLIED:

Each mL of ReBalance Antiprotozoal Oral Suspension contains 250 mg of sulfadiazine (as the sodium salt) and 12.5 mg pyrimethamine and is available in 946.4 mL (1 Quart) multiple dose child resistant, screw-capped bottles.

GENERAL INFORMATION:

For a Safety Data Sheet (SDS) or to report Adverse Reactions, call Pegasus Laboratories, Inc. at 1-800-874-9764.

Manufactured by:

Pegasus Laboratories, Inc.

Employee Owned

Pensacola, FL 32514, USA

01-2023

PRINCIPAL DISPLAY PANEL:

NDC #49427-247-11

ReBalance

Antiprotozoal Oral Suspension

(sulfadiazine and pyrimethamine)

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

Shake Well before Each Use

For oral Use in Horses Only

Keep Out of Reach of Children

Treatment for Equine Protozoal Myeloencephalitis (EPM) In Horses

Approved by FDA under NADA # 141-240

PRN Pharmacal, Pegasus Laboratories, Inc.

NET CONTENTS: 946.4 mL (One Quart)

Add image transcription here...

REBALANCE ANTIPROTOZOAL

sulfadiazine and pyrimethamine suspension

Product Information			
Product Type	PRESCRIPTION ANIMAL DRUG	**Item Code (Source)**	NDC:49427-247
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
SULFADIAZINE SODIUM (UNII: 84CS1P306F) (Sulfadiazine - UNII:0N7609K889)	Sulfadiazine	250 mg in 1 mL
Pyrimethamine (UNII: Z3614QOX8W) (Pyrimethamine - UNII:Z3614QOX8W)	Pyrimethamine	12.5 mg in 1 mL

Product Characteristics			
Color		**Score**	
Shape		**Size**	
Flavor	ALMOND	**Imprint Code**	
Contains			

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:49427-247-11	12 in 1 CARTON		
1		946 mL in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NADA	NADA141240	11/05/2004	

Labeler - Pegasus Laboratories, Inc (108454760)

Registrant - Pegasus Laboratories, Inc (108454760)

Establishment

Name	Address	ID/FEI	Business Operations
Pegasus Laboratories, Inc		108454760	manufacture, analysis, label

Revised: 12/2023 Pegasus Laboratories, Inc