

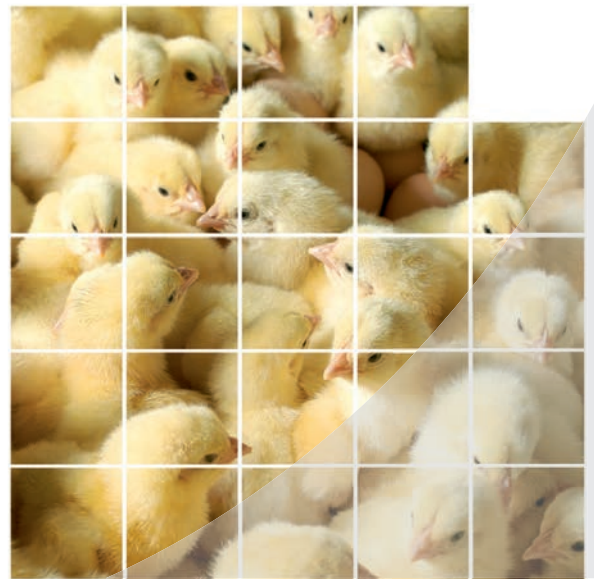
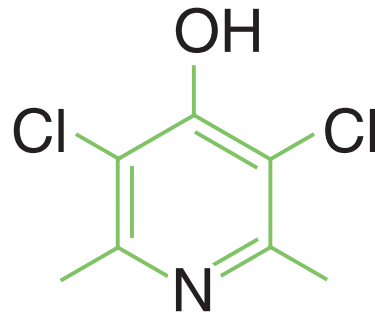
Highly effective in the prevention of coccidiosis



COXIPOL 25% Granular Premix

INTRODUCTION

Coxipol 25% is a non-dusting, granular premix which contains 250mg/g of the active ingredient clodipol. It was first marketed in 1968 and was proven safe and effective for more than two decades in the field of coccidiosis prevention. Today, poultry producers are pleading for additional coccidiosis solutions, which is one of the reasons for the revival of historically successful products to be applied in rotation programs.



STRUCTURE AND ACTIVITY

Coxipol 25% is the Huvepharma trademark for a coccidiostat product containing the active ingredient 3,5-dichloro-2,6-dimethyl-4-pyridinol (clopidol), which is a pyridone-derivative. It is effective against coccidiosis caused by *Eimeria tenella*, *E. acervulina*, *E. maxima*, *E. necatrix*, *E. brunetti*, *E. mitis* and *E. praecox*.

MODE OF ACTION

On cellular level, clopidol leads to an inhibition of the development of sporozoites and trophozoites of the mentioned *Eimeria* species.

PRODUCT CATEGORIZATION AND USE

Coxipol 25% is available as granular premix. It is a non-dusting feed additive, intended to be continuously administered in feed for the prevention of caecal and intestinal coccidiosis in broilers and replacement pullets up to 16 weeks of age. It is advised to use the product in one grow-out per year (in starter, grower or finisher feed) as part of rotation programme. Coxipol 25% is suitable for feed manufacturing use only.

INDICATIONS FOR USE

Broilers & pullets:

- Coxipol 25% is indicated for anticoccidial use against coccidiosis caused by *Eimeria tenella*, *E. acervulina*, *E. maxima*, *E. necatrix*, *E. brunetti*, *E. praecox* and *E. mitis*
- Broilers: feed containing clopidol should be fed continuously as the only ration from the time chicks are placed in floor pens for meat, taking into account the withdrawal time of 2 days.
- Pullets: feed containing clopidol should be fed continuously as the only ration up to 16 weeks of age.



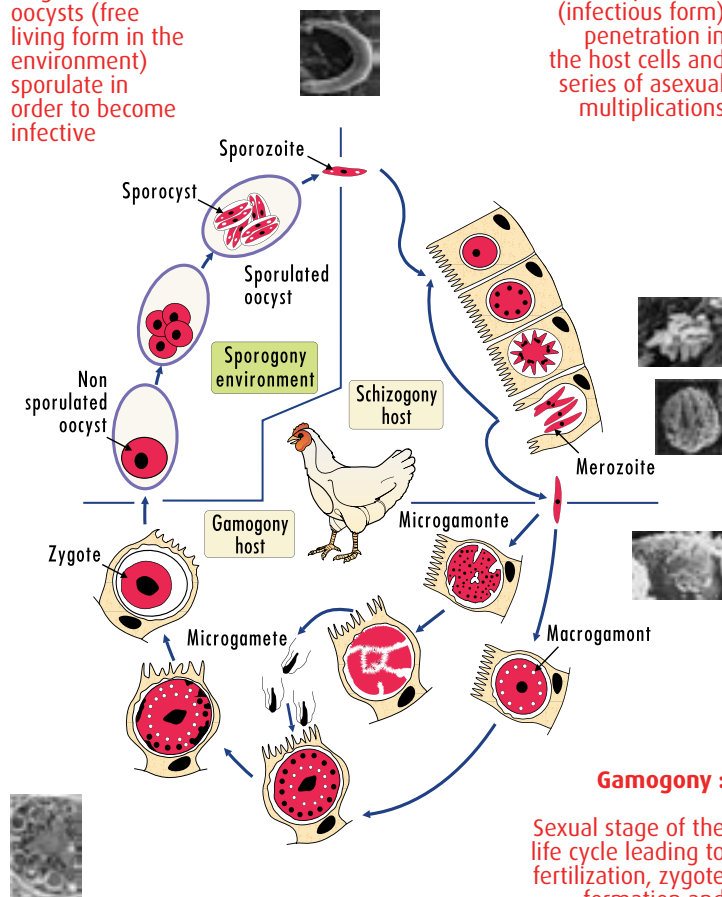
THE CYCLE OF THE PARASITE

Sporogony :

stage when oocysts (free living form in the environment) sporulate in order to become infective

Schizogony :

sporozoite (infectious form) penetration in the host cells and series of asexual multiplications



Gamogony :

Sexual stage of the life cycle leading to fertilization, zygote formation and oocyst output in the environment

PHARMACOKINETICS AND DYNAMICS

Several studies were made on the distribution and depletion of clopidol residues at different tissue locations. The sequence of maximum residue levels after stopping administration for 8 hours from high to low is the following: liver, kidneys, upper breast, lower breast and leg meat.

SAFETY

Coxipol 25% has a remarkably low order of acute oral toxicity when (accidentally) fed to a wide range of animals other than broilers and is non-hazardous to feedmill workers or poultry product consumers when handled and dosed in the correct way. The product is particularly well tolerated by chickens.

PRODUCT SPECIFICATIONS

Coxipol 25% as a granular feed additive has a whitish color and is characterized by outstanding flowability that poses no issues when running through micro-ingredient blending systems.

STABILITY

The stability of Coxipol 25% has been thoroughly studied. Storage tests in unheated and incubator conditions have demonstrated that the clopidol content of originally packaged Coxipol 25% coccidiostat as feed additive is not reduced after 18 months of storage (**Figure 1**). Stability testing of the coccidiostat in a supplemental broiler feed (at 0.0125% clopidol) demonstrated no deterioration either (**Figure 2**).

Figure 1

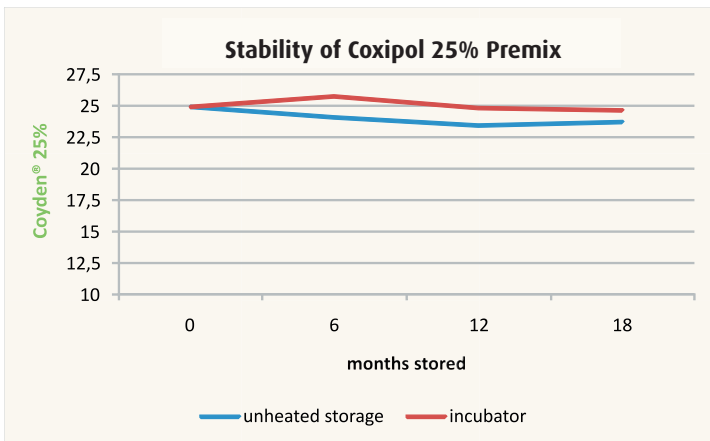
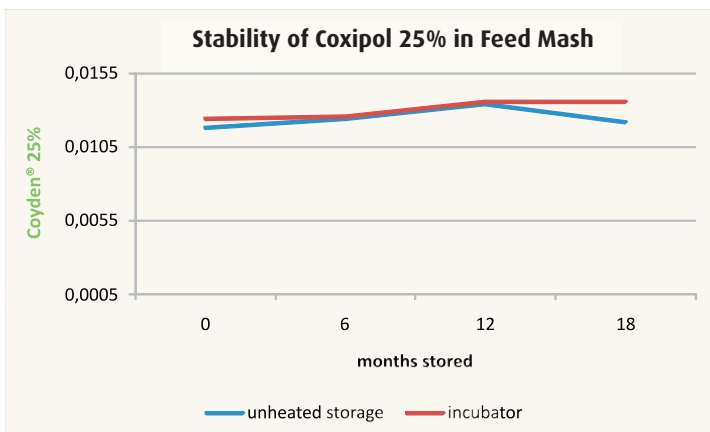


Figure 2



PRACTICAL USE

The use of anticoccidials in feed for the prevention of coccidiosis infections is common practice. Several types of molecules (ionophores and chemicals, each having a unique mode of action) have been used for years and are helping the poultry industry to overcome successfully this parasitic infection. Resistance, however, has been described for all products that have been marketed since early 1960s especially in cases where any single anticoccidial had been applied.

Coxipol can be applied safely in broilers during one grow out per year in full or shuttle programs. When used in shuttle programs with for instance ionophores, it can be supplemented as starter or grower feed. Recent field observations have shown that for "light" birds best coccidiosis control and zootechnical performances were obtained when Coxipol was supplemented in the starter diets. In birds with longer life cycle, reaching higher weights (2.5 kg), excellent coccidiosis control and zootechnical results were obtained when Coxipol was supplemented in the grower feeds of the shuttle programs. Coxipol is a high potential chemical product, which can also be used as clean-up when high coccidiosis pressure is present. Therefore Coxipol can be supplemented as a full program, from starter diet till finisher diet, which will result into a drastic decrease of the coccidial pressure and therefore will help in restoration of the efficacy of other anticoccidial products (the so called "clean-up").

CONTRAINDICATIONS

None reported.

ADVERSE REACTIONS

No adverse reactions found.

SPECIAL PRECAUTIONS

Exposure to clopidol dust may cause physical irritation of the eyes, nose, throat and skin. No chronic effects have been reported.

Acute exposure to clopidol may cause redness and itching of the eyes, runny nose, sore throat, coughing, redness and irritation of the skin.

SPECIAL PRECAUTIONS FOR USE IN ANIMALS

The product should be used as a part of a well-balanced rotation program and overuse should be avoided to minimize resistance build-up.

Do not feed clopidol to layer replacements after 16 weeks of age and to laying hens or breeding birds in production.

SPECIAL PRECAUTIONS FOR THE PERSON ADMINISTERING THE GRANULAR PREMIX TO ANIMALS

Under normal conditions of use, there is no need for specific protective precautions. General protective and hygienic measures apply: i.e. wash hands before breaks and at the end of work, avoid contact with eyes and skin, do not eat, drink, smoke or inhale. After inhalation: supply fresh air and consult a doctor in case of complaints.

After skin contact: immediately wash with water and soap and rinse thoroughly.

After swallowing: rinse out mouth and drink plenty of water. Call a doctor.

Previous experience and product information indicate the product has not caused any harmful effects.

COXIPOL 25%



TREATMENT AND CONTROL

Disease

Coccidiosis remains one of the biggest causes of economic loss in the broiler industry. It is a parasitic disease of the intestinal tract caused by *Eimeria spp.* These are small protozoans (one-celled organisms) that multiply in the intestinal tract of poultry. After a coccidiosis outbreak, the flock can develop a resistance to the exposed species of coccidia but remain non resistant to others.

Transmission and symptoms

The disease spreads from one animal to another by contact with infectious oocysts and can cause clinical disease of diarrhea resulting in dehydration and death or subclinical disease which will lead to deterioration of zootechnical performance. Coccidiosis is rarely found in birds less than three weeks of age or in birds older than three years. The signs of an outbreak include birds that are pale, droopy, tend to huddle as if cold, performance drops showing a less than regular consumption of feed and water. They can

have loose stools and/or diarrhea and often become emaciated and dehydrated. Laying hens with coccidiosis will drop egg production.

Disease elimination with Coxipol 25%

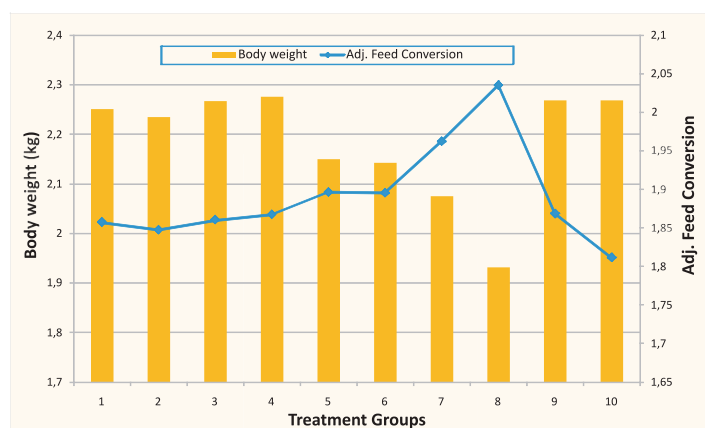
Two floor pen trials (identical protocols & study designs) were conducted in two separate research facilities to assess the current anticoccidial sensitivity of Coxipol 25% and several other chemical and ionophore anticoccidials. Coxipol 25% was used at 125 ppm in the starter feed, combined with monensin or salinomycin in the grower/finisher feed (see Figure 3). At 15 days of age, the animals were experimentally infected with 11 field isolates of *E. acervulina*, 4 of *E. maxima* and two isolates of *E. tenella*. At 21 and 42 days, intestinal lesions were scored according to the method of Johnson and Reid. After a growing period of 42 days, all remaining animals were weighed and average body weights and feed conversion efficiencies for each treatment were evaluated.

Figure 3: treatment groups

Treatment	Starter	Grower	Challenged
1	Coxipol 25% (125 ppm)	monensin (100 ppm)	Yes
2	Coxipol 25% (125 ppm)	salinomycin (60 ppm)	Yes
3	Nicarbazin 25% (125 ppm)	monensin (100 ppm)	Yes
4	Nicarbazin 25% (125 ppm)	salinomycin (60 ppm)	Yes
5	Diclazuril (1 ppm)	monensin (100 ppm)	Yes
6	Diclazuril (1 ppm)	salinomycin (60 ppm)	Yes
7	Salinomycin (60 ppm)	salinomycin (60 ppm)	Yes
8	Unmedicated / no coccidiostat	Unmedicated / no coccidiostat	Yes (control)
9	Unmedicated / no coccidiostat	Unmedicated / no coccidiostat	No (control)
10	Coxipol 25% (125 ppm)	monensin (100 ppm)	No

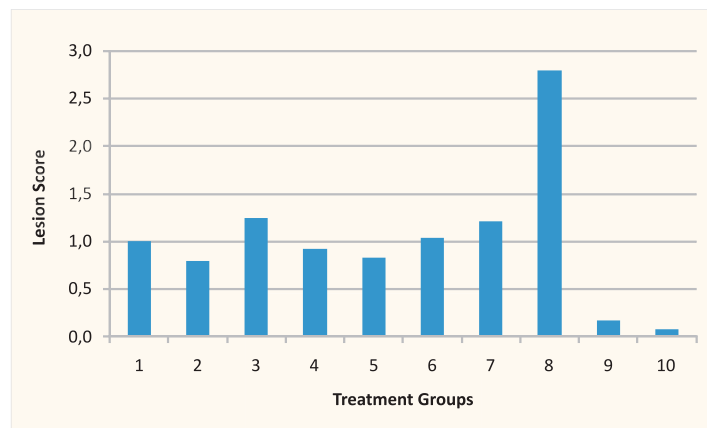
When compared with the experimentally infected nonmedicated treatment group, significant improvements in both average body weight and adjusted feed conversion were found in the Coxipol 25% treatments (with monensin or salinomycin in grower feed) (see Figure 4).

Figure 4: Average body weights, adjusted feed conversion at 42 days



Compared with the experimentally infected, non-medicated group, a significant reduction in lesion scores at 21 days of both Coxipol 25% treatments were found in both trials (see Figure 5).

Figure 5: Lesion scores at 21 days





Amount(s) to be administered and administration route

Clopidol is most frequently used at a concentration of 125 ppm which can be achieved by blending 500 g of Coxipol 25% per ton of feed. In case of severe infection the dosage can be increased up to 250 ppm.

The product must be mixed with other ingredients before feeding in order to have an optimal homogeneity and to avoid segregation. Mixing and conveying equipment should be properly cleaned to prevent carry-over.

PRACTICAL ADMINISTRATION

Coxipol 25% granular premix (clopidol) should be thoroughly and evenly mixed in the feed in accordance with current good manufacturing practice. Coxipol 25% granular premix may be used to manufacture feed containing 125 ppm to 250 ppm clopidol.

To aid in the even distribution of Coxipol 25% granular premix in the finished feed, prepare a mixture of Coxipol 25% in a portion of complete feed ingredient before mixing into the finished ration. Blend the mixture with the remainder of the finished feed and mix thoroughly.

Feed continuously, as the sole ration, depending upon management practices, degree of exposure, and feed intake levels.

WITHDRAWAL PERIOD(S)

Broiler chickens: two days

STORAGE

Store only in the original bags.

Keep in a cool, dry, well ventilated place.

Recommended storage temperature: < 30°C

PACKAGING

Coxipol 25% is packed in 20 kg bags.



Coxipol 25% is a New Zealand registered veterinary medicine, ACVM number A11356