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**S. L. Ralston**

## Anthelmintic Resistance in the Equine

Susan Ralston, VMD

Horses have the potential to be infected by over 100 species of internal parasites. These include ascarids, large and small strongyles, pinworms, bots, and tapeworms. Parasite control is necessary for the health of horses, especially where high concentrations of animals are maintained. Treatment of the horse with anti-parasitic drugs has been the major form of control of these infections. During the 1900s, over 25 products for parasite control in horses have been marketed in the United States. There are 7 major classes into which these compounds fall: phenothiazine, piperazine, organophosphates, benzimidazoles and pro-benzimidazoles, imidothiazoles (levamisole), tetrahydropyrimidines (pyrantel), and avermectins. Benzimidazoles and pro-benzimidazoles interfere with energy metabolism within the parasite; imidothiazoles, tetrahydropyrimidines, piperazine, organophosphates, and avermectins interfere with parasites' neuromuscular coordination.

In the equine, anthelmintic resistance has been reported in only one group of parasites, the cyathostomes or small strongyles, which has developed resistance to benzimidazoles, pro-benzimidazoles and pyrantel pamoate.(1) Only ivermectin and dichlorvos have maintained their original efficacy against small strongyles.

Drug resistance is manifested as a clear and obvious decrease in efficacy from the original activity of a compound or class of compounds. Resistance in a parasite population develops because there are a few worms that become refractory to the recommended dosage of a product. These parasites survive treatment and pass this ability to their offspring, resulting in the contamination of the premises with resistant strains. As this continues, the numbers of resistant worms increase and eventually the product is no longer useful in the treatment of these parasites.

There are two factors that influence parasite selection for resistance: use of

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anthelmintics and the biology of the parasite. Anthelmintic usage includes dosage and route of administration, frequency of treatment, and mechanism of action. Frequency of treatment is regarded as the main factor in selection for resistance. The more frequently a compound is used, the more likely resistance may occur. Deworming compounds that interfere with energy metabolism (benzimidazoles) are more prone to result in parasite resistance when compared to those that disrupt neuromuscular activity (ivermectin). Parasites with shorter life cycles are generally expected to manifest drug resistance sooner than those with long turnover times. This is because the genetic makeup of the parasite provides for its survival mechanism (resistance), and these genes are passed on to the progeny.

Pre- and post-treatment counts of parasite eggs and larvae per gram of feces to determine percentage change in these numbers is the most practical method to evaluate efficacy and, indirectly, whether drug resistance is present. Less than 90% reduction in the pre- vs. post-treatment number of eggs per gram indicates low efficacy and that resistant strains of parasites may be present.

Minimizing the problem of dewormer resistance in horses is complex. There are three areas to be considered: drug selection, treatment schedule, and animal management. Selecting a drug that works and administering the proper dose for the body weight of the horse are critical points. In addition, programs should be designed that will provide optimal parasite control with the least number of treatments per year. Pasture rotation may be beneficial in reducing worm numbers, as may regular removal of feces from the environment.

EQVALAN® (ivermectin) Brand Products are the ideal choice for deworming horses for many reasons. They are the broadest-spectrum products available and have high efficacy against immature parasite stages, thus eliminating generations of parasites within the host. Because of this, they may be used with less frequency than other agents, while affording optimal parasite control. In addition, there is no evidence of resistance of any horse parasite to ivermectin.

## References

1. Chapman MR, French DD, Klei TR. Evaluation of pyrantel pamoate against equine cyathostomes: resistance or lack of efficacy? in *Proceedings*. 40th Meeting of the AAVP, 1995; #27.

**EQUALAN® (ivermectin)****Product Description**

Ivermectin is derived from the avermectins, a family of potent, broad-spectrum antiparasitic agents, which are isolated from fermentation of *Streptomyces avermitilis*.

EQUALAN® (ivermectin) Liquid is a clear, ready-to-use solution with each mL containing 1% ivermectin (10 mg), 0.2 mL propylene glycol, 80 mg polysorbate 80, 9 mg sodium phosphate monobasic monohydrate, 1.3 mg sodium phosphate dibasic anhydrous, 1 mg butylated hydroxytoluene, 0.1 mg disodium edetate, 3% benzyl alcohol and purified water q.s. ad 100%.

**Product Indications**

EQUALAN Liquid is indicated for the effective treatment and control of the following parasites or parasitic conditions in horses:

**Large Strongyles:**

*Strongylus vulgaris*  
(adults and arterial larval stages)  
*S. edentatus* (adults and tissue stages)  
*S. equinus* (adults)  
*Triodontophorus* spp (adults)

**Small Strongyles** - including those resistant to some benzimidazole class compounds

(adults and fourth-stage larvae):  
*Cyathostomum* spp  
*Cylicocyclus* spp  
*Cylicostephanus* spp  
*Cylicodontophorus* spp

**Pinworms** (adults and fourth-stage larvae):

*Oxyuris equi*

**Ascarids**

(adults and third-and fourth-stage larvae):  
*Parascaris equorum*

**Hairworms** (adults):

*Trichostrongylus axei*

**Large-mouth Stomach Worms** (adults):

*Habronema muscae*

**Bots** (oral and gastric stages):

*Gastrophilus* spp

**Lungworms** (adults and fourth-stage larvae):

*Dictyocaulus arnfieldi*

**Intestinal Threadworms** (adults):

*Strongyloides westeri*

**Summer Sores** caused by *Habronema* and *Draschia* spp cutaneous third-stage larvae.

**Dermatitis** caused by neck thread-worm microfilariae, *Onchocerca* sp.

**Dosage**

EQUALAN Liquid for Horses is formulated for administration by stomach tube (nasogastric intubation) or as an oral drench. The recommended dose is 200 mcg of ivermectin per kilogram (91 mcg/lb) of body weight. Each mL contains sufficient ivermectin to treat 110 lb (50 Kg) of body weight: 10 mL will treat an 1100 lb (500 kg) horse.

**Administration**

Use a calibrated dosing syringe inserted into the bottle to measure the appropriate dose, or pour the EQUALAN Liquid into a graduated cylinder for dose measurement. Use a clean syringe if accessing the bottle to avoid contaminating the remaining product.

**Administration by stomach tube** (gravity or positive flow): The recommended dose can be used undiluted or diluted up to 40 times with clean tepid water (see Notes to Veterinarian). Use tepid water to flush any drug remaining in the tube into the horse's stomach.

**Administration by drench:** For administration by this method, an undiluted dose is usually preferred. Clear the horse's mouth of any food material, elevate the horse's head, and using a syringe, deposit the appropriate dose in the back of the mouth. In order to avoid unnecessary coughing or the potential for material to enter the trachea and lungs, do not use excessive pressure (squirting), do not use a large (diluted) dose volume, and do not deposit the dose in the laryngeal area. Increased dose

rejection may occur if the dose is deposited in the buccal space. Keep the horse's head elevated and observe the horse to insure the dose is retained.

### **Suggested Parasite Control Program**

All horses should be included in a regular parasite control program with particular attention being paid to mares, foals and yearlings. Foals should be treated initially at 6 to 8 weeks of age, and routine treatment repeated as appropriate. EQVALAN effectively controls gastrointestinal nematodes and bots in horses. Regular treatment will reduce the chances of verminous arteritis and colic caused by *S. vulgaris*. With its broad spectrum, EQVALAN is well suited to be the major product in a parasite control program.

### **Mode of Action**

Ivermectin, one of the avermectins, kills certain parasitic roundworms and ectoparasites such as mites and lice. The avermectins are different in their action from other antiparasitic agents. This action involves a chemical that serves as a signal from one nerve cell to another, or from a nerve cell to a muscle cell. This chemical, a neurotransmitter, is called gamma-aminobutyric acid or GABA.

In roundworms, ivermectin stimulates the release of GABA from nerve endings and enhances binding of GABA to special receptors at nerve junctions, thus interrupting nerve impulses - thereby paralyzing and killing the parasite. The enhancement of the GABA effect in arthropods such as mites and lice resembles that in roundworms except that nerve impulses are interrupted between the nerve ending and the muscle cell. Again, this leads to paralysis and death.

The principal peripheral neurotransmitter in mammals, acetylcholine, is unaffected by ivermectin. Ivermectin does not readily penetrate the central nervous system of mammals where GABA functions as a neurotransmitter.

### **Safety**

EQVALAN Liquid may be used in horses of all ages including mares at any stage of pregnancy. Stallions may be treated without adversely affecting their fertility. These horses have been treated with no adverse effects other than those noted under **Notes to Veterinarian**.

**Warning:** Do not use in horses intended for food purposes.

### **Precautions**

Caution: EQVALAN Liquid has been formulated specifically for use in horses **only**. This product should not be used in other animal species as severe adverse reactions, including fatalities in dogs, may result.

Refrain from smoking and eating when handling. Wash hands after use. Avoid contact with eyes. **Keep this and all drugs out of the reach of children.**

Store in a tightly closed container at room temperature.

Protect EQVALAN Liquid (undiluted or diluted) from light.

For customer service, contact Merial Customer Service, 4545 Oleatha Avenue, St. Louis, MO 63116.

### **Environmental Safety**

Studies indicate that when ivermectin comes in contact with the soil, it readily and tightly binds to the soil and becomes inactive over time. Free ivermectin may adversely affect fish and certain water-borne organisms on which they feed. Do not contaminate lakes, streams, or ground water by direct application or by improper disposal of drug containers. Dispose of drug container in an approved landfill or by incineration.

### **Notes to Veterinarian**

Swelling and itching reactions after treatment with EQVALAN have occurred in horses carrying heavy infections of neck threadworm microfilariae, *Onchocerca* sp. These reactions were most likely the

result of microfilariae dying in large numbers. Symptomatic treatment may be advisable.

Healing of summer sores involving extensive tissue changes may require other therapy in conjunction with EQVALAN. Reinfection, and measures for its prevention, should also be considered.

Special consideration should be given to the effects or potential for injury from handling, restraint, and placement of the tube during administration by stomach tube. EQVALAN Liquid should be administered by drench if the risks associated with tubing are of concern. Due to the consequences of improper administration (also see **Dosage and Administration**), EQVALAN Liquid is intended for use by a veterinarian only and is not recommended for dispensing.

EQVALAN Liquid in 1 to 20 and 1 to 40 dilutions with tap water has been shown to be stable for 72 hours under the conditions recommended for the product (i.e., at room temperature, in a tightly closed container, protected from light). The diluted product does not promote the growth of common organisms. However, prolonged storage of the diluted product cannot be recommended, as the effects of possible contaminants and interactions with untested materials are unknown.

#### **Package Information**

EQVALAN Liquid for horses (Product 25877) is available in a 100 mL plastic bottle. Each bottle contains sufficient ivermectin to treat 10-500 kg (1100 lb) horses. Contents may be poured into a graduated cylinder for dose measurement. Alternatively, a clean syringe may be inserted directly into the bottle to draw off the appropriate dose.

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Veterinary Professional Services, Merial Limited,  
2100 Ronson Road, Iselin, NJ 08830-3077. Tel 1 888 637 4251