120x189mm

# IVOSANTEL

## Injection

For Veterinary Use Only

**COMPOSITION:**

Each ml contains

Ivermectin.....10mg

Closantel.....125mg

**INDICATIONS:**

Ivosantel is endectocide and fasciolicide with strong residual power, recommended for treatment, control and prophylaxis of internal parasitosis (produced by adult and immature forms of Fasciola hepatica and gastrointestinal nematodes) and external parasitosis (lice, mange, flies, oestrosis, larval, miasis and tick. The association of Ivermectin and Closantel has demonstrated compatibility and effect of each component.

**MODE OF ACTION:**

The molecular mode of action of closantel is not completely elucidated. It is uncouplers of the oxidative phosphorylation in the cell mitochondria, which disturbs the production of ATP, the cellular "fuel". This seems to occur through suppression of the activity of succinate dehydrogenase and fumarate reductase, two enzymes involved in this process. This impairs the parasites motility and probably other processes as well. It seems that Closantel also disturbs the liquid and ion transport mechanisms in the parasites membranes. Recently it has been discovered that Closantel also inhibits chitinase in Onchocerca volvulus. Chitinase is an enzyme involved in larval molting. Its inhibition interrupts their development to adult worms. Ivermectin enhances the release of gamma amino butyric acid (GABA) at presynaptic neurons. GABA acts as an inhibitory neurotransmitter and blocks the post-synaptic stimulation of the adjacent neuron in nematodes or the muscle fiber in arthropods. By stimulating the release of GABA, Ivermectin causes paralysis of the parasite and eventual death. As liver flukes and tapeworms do not use GABA as a peripheral nerve transmitter, Ivermectin is ineffective against these parasites.

**PHARMACOKINETICS:**

After administration Cosantel is readily enters into the bloodstream. In the blood, unchanged Closantel binds strongly and almost completely (>99%) to plasma albumins. Peak plasma levels are reached 10 to 48 hours after administration. Half life in plasma is 3 to 4 weeks. Due to the strong binding to plasma albumins, Closantel residues in the tissues are rather low, the highest ones were found in the lungs and the kidneys. Closantel is poorly metabolized. About 80% of the administered dose is excreted through the feces, >98% in the form of the parent molecule,but only ~10% after intramuscular injection. Excretion half life in the organism is 2 to 3 weeks.

Ivermectin is a rather lipophilic molecule. Regardless of the delivery form (topical, oral or injection) it is well absorbed into blood and distributed throughout the host's organism. It tends to be deposited in the body fat and the liver, from where it is progressively released and metabolized. The pharmacokinetic behavior varies for each species and depends strongly on the delivery form and the formulation. Absorption into blood in cattle and sheep after subcutaneous injection varies with the vehicle. After injection with a lipophilic vehicle absorption is slower than with a hydrophilic one and persistence in the organism is longer. But the blood peak reached is also lower.The consequence is also a shorter residual effect than after injection. In cats and dogs absorption after injection is usually faster than on ruminants.

Distribution of Ivermectin to all organs and most body fluids is sufficient to achieve effective concentrations against the major parasites after oral, injectable and topical administration. Highest tissue residues are detected in body fat and liver.

Excretion of Ivermectin is independent from the delivery form and is achieved to >90% through bile and feces. Only about 2% is excreted through urine. About 45% of the eliminated ivermectin is the parent molecule and the rest are various metabolites. Excretion in goats is significantly faster than in sheep. In sheep it takes about 11 days for ivermectin to drop below the detectable level in blood, whereas in goats this level is reached 4 to 5 days after administration.

**TOXICOLOGY:**

The acute toxicity resulting from single dosing of Closantel solution in several animals,The LD50 in sheep is >40 and in cattle is >20mg/kg body weight. Acute toxic symptoms in cats will appear within 10 hours of ingestion. Symptoms may include agitation, vocalization, anorexia, mydriasis, rear limb paresis, tremors, and disorientation. Blindness, head-pressing, wall-climbing, absence of oculomotor menace reflex, and a slow and incomplete response to papillary light may also be seen. Neurologic symptoms usually diminish over several days and most animals completely recover within 2-4 weeks. Symptomatic and supportive care are recommended.Ivermectin is highly toxic to fish and extremely toxic to invertebrates. For this reason disposal of Ivermectin residues (e.g. in empty containers) in watercourses must be absolutely avoided. There is a certain environmental risk of water pollution from run-off after pour-on administration to large cattle herds.

**DOSAGE & ADMINISTRATION:**

Administer the following dose by subcutaneous route.

1ml per 50kg body weight of animal.

The administration of the total dose in two different sites is recommended, in order to avoid possible irritations.

**WITHDRAWAL TIME:**

**Meat:** 50 days.

**PRECAUTIONS:**

Do not use in lactating dairy cows.
Do not use in hypersensitive animals.
Store between 15-25°C in a cool and dry place.
Protect from light and heat.
Keep out of the reach of children.
Consult the veterinarian before use.



**Innovator's Specs.**

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