Ivermectin is a macrolide antibiotic belonging to the class of avermectin; it is extracted from a fungus discovered in Japan, *Streptomyces avermitilis*. Ivermectin exhibits broad-spectrum activity against many internal or external parasites, more specifically, nematode and arthropod parasites.

Ivermectin acts by binding the glutamate-activated Cl⁻ channels of the parasite (Cl⁻ channels do not exist in mammal cells), preventing their closure. As Cl⁻ flows into the cells, the cell membrane is hyperpolarized and no nervous signal can be transmitted. The insect is paralyzed and slowly dies. At higher concentrations, ivermectin acts as an antagonist of the GABA (γ-aminobutyric acid) neurotransmitter. In insects, those GABA neurons and receptors are primarily located in the PNS (peripheral nervous system); in mammals, they are located mainly in the CNS (central nervous system). Trematode and cestode parasitic worms have a natural resistance against ivermectin, since they do not use GABA as a PNS neurotransmitter.

Secondary effects such as inhibition of reproduction of the parasites have also been observed.

This difference in location of the GABA receptors may explain ivermectin’s rather safe use in mammals. It furthermore enables the administration of ivermectin in pregnant mammals, with the exception of rats. Indeed, ivermectin has been observed to cross the blood-brain barrier only in prenatal rats, whose barrier will not become functional until a few days after birth. This is an exception among mammals (including humans, ruminants, lagomorphs), which form a functional blood-brain barrier at the embryo stage.

Adult rats show a general slowdown during 24 h after injection. Some dog breeds (collie and collie-crosses) have shown increased sensitivity to ivermectin.

In cattle, horses and rabbits, ivermectin is partially metabolized by the liver (55%); the rest (45%) is excreted in the feces. The PO administration of ivermectin shows rapid absorption by the body and high concentration in the blood is reached relatively rapidly, in contrast to the SC injection of ivermectin (Ivomec), whose half-time absorption rate is 39.2 h (the
Absorption rate is highly dependent on the carrier, in this case glycerolformal-propyleneglycol 40:60). The drug is well distributed in all different tissues and organs, including the mucous layer of the gastrointestinal tract. High concentrations are usually found in the lungs, kidneys, skin and ears.

In rabbits, ivermectin is indicated to treat the following parasites of the GI tract: *Strongyloides* spp., *Graphidium strigosum*, *Trichostrongylus retortaeformis*. It is also efficient against ectoparasites such as ear mite, *Psoroptes cuniculi*; *Sarcoptes cuniculi*; *Notoedres cuniculi*; *Cheyletiella parasitovorax*; lice, *Haemodipsus ventricosus*; and flea, *Spilopsyllus cuniculi*.

**Adverse Effects**

In horses, injections of ivermectin can lead to edemas, due to toxins released by dying internal parasites; this last about 5 days. Dogs can suffer a shock situation for the same reason. Due to lack of detailed studies of the effects of ivermectin in young animals, its use should be avoided; if this is not possible, the fact that younger animals are more sensitive to ivermectin than adults are should be taken into account.

Ivermectin toxicosis has been reported in cattle, horses, pigs, cats and dogs. No reports are available for rabbit toxicosis (LD$_{50}$: 406 mg/kg; SC). Toxicosis is mainly related to inappropriate, off-label use, use of the large-animal formulation in dogs, or overdosage, with penetration of the blood-brain barrier. Overdosage (10 to 100 times the therapeutic value) often leads to ataxia and depression. Further signs are mydriasis (dilatation of the pupils), coma, tremors, stupor, emesis, drooling and death. Convulsions and seizures are rarely related to ivermectin toxicosis.

There is no safe and specific antidote to ivermectin. Activated charcoal, intravenous electrolyte fluids, protection of the eyes against desiccation and treatment of brachycardia are recommended. Intubation might be necessary to feed the animal. Comatose animals should be placed on a warm pad and turned regularly to avoid pressure sores. Picrotoxin has been tested; it is not the best treatment for ivermectin, and its margin of safety is narrow. Physostigmine has been shown to be beneficial, as comatose animals show a transient increase in mental alertness, enabling the diagnosis of ivermectin toxicosis.

Ivermectin interacts with benzodiazepine, each increasing the other’s toxic effect. In the combination of ivermectin and pyrantel, however, neither exerts influence on the other.
**Dosage**

Ivomec (Merck, DE) susp

- Nematodes: 0.1 mg/kg; SC
ectoparasites: 0.2-0.4 mg/kg
repeat 2-3 times, depending on parasite
50 mg/l; PO during 5 days, repeat after one week

Eqvalan (Biokema AG, CH) paste

- 50 mg/l; PO during 5 days,
Repeat after one week

Eraquell (Virbac AG, CH) paste

- 50 mg/l; PO during 5 days,
repeat after one week

**Further Information**


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