LEVATRİZOL

Oral Tablets

375 mg Levamisole HCl / 600 mg Triclabendazole

Routine anthelmentic treatment and control programme

High-risky zones: Whole herd should be treated at 10-week intervals for prophylaxis from March-April to October-November. An application may be needed in January.

Medium-risky zones: Treatment should be given at 10-12 weeks intervals beginning from high risk months for liver flukes (from September to January-February) A supportive application in the spring will help reduce the severity of the infection in the following autumn.

Treatment of acute outbreaks: Treatment should be started as soon as possible after diagnosis, The interval of application in subacute cases is 5-6 weeks.

WITHDRAWAL PERIOD

Cattle bred for meat and offal should not be sent to slaughter during the treatment and following 56 days from the last drug administration. **It is not used during lactation and last three months of the pregnancy in dairy cattle producing milk for human consumption.**

Levatrizol® Oral Tablet Veterinary Anthelmintic COMPOSITION It is a cream-white coloured, with a notch at one side and other side is straight, homogeneous-looking oblong tablet and each tablet contains 375 mg Levamisole HCl and 600 mg Triclabendazole. PHARMACOLOGICAL PROPERTIES Pharmacodynamic properties: Levamisole is a cholinergic agonist compound which belongs to tetrahydroimidazoles. Antinematodal activity is caused by the blockage of the nervous system by providing continuous stimulation of parasite autonomic ganglia. It also inhibits the carbonhydrate metabolism of parasite by inhibiting the activity of the fumarate reductase enzyme, as is the case with benzimidazoles. The development of resistance to levamisole occurs with changes in the general characteristics of the acetylcholine receptor population. Triclabendazole, is a halogenated fasciolicide and belongs to benzimidazole group. It is effective against all young forms and adult forms of liver trematodes. Triclabendazole binds to the tubulin structure of trematodes and disrupts the intracellular transport mechanism and causes multi-directional inhibition of energy metabolism. It also inhibits protein synthesis. In the development of resistance to triclabendazole; I. Progressive loss of susceptible betatubulin gene isotype, the emergence of a resistant beta-tubulin gene isotype with a point mutation resulting from tyrosine coding instead of phenylalanine, II. Change of drug intake and metabolism, III. P-glycoprotein-linked flow pumps are known to be drug carriers. Pharmacokinetic properties: When administered orally, rapidly disperses in rumen and reachs the maximum blood concentration within 2-4 hours. The half-life of the compound is 9.3 hours and it is excreted through urine (approximately 68-78%) and feces (approximately 17-33%) within 72 hours. When administered orally, triclabendazole is rapidly absorbed through the gastrointestinal tract, it initiates the antiparasitic activity and reaches to maximum blood concentration after 18 hours. Sulfones, sulfoxides, ketones and 4-hydroxy derivatives present in plasma as main metabolites. Within 7 days, 81.4% of total excreted through urine (2,2%) and faeces (76%) in cattle. Plasma protein binding rate was found to be higher than 99%. INDICATIONS FOR USE, SPECIFYING THE TARGET SPECIES LEVATRIZOL Oral Tablet is used in the prevention and treatment of parasitic invasions caused by levamisole and triclabendazole susceptible helminths in cattle not in lactation period. Abomasum nematodes: Haemonchus spp., adult, L4 and immature forms (Ostertagia spp. has been reported to be effective in inhibiting larvae) of Ostertagia spp., Small intestine nematodes: Adult and larval forms of Cooperia spp, Trichostrongylus spp., Nematodirus spp, Bunostomum spp. Large intestine nematodes: adult and larval forms of Oesophagostomum spp. Lungworms: Adult and larval forms of Dictyocaulus spp. Liver trematodes: Adult forms of Fasciola hepatica, as well as tissue invasion and is responsible for the most damaged stage of infection is effective on immature trematodes. AMOUNTS TO BE ADMINISTERED AND ADMINISTRATION ROUTE Unless otherwise recommended by the veterinarinarians; Pharmacological dose for cattle 12 mg triclabendazole/kg body weight and 7.5 mg levamisole/kg body weight. It is administered orally with the help of some water. It is used as 1 tablet per 50 kg body weight in cattle. Practical dosage table; For heaver cattle, 1 tablet is added per 50 kg body weight. Unfinished tablets should be used within 7 days. SPECIAL CLINIC INFORMATION AND SPECIAL WARNINGS FOR EACH TARGET SPECIES Wrong use of anthelmintics may cause increased resistance in parasites, therefore should be administered within an appropriate programme. When used against resistant strains against levamisole and triclabendazole, the effect is reduced. Cachectic and severely stressed animals should be observed after application. It should not be administered to sick and weak animals. Recommended doses should not be exceeded and dose should be calculated carefully according to body weight. The same application should be applied to animals that are included in the herd within programme. Routine anthelmentic treatment and control programme High-risky zones: Whole herd should be treated at 10-week intervals for prophylaxis from March-April to October-November. An application may be needed in January. Medium-risky zones: Treatment should be given at 10-12 weeks intervals beginning from high risk months for liver flukes (from September to January-February) A supportive application in the spring will help reduce the severity of the infection in the following autumn. Treatment of acute outbreaks: Treatment should be started as soon as possible after diagnosis, The interval of application in subacute cases is 5-6 weeks. In order to reduce the risk of resistance development to the product and to provide effective treatment, the following points should be considered: Long-term and repeated administration of other antiparasitic drugs in the same group should be avoided with chemical substances similar to the active substances. Dose calculation and application errors should be avoided and care should be taken to use the appropriate dose. Especially low doses may cause resistance. When suspicion of resistance to anthelmintics is suspected, tests (for example, reduction in the number of parasitic eggs in feces) can be used to obtain the correct conclusion. When resistance development is determined, an anthelmintic should be used which has a different pharmacological class and a different mechanism of action. Levamisole resistance has been reported in Teladorsagia species in cattle in developed countries such as New Zealand. Triclabendazole resistance was first identified in the field isolates of Fasciola hepatica in Australia in 1995, and then triclabendazole resistance was detected in sheep and cattle farms in Europe (the Netherlands and Spain). Therefore, the use of this product should be based on local (regional or farm) epidemiological information on susceptibility to nematodes and recommendations on ways to limit subsequent selection against anthelmintic resistance. ADVERSE REACTIONS Side effects are less likely to occur when administered at the recommended dose. However, depending on the levamisole, symptoms such as vomiting, salivation and muscle tremors may develop, if rare. Repeated doses may cause such as fever, muscle aches and allergic reactions on skin. Since the treatment index of levamisole is narrow, dosing should be done with caution. Skin irritation may occur due to triclabendazole. In Australia, after triclabendazole treatment, inflammation of the skin has been observed in the non-pigmented skin of the cows (teat on udder and nose) due to photosensitivity. INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION • Piperazine salts should not be used together due to its antagonistic effect. • Use with tetrahydropyrimidines (salts of pyrantel and morantel) may lead to increased toxicity. • Due to its nicotinic effects it should not be used with organic phosphorus compounds (trichlorfon, dichlorvos, etc.), phenothiazines, diethylcarbamazine, procaine and phenicols. OVERDOSE (SYMPTOMS, EMERGENCY PROCEDURES, ANTIDOTES) Overdose applications (5 times of the recommended dose) can lead to levamisole poisoning. Excessive salivation, nausea, vomiting, urination, defecation, pupillary constriction, hypersensitivity and slight muscle tremors can be observed. These symptoms last within 1-4 hours. Triclabendazole is more reliable. Levamisole does not have a specific antidote. Nicotine antagonists, anticholinergic and anti-alpha adrenergic drugs can be used in intoxications. In this case atropine is quite useful, to control of parasympathetic and central nerve symptoms it should be administered intravenously. However, only atropine does not reduce mortality. Supportive applications are very important. Since the cause of death in acute intoxications is asphyxia due to respratory failure, oxygen administration is vital. When taken orally, the stomach and intestines must be emptied and activated charcoal should be given. WITHDRAWAL PERIOD Cattle bred for meat and offal should not be sent to slaughter during the treatment and following 56 days from the last drug administration. It is not used during lactation and last three months of the pregnancy in dairy cattle producing milk for human consumption. CONTRAINDICATIONS Avoid administered to animals known to be sensitive to levamisole and triclabendazole. It should not be administered to animals with liver and renal failure. It should not be used in young dairy cattle, newborns. Organophosphorus insecticides should not be applied 14 days before and after of levamisole application. It should not be used in without target species. Intoxication and even death can be observed at normal doses due to the race and herd sensitivity of the goats against levamisole. Even at a dose of 20 mg / kg levamisole in horses can lead to death. Toxic for cats and dogs that may cause death. Use during pregnancy and lactation It is safe to use during pregnancy and lactation periods. It should not be used in the last three months of pregnancy in animals obtained from milk for human consumption. GENERAL WARNINGS • Consult to a veterinarian before use and in case of unexpected effects. • Keep out of the sight and reach of children SPECIAL PRECAUTIONS TO BE TAKEN BY THE PERSON ADMINISTERING THE VETERINARY MEDICINAL PRODUCT TO ANIMALS Do not drink or eat or smoke during the administration. In case of contamination, wash your eyes and skin immediately and take off the clothes. Although rarely observed, levamisole may cause idiosyncratic reactions and serious blood diseases in humans during or shortly after administration of the product. In case of dizziness, nausea, vomiting, abdominal pain, mouth and throat pain or fever, seek medical attention immediately. STORAGE CONDITIONS AND SHELF LIFE Shelf life is 48 months from the manufacturing date when it is stored at room temperature below 25°C, away from sunlight without refrigerate and freeze and in original package. Unfinished tablets should be used within 7 days. DISPOSAL AFTER APPLICATION AND WARNINGS FOR NON-TARGET SPECIES Any unused veterinary medicinal product or waste materials derived from such veterinary medicinal products should be disposed of in accordance with local requirements. Since triclabendazole contains toxic effects for fish and aquatic organisms, care should be taken not to mix with water resources. It should be noted that the active substance and metabolites of the product are excreted in feces and urine for 10 days. NATURE AND COMPOSITION OF IMMEDIATE PACKAGING Transparent PVC foil and grey coloured, with one side printed aluminum foil blisters are used. One blister containing 10 tablets is presented in cardboard box with the leaflet. TERMS OF SALE Sold at pharmacies and veterinary clinics with veterinary prescription only. MARKETING AUTHORISATION DATE AND NUMBER: 27.07.2005/14-089 NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER DEVA Holding AŞ Halkalı Merkez Mah. Basın Ekspres Cad. No:1 Küçükçekmece/İstanbul/TURKEY Tel: +90 212 692 92 92 Fax: +90 212 697 34 89 e-mail: vetas@vetas.com.tr NAME AND ADDRESS OF THE MANUFACTURER DEVA Holding A.Ş. Çerkezköy Organize Sanayi Bölgesi, Karaağaç Mah. Fatih Bulvarı No.26 Kapaklı/Tekirdağ/TURKEY Tel: +90 282 758 17 71 Fax: +90 282 758 17 70

Body Weight	Tablet
100 kg	2 tablets
125 kg	2,5 tablets
150 kg	3 tablets
200 kg	4 tablets

Body Weight	Tablet
250 kg	5 tablets
300 kg	6 tablets
350 kg	7 tablets
400 kg	8 tablets

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Please contact our company for more information. **DEVA HOLDİNG A.Ş.** Halkalı Merkez Mah. Basın Ekspres Cad. No:1 34303 Küçükçekmece / İSTANBUL Tel: 0212 692 92 92 Faks: 0212 697 34 89 • www.vetas.com.tr

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STRONG SYNERGY & EFFECT
WIDE SPECTRUM

Vetaş

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INDICATIONS FOR USE

LEVATRIZOL Oral Tablet is used in the prevention and treatment of parasitic invasions caused by levamisole and triclabendazole susceptible helminths in cattle not in lactation period.

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Small intestine nematodes: Adult and larval forms of *Cooperia spp, Trichostrongylus spp., Nematodirus spp, Bunostomum spp.*
Large intestine nematodes: Adult and larval forms of *Oesophagostomum spp.*
Lungworms: Adult and larval forms of *Dictyocaulus spp.*
Liver trematodes: Adult forms of *Fasciola hepatica,* as well as tissue invasion and is responsible for the most damaged stage of infection is effective on immature trematodes.

AMOUNTS TO BE ADMINISTERED and ADMINISTRATION ROUTE

Pharmacological dose for cattle

12 mg triclabendazole/kg body weight and 7.5 mg levamisole/kg body weight.
It is administered orally with the help of some water.
It is used as 1 tablet per 50 kg body weight in cattle.

Practical dosage table; 1 TABLET / 50 KG

Body Weight	Tablet
100 kg	2 tablets
125 kg	2,5 tablets
150 kg	3 tablets
200 kg	4 tablets
250 kg	5 tablets
300 kg	6 tablets
350 kg	7 tablets
400 kg	8 tablets