(For the use only of a registered Medical Practitioner or a Hospital or a Laboratory)

Albendazole Tablet USP 400 mg
AEROALBEN™

COMPOSITION:

Each Uncoated tablet contains:
Albendazole USP..... 400 mg
Excipients..... q.s.

DESCRIPTION:

Albendazole tablets, USP 400 mg is an oral formulation of the synthetic Albendazole A benzimidazole broad-spectrum anthelmintic structurally related to mebendazole that is effective against many diseases.

PHARMACOLOGICAL PROPERTIES

Pharmacokinetics:

Oral absorption of albendazole varies among species, with 1–5% of the drug being successfully absorbed in humans, 20–30% in rats, and 50% in cattle.

The absorption also largely depends on gastric pH. People have varying gastric pHs on empty stomachs, and thus absorption from one person to another can vary wildly when taken without food. Generally, the absorption in the GI tract is poor due to albendazole's low solubility in water. It is, however, better absorbed than other benzimidazole carbamates. Food stimulates gastric acid secretion, lowering the pH and making albendazole more soluble and thus more easily absorbed. Oral absorption is especially increased with a fatty meal, as albendazole dissolves better in lipids, allowing it to cross the lipid barrier created by the mucus surface of the GI tract. To target intestinal parasites, albendazole is taken on an empty stomach in order to stay within the gut.

Absorption is also affected by how much of the albendazole is degraded within the small intestine by metabolic enzymes in the vili.

Albendazole undergoes very fast 1st-pass metabolism in all species, such that the unchanged drug is undetectable in plasma. Most of it is oxidized into albendazole sulfoxide (also known as ricobendazole and albendazole oxide in the liver by cytochrome P450 oxidases (CYPs) and a flavin-containing monooxygenase (FMO), which was discovered later. In humans, the cytochrome P450 oxidases are thought to include CYP3A4 and CYP1A1, while those in the rats are thought to be CYP2C6 and CYP2A1.

While oxidation to albendazole sulfoxide by FMO produces R(+) enantiomers, while oxidation the cytochromes and by some enzymes in the gut epithelium produce S(-). Different species produce the R(+) and S(-) enantiomers in different quantities; humans, dogs, and most other species produce the R(+) enantiomer more (with the human AUC ratio being 80:20). Compared to the S(-) enantiomer, the R(+) has greater pharmacological activity, lasts longer in the bloodstream, is found in higher concentrations in the infected host tissues, and is found in higher concentrations within the parasites themselves. Some albendazole is also converted to hydroxyalbendazole, mainly by CYP2J2.

Albendazole sulfoxide is converted to the inactive albendazole sulfone by cytochrome P450 oxidases, thought to include CYP3A4 and/or CYP2C. Other inactive metabolites include: 2-aminosulfone, ω-hydroxysulfone, and β-hydroxysulfone. The major final metabolites that are excreted by humans are:

- methyl [5-(propylsulfonyl-1H-benzimidazol-2-yl)] carbamate,
- methyl [6-hydroxy 5-(n-propylsulfonyl)-1H-benzimidazole-2-yl)] carbamate,
- methyl [5-(n-propylsulfinyl)-1H-benzimidazole-2-yl)] carbamate,
- 5-(n-propylsulfonyl)-1H-benzimidazole-2-yl amine, and
- 5-(n-propysulfinyl)-1H-benzimidazole-2-yl amine.

There are also some minor hydroxylated sulfated or glucuronidated derivatives. No unchanged albendazole is excreted, as it is metabolized too quickly.

In humans, the metabolites mostly excreted in the bile, with only a small amount being excreted in the urine (less than 1%) and feces.

MECHANISM OF ACTION

As a vermicide, albendazole causes degenerative alterations in the intestinal cells of the worm by binding to the colchicine-sensitive site of β-tubulin, thus inhibiting its polymerization or assembly into microtubules (it binds much better to the β-tubulin of parasites than that of mammals). Albendazole leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites, and depletes their glycogen stores. Albendazole also prevents the formation of spindle fibers needed for cell division, which in turn blocks egg production and development; existing eggs are prevented from hatching. Cell motility, maintenance of cell shape, and intracellular transport are also disrupted. At higher concentrations, it disrupts the helminthes' metabolic pathways by inhibiting metabolic enzymes such as malate dehydrogenase and fumarate reductase, with inhibition of the latter leading to less energy produced by the Krebs cycle. Due to diminished ATP production, the parasite is immobilized and eventually dies.

Some parasites have evolved to have some resistance to albendazole by having a different set of acids comprising β-tubulin, decreasing the binding affinity of albendazole.

INDICATIONS AND USAGE:

Albendazole is an effective treatment for:

Flatworms

Fasciolosis

Cestodes (tapeworms), as an alternative to praziquantel or niclosamide for adult beef tapeworms (Taenia saginata) and as an alternative to praziquantel for pork tapeworms (T. solium). It is also given for infections by T. crassiceps. Though praziquantel is often better at treating tapeworm infections, albendazole is used more often in endemic countries due to being cheaper and having a broader spectrum.

Nematodes

Ascariasis, which can be cured with a single dose of albendazole.

Baylisascariasis, caused by the raccoon roundworm. Corticosteroids are sometimes added in cases of eye and CNS infections.

Enterobiasis (pinworm infection)

Filariasis; since albendazole's disintegration of the microfilarie ("pre-larva") can cause an allergic reaction, antihistamines or corticosteroids are sometimes added to treatment. In cases of lymphatic filariasis (elephantiasis) caused by Wuchereria bancrofti or Brugia malayi, albendazole is sometimes given as an adjunct to ivermectin or diethylcarbamazine in order to suppress microfilaremia. It can also be given for loa loa filariasis as an adjunct or replacement to diethylcarbamazine. Albendazole has an embryotoxic effect on Loa loa adults and thus slowly reduces microfilaremia.

Gnathostomiasis when caused by Gnathostoma spinigerum. Albendazole has a similar effectiveness to ivermectin in these cases, though it needs to be given for 21 days rather than the 2 days needed for ivermectin.

Gongylonemiasis

Hookworm infections, including cutaneous larva migrans caused by hookworms in the genus Ancylostoma. A single dose of albendazole is sufficient to treat intestinal infestations by A. duodenale or Necator americanus

Intestinal capillariasis, as an alternative to mebendazole

Mansonelliasis when caused by Mansonella perstans. Albendazole works against the adult worms but not against the younger microfilariae.

Trichostrongyliasis, as an alternative to pyrantel pamoate. A single dose is sufficient for treatment.

Trichuriasis (whipworm infection), sometimes considered as an alternative to mebendazole and sometimes considered to be the drug of choice. Only a single dose of albendazole is needed. It can also be given with ivermectin.

Giardiasis, as an alternative or adjunct to metronidazole, especially in children

Microsporidiosis, including ocular microsporidiosis caused by Encephalitozoon hellem or E. cuniculi, when combined with topical fumagillin

Granulomatous amoebic encephalitis, when caused by the ameba Balamuthia mandrillaris, in combination with miltefosine and fluconazole

Arthropods

Crusted scabies, when combined with topical crotamiton and salicylic acid

Head lice infestation, though ivermectin is much better

Intestinal myiasis

Though albendazole is effective in treating many diseases, it is only FDA-approved for treating hydatid disease caused by dog tapeworm larvae and neurocysticercosis caused by pork tapeworm larvae.

ADVERSE REACTIONS:

The most common side effects by albendazole are, experienced by over 10% of people, headache and abnormal liver function. Elevation of liver enzymes occur in 16% of patients receiving treatment specifically for hydatid disease and goes away when treatment ends. The liver enzymes normally increase to two to four times the normal levels (a mild to moderate increase). An estimated 1–10% of people experience abdominal pain, nausea or vomiting, dizziness or vertigo, increased intracranial pressure, meningeal signs, temporary hair loss, and fever. The headache, nausea, and vomiting are thought to be caused by the sudden destruction of cysticerci (tapeworm larvae), which causes acute inflammation. Fewer than 1% of people get hypersensitivity reactions (such as rashes and hives), leukopenias (drop in white blood cell levels) such as agranulocytosis and granulocytopenia, thrombocytopenia (reduced platelet count), pancytopenia (drop in white blood cells, red blood cells, and platelets), hepatitis, acute liver failure, and acute renal failure, irreversible bone marrow suppression, and aplastic anemia.

Side effects can be different when treating for hydatid disease versus neurocysticercosis; for example, those being treated for the former are more likely to experience elevated liver enzymes and abdominal pain; those being treated for the latter are more likely to experience headache. Those being treated for retinal neurocysticercosis can face retinal damage if they are not first checked for ocular cysticeri; since changes to existing lesions in the eye by albendazole can cause permanent blindness.

INTERACTIONS:

The antiepileptics carbamazepine, phenytoin, and phenobarbital lower the plasma concentration and the half life of albendazole sulfoxide's R(+) enantiomer.

The antacid cimetidine heightens serum albendazole concentrations, increases the half life of albendazole, and doubles albendazole sulfoxide levels in bile. It was originally thought to work by increasing albendazole bioavailability directly; however, it is now known that cimetidine inhibits the breakdown of albendazole sulfoxide by interfering with CYP3A4. The half-life of albendazole sulfoxide thus increases from 7.4 hours to 19 hours. This might be a helpful interaction on more severe cases, because it boosts the potency of albendazole. Paradoxically, cimetidine also inhibits the absorption of albendazole by

OVER DOSAGE:

Because of its low solubility, albendazole often cannot be absorbed in high enough quantities to be toxic. The oral LD50 of albendazole in rats was found to be 2,500 mg/kg. It takes 20 times the normal dose to kill a sheep, and 30 times the normal dose to kill cattle. Overdose affects the liver, testicles, and GI tract the most. It can manifest with lethargy, loss of appetite, vomiting, diarrhea, intestinal cramps, dizziness, convulsions, and sleepiness. There is no specified antidote.

SHELF LIFE: Refer to carton and label.

PRESENTATION: 10 X 2 Albendazole Tablets USP as blister packing.

Special precautions for storage: Store in a cool dry & dark place. Protect from light & exposure.

Dosage: As directed by the physician.

Número de registro.:
Código neutral: HP/Drugs/09/92

Manufactured for: Area Biotech Pvt Ltd.
Marketed and Exported By:
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