ZENTEL

Albendazole

QUALITATIVE AND QUANTITATIVE COMPOSITION

Tablet containing 400 mg albendazole.
2 % w/v suspension to be taken orally; 2 g albendazole per 100 mL.

CLINICAL INFORMATION

Indications

ZENTEL is a benzimidazole carbamate with anthelmintic and anti-protozoal activity against the following intestinal and tissue parasites: Roundworm (Ascaris lumbricoides), pinworm (Enterobius vermicularis), hookworm (Necator americanus, Ancylostoma duodenale), whip-worm (Trichuris trichiura), threadworm (Strongyloides stercoralis), tapeworm (Taenia spp and Hymenolepis nana only in the case of associated parasitism), Chlonorchiasis (Chlonorchis sinensis), Opisthorchiasis (Opisthorchis viverrini) and cutaneous larva migrans; Giardiasis (G.lamblia, G.duodenalis, G.intestinalis, Lamblia intestinalis) in children.

Dosage and Administration

Pharmaceutical Form:

Tablet.
Suspension.

Dosage

Indications	Age	Dose	Period
- Roundworm - Pinworm* - Hookworms - Whipworm	Adults and children over 2 years of age.	400 mg [one 400 mg tablet(s) or 10 mL 4% or 20 mL 2% suspension]#	Single dose.
	Children 1-2 years	200 mg (5 mL 4% or	Single dose.

	of age.	10 mL 2% suspension)	
- Strongyloidiasis - Taeniasis - Hymenolepiasis[=]	Adults and children over 2 years of age.	400 mg (#see above)	One dose per day for 3 days.
- Chlonorchiasis - Opisthorchiasis	Adults and children over 2 years of age.	400 mg (#see above)	Two doses per day for 3 days.
- Cutaneous larva migrans	Adults and children over 2 years of age.	400 mg	One dose per day for 1 to 3 days.
- Giardiasis	Children 2 – 12 years of age only.	400 mg (#see above)	One dose per day for 5 days.

[*]In order to obtain a complete cure in the case of pinworm infestation, prescribe strict measures of hygiene, also treat the relatives and individuals sharing the same housing.

[=]In cases of proven Hymenolepiasis, retreatment in 10 to 21 days is recommended.

Method of Administration

If the patient is not cured after three weeks, a second course of treatment is indicated.

No special procedures, such as fasting or purging, are required.

The tablets can be chewed or taken with water. Some people, particularly young children, may experience difficulties swallowing the tablets whole and should be encouraged to chew the tablets with a little water, alternatively the tablets may be crushed.

Special Patient Populations

- **Elderly**

Experience in patients 65 years of age or older is limited. Reports indicate that no dosage adjustment is required, however, *ZENTEL* should be used with caution in elderly patients with evidence of hepatic dysfunction (see *Hepatic Impairment* and *Pharmacokinetics*).

- **Renal impairment**

Since renal elimination of albendazole and its primary metabolite, albendazole sulfoxide, is negligible, it is unlikely that clearance of these compounds would be altered in these patients. No dosage adjustment is required, however, patients with evidence of renal impairment should be carefully monitored.

- **Hepatic impairment**

Since albendazole is rapidly metabolised by the liver to the primary pharmacologically active metabolite, albendazole sulfoxide, hepatic impairment would be expected to have significant effects on the pharmacokinetics of albendazole sulfoxide. Patients with abnormal liver function test results (transaminases) prior to commencing albendazole therapy should be carefully monitored.

Contraindications

ZENTEL should not be administered during pregnancy, or in women thought to be pregnant.

ZENTEL is contraindicated in patients with a known history of hypersensitivity to the drug (albendazole or constituents).

Warnings and Precautions

In order to avoid administering *ZENTEL* during early pregnancy, women of childbearing age should initiate treatment during the first week of menstruation or after a negative pregnancy test.

Treatment with *ZENTEL* may uncover pre-existing neurocysticercosis, particularly in areas with high taenosis infection. Patients may experience neurological symptoms e.g. seizures, increased intracranial pressure and focal signs as a result of an inflammatory reaction caused by death of the parasite within the brain. Symptoms may occur soon after treatment, appropriate steroid and anticonvulsant therapy should be started immediately.

Excipients

ZENTEL tablets contain sunset yellow FCF (E110 or FD&C Yellow No 6) which may cause allergic-type reactions.

ZENTEL suspension contains benzoic acid which is a mild irritant to the skin, eyes and mucous membrane. It may increase the risk of jaundice in newborn babies.

Interactions

Cimetidine, praziquantel and dexamethasone has been reported to increase the plasma levels of the albendazole active metabolite responsible for the systemic efficacy of the product.

Ritonavir, phenytoin, carbamazepine and phenobarbital may have the potential to reduce plasma concentrations of the active metabolite of albendazole; albendazole sulfoxide. The clinical relevance of this is unknown, but may result in decreased efficacy, especially in the treatment of systemic helminth infections. Patients should be monitored for efficacy and may require alternative dose regimens or therapies.

Pregnancy and Lactation

Pregnancy

ZENTEL should not be administered during pregnancy or in women thought to be pregnant (see *Contraindications*).

Lactation

It is not known whether albendazole or its metabolites are secreted in human breast milk. Thus *ZENTEL* should not be used during lactation unless the potential benefits are considered to outweigh the potential risks associated with treatment.

Effects on Ability to Drive and Use Machines

There have been no studies to investigate the effect of *ZENTEL* on driving performance or the ability to operate machinery. However, when driving vehicles or operating machinery, it should be taken into account that dizziness has been reported after using *ZENTEL* (see Adverse Reactions).

Adverse Reactions

Data from large clinical studies were used to determine the frequency of very common to rare undesirable reactions. The frequencies assigned to all other undesirable reactions (i.e. those occurring at < 1/1000) were mainly determined using post-marketing data and refer to a reporting rate rather than a true frequency.

The following convention has been used for the classification of frequency:

Very common	≥1/10
Common	≥1/100 to <1/10
Uncommon	≥ 1/1000 to < 1/100
Rare	≥ 1/10,000 to < 1/1000
Very rare	< 1/10,000

Immune system disorders
Rare: Hypersensitivity reactions including rash, pruritis and urticaria.

Nervous system disorders
Uncommon: Headache and dizziness.

Gastrointestinal disorders
Uncommon: Upper gastrointestinal symptoms (e.g. epigastric or abdominal pain, nausea, vomiting) and diarrhoea.

Hepatobiliary disorders
Rare: Elevations of hepatic enzymes

Skin and subcutaneous tissue disorders
Very rare: Erythema multiforme, Stevens-Johnson syndrome

Overdose

Treatment

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamics

ATC code

P02CA03

Mechanism of Action

Albendazole exhibits larvicidal, ovicidal and vermicidal activity, and it is thought to exert its anthelmintic effect by inhibiting tubulin polymerisation. This causes the disruption of the helminth metabolism, including energy depletion, which immobilises and then kills the susceptible helminth.

Pharmacokinetics

Absorption

In man, albendazole is poorly absorbed (less than 5%) following oral administration.

The systemic pharmacological effect of albendazole is augmented if the dose is administered with a fatty meal, which enhances the absorption by approximately five-fold.

Distribution

Following oral administration of a single dose of 400 mg albendazole, the pharmacologically active metabolite, albendazole sulfoxide, has been reported to achieve plasma concentrations from 1.6 to 6.0 micromol/L when taken with breakfast.

Metabolism

Albendazole rapidly undergoes extensive first-pass metabolism in the liver, and is generally not detected in plasma. Albendazole sulfoxide is the primary metabolite, which is thought to be the active moiety in effectiveness against systemic tissue infections.

Elimination

The plasma half-life of albendazole sulfoxide is 8.5 hours.

Albendazole sulfoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion appearing in the urine.

Special Patient Populations

- **Elderly**

Although no studies have investigated the effect of age on albendazole sulfoxide pharmacokinetics, data in 26 hydatid cyst patients (up to 79 years) suggest pharmacokinetics similar to those in young healthy subjects. The number of elderly patients treated for either hydatid disease or neurocysticercosis is limited, but no problems associated with an older population have been observed.

- **Renal Impairment**

The pharmacokinetics of albendazole in patients with impaired renal function have not been studied.

- **Hepatic Impairment**

The pharmacokinetics of albendazole in patients with impaired hepatic function have not been studied.

Clinical Studies

No Text.

NON-CLINICAL INFORMATION

Albendazole has been shown to be teratogenic and embryotoxic in rats and rabbits. Albendazole was negative for evidence of mutagenicity or genotoxicity in a panel of in vitro (including Ames inactivated and activated) and in vivo tests. In long-term toxicity studies conducted in rats and mice at daily doses of up to 30 times the recommended human doses, no treatment-related tumour formation was seen.

PHARMACEUTICAL INFORMATION

List of Excipients

Tablets 400 mg	**Suspension (2%)**
Lactose	Aluminium magnesium silicate
Microcrystalline cellulose	Carboxymethylcellulose sodium
Maize starch	Glycerin
Croscarmellose sodium	Polysorbate 80
Povidone K30	Sorbitan monolaureate
Sodium lauryl sulphate	Potassium sorbate
Sunset yellow FCF (E110 or FD&C Yellow No 6) (see *Warnings and Precautions*)	Benzoic acid (see *Warnings and Precautions*)
Sodium saccharin	Sorbic acid
Magnesium stearate*	Silicone antifoam 1510
Flavourings	Saccharin sodium
	Flavourings

Shelf-Life

The expiry date is indicated on the packaging.

Storage

The storage conditions are detailed on the packaging.

Nature and Contents of Container

Tablets: Blister packs, polypropylene containers and cap.

Suspensions: Glass/Plastic bottle with polypropylene cap.

Incompatibilities

There are no special requirements for use on handling of this product

Use and Handling

Suspensions: Shake well before use.

Not all presentations are available in every country.

Name and address of the holder of the certificate of registration

GlaxoSmithKline South Africa (Pty) Ltd
57 Sloane Street
Bryanston, 2021
South Africa

Manufacturer

Tablet:

GlaxoSmithKline Consumer Healthcare S.A. (Pty) Ltd, 39 Hawkins Avenue, Epping Industria 1, 7460

Suspension:

Farmaclair, 440 Avenue du Général de Gaulle, 14200 Hérouville, Saint Clair, France

Registration details

Tablet:

Botswana: Reg No BOT1101811 (A/B) S2

Malawi: Reg No PMPB/PL270/150 P

Namibia: Reg No 10/12/0373 NS2

Zambia: Reg No 179/022 POM

Zimbabwe: Reg No 2014/7.7/4838 P

Suspension:

Botswana: Reg No BOT9900418 S2

Malawi: Reg No PMPB/PL270/63 P

Namibia: Reg No 90/12/001614 NS2

Zambia: Reg No 179/033 POM

Zimbabwe: Reg No 83/7.7/1656 P

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