Pharma Code Ref. No. 45

ZENTEL
Albendazole

Pharma Code Ref. No. 45

QUALITATIVE AND QUANTITATIVE COMPOSITION
Tablet containing 400 mg albendazole.
4 % w/v suspension to be taken orally; 4 g albendazole per 100 mL.
2 % w/v suspension to be taken orally; 2 g albendazole per 100 mL.

CLINICAL INFORMATION

Indications
ZENTEL is a benzimidazole carbamate with antihelmintic and antiprotozoal activity against the following intestinal and tissue parasites: Round-worm (Ascaris lumbricoides), pin-worm (Enterobius vermicularis), hook-worm (Necator americanus, Ancylostoma duodenale), whip-worm (Trichuris trichiura), thread-worm (Strongyloides stercoralis), tape-worm (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 of age.	200 mg (5 mL 4% or 10 mL 2% suspension)	Single dose.
- 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 pin-worm 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 contra-indicated 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

62000000056463/1020

Pharma Code Ref. No. 45

Version: 2

Harmony AMS
Artwork Information Panel

Manufacturing Site Number:
62000000056463

Manufacturing Site(s):
GSK_CAPE TOWN_SOUTH AFRICA

Product Market Trade Name:
Zentel

Approving Market(s):
CFUN-GRA Labelling-General Export Pack

Print Process:
Offset - Lithography

Colour Standard Reference:
For Colour Standard Reference, please match to exisitng component P7193ZA

Technical Drawing (Do NOT include version number):
CT_LF_ZENTEL_125X560MM_DWG

Material Spec. (Do NOT include version number):
N/A

Material Type: White Paper	SUBSTRATE

Total Colours & Varnishes: 1

		BLACK	

Total Special Finishes: 0

Body Text Size:
8.0pt

Smallest Text Size:
8.0pt

Leading:
10.0pt

Horizontal Scale:
100%

Microtext:
N

Additional Info (1):
N/A

Additional Info (2):
N/A

Additional Info (3):
N/A

200 mm Measuring Bar

If an e-banner DOES NOT appear on the top of this document, THEN this document has NOT been printed from the Harmony system.

AIP_Production_V_INDD - 04_2017 - Harmony - Version 2

IMPORTANT

GSK LOC is responsible to approve the change documentation, artwork brief and final artwork, ensuring that it is accurate, consistent and complete.

GSK SDC is responsible for site technical requirements and pre-press suitability.

GSK Market is responsible to advise SDC when changes required impact the following:

Formulation
Tablet embossing
Storage conditions
Shelf Life

NOTE TO MARKET

Local approvers must ensure that trade mark and copyright statements included in the brief comply with guidance provided by Legal: Global Trade Marks.

CAPE TOWN

Site Additional Artwork Information Panel

Production Site:
GSK_CAPE TOWN_SOUTH AFRICA

Item Code/Date Code:
62000000056463/1020

Superseded Item Code/Date Code:
P7193ZA/0320

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%, 4%)
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

* Magnesium Stearate is of vegetable origin.

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.

Manufactured and Packaged by:
GlaxoSmithKline Consumer Healthcare South Africa (Pty) Ltd.*
39 Hawkins Avenue
Epping Industria 1, 7460
Cape Town, South Africa
*Member of GSK group of companies

Version number: GDS27/IPI11

Date of issue: 28 May 2020

62000000056463/1020

Pharma Code Ref. No. 45

Version: 2

Harmony AMS
Artwork Information Panel

Manufacturing Site Number:
62000000056463

Manufacturing Site(s):
GSK_CAPE TOWN_SOUTH AFRICA

Product Market Trade Name:
Zentel

Approving Market(s):
CFUN-GRA Labelling-General Export Pack

Print Process:
Offset - Lithography

Colour Standard Reference:
For Colour Standard Reference, please match to exisitng component P7193ZA

Technical Drawing (Do NOT include version number):
CT_LF_ZENTEL_125X560MM_DWG

Material Spec. (Do NOT include version number):
N/A

Material Type: White Paper	SUBSTRATE

Total Colours & Varnishes: 1

		BLACK	

Total Special Finishes: 0

Body Text Size:
8.0pt

Smallest Text Size:
8.0pt

Leading:
10.0pt

Horizontal Scale:
100%

Microtext:
N

Additional Info (1):
N/A

Additional Info (2):
N/A

Additional Info (3):
N/A

200 mm Measuring Bar

If an e-banner DOES NOT appear on the top of this document, THEN this document has NOT been printed from the Harmony system.

AIP_Production_V_INDD - 04_2017 - Harmony - Version 2

IMPORTANT

GSK LOC is responsible to approve the change documentation, artwork brief and final artwork, ensuring that it is accurate, consistent and complete.

GSK SDC is responsible for site technical requirements and pre-press suitability.

GSK Market is responsible to advise SDC when changes required impact the following:

Formulation
Tablet embossing
Storage conditions
Shelf Life

NOTE TO MARKET

Local approvers must ensure that trade mark and copyright statements included in the brief comply with guidance provided by Legal: Global Trade Marks.

CAPE TOWN

Site Additional Artwork Information Panel

Production Site:
GSK_CAPE TOWN_SOUTH AFRICA

Item Code/Date Code:
62000000056463/1020

Superseded Item Code/Date Code:
P7193ZA/0320

62000000056463/1020