Summary of Product Characteristics for Pharmaceutical Products

1. **Name of the medicinal product:**
   Nil worm tablets 400mg (Chewable)
2. **Qualitative and quantitative composition**
   Each chewable uncoated tablet contains:
   Albendazole USP…….400mg
   Excipients with potential clinical effect
   Each tablet contains about 150 mg of lactose monohydrate and 2.4mg of sunset yellow colour.
3. **Pharmaceutical form**
   Orange coloured capsule shaped uncoated chewable tablet with break line on one side and other side plain. (the break line is only to facilitate breaking for ease of swallowing and not to divide into equal doses)
4. **Clinical particulars**

4.1 Therapeutic indications

Nil worm is a broad-spectrum anthelmintic used for the treatment of the following infections:

Cestode infections (tapeworms)

Nil worm is indicated for the treatment of Echinococcus multilocularis and E. granulosus infections before or after surgery or where surgery is not suitable.

Nil worm is further indicated for the treatment of neurocysticercosis caused by larval forms of the pork tapeworm, Taenia solium. It may also be given for preventive chemotherapy of Taenia solium taeniasis in endemic populations, where other alternatives are not available.

Lymphatic filariasis

Nil worm is indicated together with ivermectin and/or diethylcarbamazine for the elimination of lymphatic filariasis.

Treatment is given to the entire eligible population in endemic areas through a mass drug administration programme.

Other nematode infections (roundworms)

Nil worm is effective for the treatment of various nematode infections. Nil worm can be used, alone or in combination with other medicines, for the control of soil-transmitted helminthiasis (ascariasis, trichuriasis and hookworm infections) through mass drug administration programmes.

4.2 Posology and method of administration

Posology

Cestode infections (tapeworms)

Adults

In adults over 60 kg, the usual dose for treatment of echinococcosis or Taenia solium neurocysticercosis is 400 mg twice a day. In adults up to 60 kg, the dose is 15 mg/kg daily in 2 divided doses (maximum 800 mg daily).

For cystic echinococcosis, Nil worm treatment is continued for 3 to 6 months or longer.

For alveolar echinococcosis treatment should be given for at least 2 years and may be continued for many years, reviewed at 2-year intervals.

For neurocysticercosis, treatment with Nil worm is usually for 10–14 days but can be increased to up to 30 days or more for extraparenchymal cysts (e.g. in the ventricles or subarachnoid space).

Children

Only limited data are available on the use of Nil worm in children for cestode infections.

Mass drug administration

In mass drug administration programmes for preventive chemotherapy of taeniasis where other alternatives are not available, Nil worm may be given to endemic populations from 2 years of age in a dose of 400 mg daily for 3 consecutive days. Because of the risk of triggering latent neurocysticercosis, a reporting system must be in place with active surveillance and referral of any neurological adverse events.

Nematode infections

For the elimination of lymphatic filariasis and the control of soil-transmitted helminthiasis (ascariasis, trichuriasis, or hookworm disease), a single oral dose of Nil worm is normally given once a year in mass treatment programmes. The dose may be given twice a year at 6-monthly intervals, if required, in line with national treatment plans. For lymphatic filariasis, Nil worm is given together with diethylcarbamazine, or ivermectin, or both.

Adults and children aged over 2 years

In adults and children aged over 2 years, the dose of Nil worm for mass drug administration is 400 mg.

Children aged 1–2 years

In children aged 1–2 years, the dose of Nil worm for the control of soil-transmitted helminthiasis is 200 mg (half a tablet).

Nil worm is not used in children below 2 years for the elimination of lymphatic filariasis.

Special populations

Renal impairment

No dose adjustment is required.

Hepatic impairment

Caution should be used if Nil worm is given to patients with liver disease, since Nil worm is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

Method of administration

Oral use.

For young children or patients not able to swallow the tablets whole, the tablets may be crushed and added to a small amount of semi-solid food or liquid, all of which should be swallowed immediately.

Nil worm should be taken with a meal for the prevention and treatment of tissue infections such as echinococcosis, neurocysticercosis and lymphatic filariasis. Taking Nil worm with a fatty meal improves its bioavailability and leads to higher blood levels (see section 5.2).

For treatment of intestinal infections such as taeniasis or soil-based helminth infections, Nil worm should be taken at least 2 hours after a meal and 30 minutes before the next meal. This leads to higher intestinal and lower systemic Nil worm levels, which is desirable in these conditions.

4.3 Contraindications

Hypersensitivity to the active substance, other benzimidazoles or to any excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Pre-existing neurocysticercosis

Treatment with Nil worm may uncover pre-existing neurocysticercosis, particularly in areas where taeniasis is common.

Patients may experience neurological symptoms such as 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 develop rapidly after treatment, and appropriate corticosteroid and anticonvulsant therapy should be given straight away.

Risk of retinal damage in patients with retinal neurocysticercosis

Cysticercosis may, in rare cases, involve the retina. Before starting therapy for neurocysticercosis, the patient should be examined for the presence of retinal lesions. If such lesions are present, the need for anticysticeral therapy should be weighed against the possibility of retinal damage caused by Nil worm-induced changes to the retinal lesion.

Hepatic effects

Patients undergoing treatment for echinococcosis should have their liver function tested before the start of treatment and regularly (ideally every 2 weeks) during treatment. Patients with disturbed liver function tests before starting Nil worm should be carefully evaluated, since the medicine is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

Mild to moderate elevations of liver enzymes have been reported frequently with prolonged Nil worm treatment. Enzyme abnormalities are usually reversible on discontinuation of treatment. In prolonged higher- dose Nil worm therapy for echinococcosis there have been rare reports of severe hepatic abnormalities such as jaundice and histological hepatocellular damage, which may be irreversible.

If enzymes are significantly increased (greater than twice the upper limit of normal) during treatment, Nil worm should be discontinued. Nil worm treatment may be reinstituted when levels have returned to normal limits, but liver function should be monitored frequently during repeat therapy.

Bone marrow suppression

Nil worm can cause bone marrow suppression and therefore blood counts are needed at the start and ideally every two weeks thereafter during treatment for echinococcosis. Patients with liver disease, including hepatic echinococcosis, may be more susceptible to bone marrow suppression leading to pancytopenia, aplastic anaemia, agranulocytosis and leucopenia and therefore warrant closer monitoring of blood counts.

Nil worm should be discontinued if clinically significant decreases in blood cell counts occur.

Excipients

Patients with congenital lactase deficiency, galactosaemia or glucose-galactose intolerance must not be given this medicine unless strictly necessary. The small amount of lactose in each dose may cause symptoms of intolerance in other patients.

Patients who are allergic to cow's milk proteins must not be given this medicine unless strictly necessary.

Nil worm contains Sunset yellow colour. This may cause allergic reactions.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine, dexamethasone and praziquantel may all increase the plasma concentration of the active metabolite of Nil worm, Nil worm sulfoxide. Carbamazepine, phenobarbital, phenytoin and ritonavir may reduce plasma concentrations of the active metabolite of Nil worm. 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.

4.6 Pregnancy and Lactation

Women of childbearing potential

Pregnancy should be avoided in women treated with Nil worm. Adequate contraceptive measures should be taken, particularly with prolonged treatment.

Pregnancy

There are no adequate and well-controlled studies of Nil worm administration in pregnant women. Limited data from inadvertent single-dose administration of Nil worm during the first trimester have not demonstrated an increased incidence of congenital anomalies. However, animal studies with Nil worm have revealed evidence of teratogenicity in rats and rabbits (see section 5.3), and therefore preventive chemotherapy with Nil worm is not recommended in the first trimester of pregnancy.

In general, Nil worm should be used in pregnant women only if there are no alternatives and the potential benefit justifies the potential risk to the fetus.

Breast-feeding

Nil worm and its active metabolite pass into breast milk in very small amounts; it is generally considered compatible with breast-feeding, particularly in single doses.

Fertility

There are no data on the effects of Nil worm on human male or female fertility. Animal studies indicate no effects of Nil worm on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Nil worm is unlikely to affect the ability to drive or operate machinery. However, patients should be advised to consider if their clinical status, including any undesirable effects of the medicine, allows them to perform skilled tasks safely.

4.8 Undesirable effects

Data from clinical trials and post-marketing surveillance were used to estimate the frequency of adverse events linked to Nil worm.

The adverse reactions considered related to Nil worm are listed below by body system, organ class and absolute frequency. Frequencies are defined as very common (≥ 1/10), common (1/100 to 1/10), uncommon (1/1000 to 1/100), rare (1/10 000 to 1/1000), and very rare (< 1/10 000).

Short duration of treatment

Blood and lymphatic system disorders

Rare Low red cell count

Immune system disorders

Rare Hypersensitivity reactions including rash, pruritus and urticaria

Nervous system disorders

Uncom Headache, dizziness

mon	
Gastrointestinal disorders	
Commo n	Upper gastrointestinal symptoms (e.g. epigastric or abdominal pain, nausea, vomiting)
Uncom mon	Diarrhoea
Hepatobiliary disorders	
Rare	Elevations of hepatic enzymes
Skin and subcutaneous tissue disorders	
Uncom mon	Itchiness, skin rashes
Very rare	Erythema multiforme, Stevens-Johnson syndrome
Musculoskeletal and connective tissue disorders	
Rare	Bone pain
Renal and urinary disorders	
Rare	Proteinuria

Longer duration of treatment

Blood and lymphatic system disorders	
Uncom mon	Leucopenia
Rare	Low red cell count
Very rare	Pancytopenia, aplastic anaemia, agranulocytosis
Immune system disorders	
Uncom mon	Hypersensitivity reactions including rash, pruritus and urticaria
Nervous system disorders	
Very commo n	Headache
Commo n	Dizziness
Gastrointestinal disorders	
Commo n	Gastrointestinal disturbances (abdominal pain, nausea, vomiting)
Hepatobiliary disorders	
Very commo n	Mild to moderate elevations of hepatic enzymes
Uncom mon	Hepatitis[1]
Skin and subcutaneous tissue disorders	
Commo n	Reversible alopecia (thinning of hair, and moderate hair loss)
Very rare	Erythema multiforme, Stevens-Johnson syndrome
Musculoskeletal and connective tissue disorders	
Rare	Bone pain

Renal and urinary disorders		
Rare	Proteinuria	
General disorders		
Common	Fever	

[1] With prolonged Nil worm treatment for echinococcosis there have also been reports of severe hepatic abnormalities, including jaundice and hepatocellular damage which may be irreversible.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Pharmacy and Poisons Board-Pharmacovigilance Electronic Reporting System (PvERS); *https://pv.pharmacyboardkenya.org* .

4.9 Overdose

In case of overdosage, symptomatic therapy and general supportive measures are recommended.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antihelmintics, benzimidazole derivatives,
ATC code: P02CA03.

Mechanism of action

Nil worm is a benzimidazole derivative that causes degenerative alterations in the tegument and intestinal cells of the parasite and blocks their energy production, ultimately leading to immobilisation and death of the parasite. It works by binding to the colchicine-sensitive site of tubulin, thus inhibiting its assembly into microtubules. As cytoplasmic microtubules are critical in promoting glucose uptake, the glycogen stores of the parasites are depleted. Nil worm exhibits larvicidal, ovicidal and vermicidal activity against helminth parasites. At lower doses the anthelminthic action of Nil worm is thought to be mainly intra-intestinal. However, at higher doses, sufficient is absorbed and metabolised to the active sulfoxide metabolite to have a therapeutic effect against tissue parasites.

A number of studies have suggested that therapeutic doses of benzimidazoles are only parasitostatic against
E. multilocularis. Nonetheless, after several years of Nil worm treatment, treatment interruption may be considered, in the absence of progression of the lesions assessed by conventional imaging, and indirect assessment of viability using PET/CT. Although it does not provide direct evidence of *E. multilocularis* viability, and recurrence may occur, this technique, together with the follow-up of specific serum antibodies, may support decision-making and follow-up after Nil worm withdrawal in highly selected patients.

5.2 Pharmacokinetic properties

The absorption characteristics of Nil worm have been determined in healthy subjects under fed conditions as follows:

Pharmacokinetic variable	**Mean value* (±standard deviation)**
	Nil worm
Maximum concentration (Cmax) ng/mL	84 ± 89
Area under the curve (AUC0-∞), a measure of the extent of absorption ng.h/Ml	314 ± 368
Time to attain maximum concentration (Tmax) # hour	4.0 (1.33 – 5.0)

Pharmacokinetics of Nil worm

General	
	Nil worm concentrations are negligible or undetectable in plasma as it is rapidly converted into the sulfoxide metabolite prior to reaching the systemic circulation. The systemic anthelmintic activity has been attributed to this primary metabolite, Nil worm sulfoxide. Maximal plasma concentrations of Nil worm sulfoxide are typically achieved 2 to 5 hours after dosing.
Absorption	
Absolute bioavailability	Not available
Oral bioavailability	Nil worm is poorly absorbed from the gastrointestinal tract (< 5%) due to its low aqueous solubility.

Food effect	Absorption is significantly enhanced (approximately 5-fold) if Nil worm is taken with a fatty meal. Following a single 400 mg oral dose of Nil worm, the maximum plasma concentration of Nil worm sulfoxide was 0.4–1.6 µmol/L in fasting patients and 1.8–6.0 µmol/L when taken with breakfast (estimated fat content 40 g).
Distribution	
Volume of distribution (mean)	Not available
Plasma protein binding *in vitro*	Nil worm sulfoxide is 70% bound to plasma protein.
Tissue distribution	Nil worm sulfoxide is widely distributed throughout the body; it has been detected in urine, bile, liver, cyst wall, cyst fluid, and cerebral spinal fluid.
Metabolism	
	Nil worm rapidly undergoes extensive first-pass metabolism in the liver to Nil worm sulfoxide, and is generally not detected in plasma. Nil worm sulfoxide is further metabolised to Nil worm sulfone and other primary oxidative metabolites.
Active metabolite(s)	Nil worm sulfoxide
Elimination	
Elimination half life	The terminal elimination half-life of Nil worm sulfoxide typically ranges from 8 to 12 hours.
Mean systemic clearance (Cl/F)	
Excretion	Following oral administration, Nil worm has not been detected in human urine. Nil worm sulfoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion appearing in the urine.
Pharmacokinetic linearity	
	Plasma concentrations of Nil worm sulfoxide increase in a dose-proportional manner over the therapeutic dose range following ingestion of a fatty meal.
Drug interactions *(in vitro*)	
Transporters	Not available

Metabolising enzymes	Not available

Special populations

Renal impairment

Since renal elimination of Nil worm and its primary metabolite, Nil worm sulfoxide, is negligible, it is unlikely that clearance of these compounds would be altered in these patients.

Liver impairment

In patients with evidence of extrahepatic obstruction, the systemic availability of Nil worm sulfoxide was increased 7-fold.

Elderly patients

Although no studies have investigated the effect of age on Nil worm sulfoxide pharmacokinetics, data suggest that the pharmacokinetics are similar to those in young healthy subjects.

Children

Following single-dose administration of 200 to 300 mg (approximately 10 mg/kg) Nil worm to paediatric patients with hydatid cyst disease (age range 6 to 13 years), Nil worm sulfoxide pharmacokinetics were similar to those observed in fed adults.

5.3 Preclinical safety data

General toxicity

Studies of up to 6 months in mice, rats and dogs recognised the haematopoietic system and the liver as target organs of toxicity.

Genotoxicity

In genotoxicity tests, Nil worm was found negative in an Ames Salmonella/microsome plate mutation assay, Chinese hamster ovary chromosomal aberration test, and in vivo mouse micronucleus test. In the in vitro BALB/3T3 cells transformation assay, Nil worm produced weak activity in the presence of metabolic activation while no activity was found in the absence of metabolic activation.

Carcinogenicity

Long-term carcinogenicity studies in mice and rats found no evidence of increased incidence of tumours was found in the mice or rats at up to 400 mg/kg/day and 20 mg/kg/day, respectively.

Effects on reproduction

Nil worm did not affect male or female fertility in the rat at an oral dose level of 30 mg/kg/day.

Nil worm was teratogenic (embryotoxicity and skeletal malformations) in pregnant rats and rabbits. The teratogenic response in the rat occurred at oral doses of 10 and 30 mg/kg/day during gestation days 6 to 15, and in pregnant rabbits at oral doses of 30 mg/kg/day during gestation days 7 to 19. In the rabbit study, maternal toxicity (33% mortality) occurred at 30 mg/kg/day. In mice, no teratogenic effects were observed at oral doses up to 30 mg/kg/day administered during gestation days 6 to 15.

6. Pharmaceutical Particulars

6.1 List of Excipients

Excipients	**Specification**	**Quantity (mg)/ Tablet**
Lactose	BP	155.000mg
Microcrystalline cellulose	BP	100.000mg
Maize starch	BP	200.600mg
Maize starch (for paste)	BP	40.000mg
Sunset yellow colour	IH	2.400mg
Povidone	BP	10.500mg
Saccharin sodium	BP	8.000mg
Polysorbate 80	BP	12.000
Flavor Orange	IH	6.000mg
Magnesium Stearate	BP	5.500mg
Croscarmellose sodium	BP	30.000mg
Croscarmellose sodium (lubricant)	BP	15.000mg

6.2 Incompatibilities

Not applicable.

6.3 Shelf-Life

36 months

6.4 Special Precautions for storage

Store below 30°C in a cool and dry place.
Protect from light.
Discard the product 30 days after initial opening.
Keep out of reach of children.

6.5 Nature and Content of container

Alu-PVC blister pack of 1 tablet.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing Authorization Holder

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8. Marketing Authorization Number

CTD8476

9. Date of first authorization/renewal of the authorization

29/06/2023

10. Date of revision of the text

10th May, 2025