SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

1. NAME OF THE MEDICINAL PRODUCT

NILWORM (Albendazole Tablets 400 mg (chewable))

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition:

Each uncoated chewable tablet contains:

Albendazole USP 400 mg

Colour: Sunset yellow supra

Excipients: q.s.

S.N.	Ingredients	Spec.	Qty/ Tab (mg)	Ovg. %	Function
1	Albendazole	USP	400.00	--	Active
2	Lactose	BP	155.00	--	Diluent
3	Micro crystalline cellulose	BP	100.00	--	Diluent
4	Maize starch	BP	200.60	--	Binder
5	Croscarmellose sodium	BP	30.00	--	Superdisintegrant
6	Maize starch (for paste)	BP	40.00	--	Binder
7	Povidone	BP	10.50	--	Diluent
8	Polysorbate 80	BP	12.00	--	Solubilizer
9	Saccharin Sodium	BP	8.00	--	Sweetening agent
10	Colour sunset yellow	INH	2.40	--	Colour
	Lubricant				
11	Orange flavour	INH	6.00	--	Flavour
12	Croscarmellose sodium	BP	15.00	--	Superdisintegrant
13	Magnesium stearate	BP	5.50	--	Lubricant
	Total		**985.00**		

USP: United States Pharmacopoeia

BP: British Pharmacopoeia

INH: IN- House specification

Average weight of uncoated tablet: 985.00 mg ± 5.0%

3. PHARMACEUTICAL FORM

Uncoated chewable tablet

4.CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

i) Symptomatic relief of rheumatic aches and pains and of influenza, feverishness and feverish colds

ii) For the treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, Echinococcus granulosus.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Route of administration: Oral

Age 12 to 24 months: 200 mg as a single dose

Adults & children (over two years): One of Albendazole Tablet 400 mg chewable as a single dose in cases of Enterobius vermicularis, Trichuris trichiura, Ascaris lumbricoides, Ancylostoma duodenale and Necator americanus.

In cases of strongyloidiasis or taeniasis, one of Albendazole tablets 400 mg chewable as a single dose should be given for three consecutive days.

Giardiasis: One of Albendazole tablets 400 mg chewable once daily for five days.

In hydatid disease (Echinococcosis): In the treatment of echinococcosis, (Albendazole) is given by mouth with meals in a dose of 400 mg twice daily for 28 days for patients weighing over 60 kg.

A dose of 15 mg/kg body weight daily in two divided doses (to a maximum total daily dose of 800 mg) is used for patients weighing less than 60 kg.

For cystic echinococcosis: the 28-days course may be repeated after 14 days without treatment to a total of three treatment cycles. For alveolar echinococcosis, cycles of 28 days of treatment followed by 14 days without treatment may need to continue for months or years. When three courses of therapy have been given in the pre or post surgical setting, optimal killing of cyst contents is achieved.

4.3 CONTRAINDICATIONS

It is contraindicated in patients with known Hypersensitivity to the Benzimidazole class of compounds or any components of Albendazole.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Rare fatalities have been reported due to granulocytopenia or pancytopenia. Albendazole has been shown to cause bone marrow suppression, aplastic anemia, and agranulocytosis in patients with and without underlying hepatic dysfunction. Blood counts should be monitored at the beginning of each 28-day cycle

of therapy, and every 2 weeks while on therapy with Albendazole in all patients. Patients with liver disease, including hepatic echinococcosis, appear to be more at risk for bone marrow suppression leading to pancytopenia, aplastic anemia, agranulocytosis, and leukopenia attributable to Albendazole and warrant closer monitoring of blood counts. Albendazole should be discontinued in all patients if clinically significant decreases in blood cell counts occur.

Albendazole should not be used in pregnant women except in clinical circumstances where no alternative management is appropriate. Patients should not become pregnant for at least 1 month following cessation of Albendazole therapy. If a patient becomes pregnant while taking this drug, Albendazole should be discontinued immediately. If pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Precautions: Patients being treated for neurocysticercosis should receive appropriate steroid and anticonvulsant therapy as required. Oral or intravenous corticosteroids should be considered to prevent cerebral hypertensive episodes during the first week of anticysticeral therapy.

Pre-existing neurocysticercosis may also be uncovered in patients treated with Albendazole for other conditions. 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.

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

4.5 INTERACTION WITH OTHER MEDICINAL PRODUCTS AND PHARMACEUTICAL FORM

Dexamethasone

Steady-state trough concentrations of Albendazole Sulfoxide were about 56% higher when 8 mg Dexamethasone was co-administered with each dose of Albendazole (15 mg/kg/day) in 8 neurocysticercosis patients.

Praziquantel

In the fed state, Praziquantel (40 mg/kg) increased mean maximum plasma concentration and area under the curve of Albendazole Sulfoxide by about 50% in healthy subjects (n = 10) compared with a separate group of subjects (n = 6) given Albendazole alone. Mean Tmax and mean plasma elimination half-life of Albendazole Sulfoxide were unchanged. The pharmacokinetics of Praziquantel were unchanged following coadministration with Albendazole (400 mg).

Cimetidine

Albendazole Sulfoxide concentrations in bile and cystic fluid were increased (about 2-fold) in hydatid cyst patients treated with Cimetidine (10 mg/kg/day) (n = 7) compared with Albendazole (20 mg/kg/day) alone (n = 12). Albendazole Sulfoxide plasma concentrations were unchanged 4 hours after dosing.

Theophylline

The pharmacokinetics of Theophylline (Aminophylline 5.8 mg/kg infused over 20 minutes) was unchanged following a single oral dose of Albendazole (400 mg) in 6 healthy subjects.

4.6 PREGNANCY AND LACTATION

Albendazole should not be used in pregnant women except in clinical circumstances where no alternative management is appropriate. Patients should not become pregnant for at least 1 month following cessation of Albendazole therapy. If a patient becomes pregnant while taking this drug, Albendazole should be discontinued immediately. If pregnancy occurs while taking this drug, the patient should be apprised of the potential hazard to the fetus.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

None such data reported.

4.8 UNDESIRABLE EFFECTS

i. There have been rare reports of granulocytopenia, pancytopenia, agranulocytosis, or thrombocytopenia.
ii. Patients with liver disease, including hepatic echinococcosis, appear to be more at risk of bone marrow suppression.
iii. Immune system disorders, Hypersensitivity reactions, including rash and urticaria.

4.9 OVERDOSAGE

If poisoning or excessive overdosage is suspected it is recommended, on general principles, that vomiting be induced or gastric lavage be performed, and such symptomatic supportive therapy be administered as appears indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMICS PROPERTIES

Therapeutic category: Anthelmintic

Mechanism of action

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by binding to the colchicine-sensitive site of tubulin, thus inhibiting its polymerization or assembly into microtubules. The loss of the cytoplasmic microtubules leads to impaired uptake of glucose by the larval and adult stages of the susceptible parasites and depletes their glycogen stores. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventually dies.

Albendazole also has been shown to inhibit the enzyme fumarate reductase, which is helminth-specific. This action may be considered secondary to the effect on the microtubules due to the decreased absorption of glucose.

This action occurs in the presence of reduced amounts of nicotinamide-adenine dinucleotide in reduced form (NADH), which is a coenzyme involved in many cellular oxidation-reduction reactions.

Albendazole has larvicidal effects in necatoriasis and ovicidal effects in ascariasis, ancylostomiasis, and trichuriasis.

5.2 PHARMACOKINETIC PROPERTIES

Absorption and Metabolism

Albendazole is poorly absorbed from the gastrointestinal tract due to its low aqueous solubility. Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted to the sulfoxide metabolite prior to reaching the systemic circulation. The systemic anthelmintic activity has been attributed to the primary metabolite, albendazole sulfoxide. Oral bioavailability appears to be enhanced when albendazole is co-administered with a fatty meal (estimated fat content 40 g) as evidenced by higher (up to 5-fold on average) plasma concentrations of albendazole sulfoxide as compared to the fasted state.

Maximal plasma concentrations of albendazole sulfoxide are typically achieved 2 to 5 hours after dosing and are on average 1.31 mcg/mL (range 0.46 to 1.58 mcg/mL) following oral doses of albendazole (400 mg) in 6 hydatid disease patients, when administered with a fatty meal. Plasma concentrations of albendazole sulfoxide increase in a dose-proportional manner over the therapeutic dose range following ingestion of a fatty meal (fat content 43.1 g). The mean apparent terminal elimination half-life of albendazole sulfoxide typically ranges from 8 to 12 hours in 25 normal subjects, as well as in 14 hydatid and 8 neuro cysticercosis patients.

Following 4 weeks of treatment with albendazole (200 mg three times daily), 12 patients' plasma concentrations of albendazole sulfoxide were approximately 20% lower than those observed during the first half of the treatment period, suggesting that albendazole may induce its own metabolism.

Distribution

Albendazole sulfoxide is 70% bound to plasma protein and is widely distributed throughout the body; it has been detected in urine, bile, liver, cyst wall, cyst fluid, and cerebral spinal fluid (CSF). Concentrations in plasma were 3- to 10-fold and 2- to 4-fold higher than those simultaneously determined in cyst fluid and CSF, respectively. Limited in vitro and clinical data suggest that albendazole sulfoxide may be eliminated from cysts at a slower rate than observed in plasma.

Metabolism and Excretion

Albendazole is rapidly converted in the liver to the primary metabolite, albendazole sulfoxide, which is further metabolized to albendazole sulfone and other primary oxidative metabolites that have been identified in human urine. Following oral administration, albendazole has not been detected in human

urine. Urinary excretion of albendazole sulfoxide is a minor elimination pathway with less than 1% of the dose recovered in the urine. Biliary elimination presumably accounts for a portion of the elimination as evidenced by biliary concentrations of albendazole sulfoxide similar to those achieved in plasma.

Special Populations

Patients with Impaired Renal Function

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

5.3 PRECLINICAL SAFETY DATA

Not applicable

6.PHARAMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

S.N.	Excipients	Specification
1	Lactose	As per BP
2	Micro crystalline cellulose	As per BP
3	Maize starch	As per BP
4	Croscarmellose sodium	As per BP
5	Maize starch (for paste)	As per BP
6	Povidone	As per BP
7	Polysorbate 80	As per BP
8	Saccharin sodium	As per BP
9	Colour sunset yellow	As per INH
10	Orange flavour	As per INH
11	Magnesium stearate	As per BP

BP: British Pharmacopoeia

INH: IN- House specification

6.2 INCOMPATIBILITY

None such data reported

6.3 SHELF LIFE

36 months (3 years)

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 30°C. Protected from light.

6.5 NATURE AND CONTENTS OF CONTAINER

Blister pack of 1 tablet

6.6 SPECIAL PRECAUTIONS FOR DISPOSABLE AND OTHER HANDLING

None such special precautions for disposing and handling applies for this product.