SUMMARY OF PRODUCT CHARACTERSTICS

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1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Product Name **: UBENZOLE – 400 (Albendazole Tablets USP 400mg)**
Strength **:** 400 mg
Pharmaceutical Form **:** Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Label Claim:
Each uncoated Chewable tablet contains:
Albendazole USP ..... .400 mg
Excipients .....q.s.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Light orange coloured, oblong, biconvex uncoated chewable tablet.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Single dose or short term courses of Ubenzole-400 are indicated in the treatment of single or mixed infestations of intestinal and tissue parasites, in adults and children over 2 years of age.

Clinical studies have shown Ubenzole-400 to be effective in the treatment of infections caused by:

Enterobius vermicularis (pinworm/threadworm), Ascaris lumbricoides (roundworm), Ancylostoma duodenale and Necator americanus (hookworms), Trichuris trichiura (whipworm), Strongyloides stercoralis, animal hookworm larvae causing cutaneous larva migrans, and the liver flukes Opisthorchis viverrini and Clonorchis sinensis.

Ubenzole-400 is also indicated for the treatment of Hymenolepis nana when other susceptible helminths species are present. Treatment courses should be extended to 3 days.

4.2 Posology and method of administration

Dosage of Albendazole varies, depending on which of the following parasitic infections is treated. In young children, the tablets should be crushed or chewed and swallowed with a glass of water.

Indication	**Weight of the patient**	**Dose**	**Duration**

Hydatidologie	60 kg or more	400 mg twice a day, with meals	28 day cycle with a 14-day albendazole free interval, for a total of 3 cycles
	Under 60 kg	15 mg / kg / day in doses divided twice daily with meals (maximum total daily dose of 800 mg)	
	NOTE: When administering Albendazole in the post-surgical setting in pre-ou, killing optimal content of the cyst is achieved when 3 courses of therapy have been given.		
Neurocysticercosis	60 kg or more	400 mg twice a day, with meals	8-30 days
	under 60 kg	15 mg / kg / day in doses divided twice daily with meals (maximum total daily dose of 800 mg)	

Patients treated for neurocysticercosis should receive a corticosteroid and anticonvulsant as required. Oral or intravenous corticosteroids should be considered to avoid cerebral episodes of high blood pressure during the first week of treatment.

4.3 Contraindications

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

Albendazole has been shown to be teratogenic and embryotoxic in rats and rabbits. Women of childbearing age should be advised to take effective precautions against conception during and within one month of completion of treatment with Ubenzole-400.

Albendazole is contraindicated in persons who are known to be hypersensitive to albendazole, other benzimidazole derivatives, or any component of the tablets.

4.4 Special warnings and special precautions for use

Rare deaths associated with the use of the Ubenzole have been reported due to granulocytopenia Albendazole or pancytopenia has been shown to cause suppression of the bone marrow, aplastic anemia and agranulocytosis in patients with and without underlying liver dysfunction. Blood count should be monitored at the beginning of each cycle of 28 days of therapy, and every 2 weeks during treatment with a albendazole in all patients. Patients with liver disease, including liver echinococcosis, seem to be more at risk of removal of the bone marrow causing a pancytopenia, aplastic anemia, agranulocytosis and leukopenia attributable to albendazole and so warrant closer monitoring of blood counts. Albendazole should be interrupted in all patients, if a clinically significant decrease in the number of blood cells occur.

Albendazole should not be used in pregnant women, except in clinical circumstances where no alternative is appropriate. Patients should not become pregnant for at least a month after

discontinuation of the therapy of albendazole. If a patient becomes pregnant while she is taking this drug, albendazole should be discontinued immediately. If a pregnancy occurs while taking this drug, the patient should be informed of the potential risk to the fetus.

Precautions:

General
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.

Laboratory tests

The white blood cell count

Albendazole has been shown to cause occasional (less than 1% of treated patients) reversible reductions in total number of white blood cells. Rarely, deeper cuts may be encountered, including granulocytopenia, agranulocytosis, or a pancytopenia. Complete blood count should be done at the beginning of each cycle of 28 days and all treatment 2 weeks during each cycle of 28 days for all patients. Patients with liver disease, including liver echinococcosis, seem to be more at risk of bone marrow suppression and warrant closer monitoring of blood counts. Albendazole should be interrupted in all patients, if a clinically significant decrease in the number of blood cells occur.

Liver function

In clinical trials, treatment with albendazole has been associated with slight elevations to moderate liver enzymes in about 16% of patients. These elevations have generally returned to normal after stopping the treatment. He's also been cases of acute hepatic failure of uncertain causation and hepatitis.

Tests of liver function (transaminases) must be made before the start of each cycle of treatment and at least every 2 weeks during treatment. If the liver enzymes exceeded twice the upper limit of normal, consideration should be given to the treatment of albendazole depending on the circumstances of each patient. Restart the treatment in patients whose liver enzymes albendazole is are standardized without treatment is an individual decision which must take account of the risk / benefit of the use of albendazole further. Laboratory tests must be performed frequently if albendazole treatment is restarted.

Patients with abnormal liver function test results are at increased risk of Hepatotoxicity and suppression of the bone marrow. The treatment should be discontinued if liver enzymes are significantly increased or clinically significant reductions in the number of blood cells occur.

4.5 Interaction with other FPP and other forms of interaction

Dexamethasone
Steady-state trough concentrations of albendazole sulfoxide were about 56% higher when 8 mg dexamethasone was coadministered 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) were unchanged following a single oral dose of albendazole (400 mg) in 6 healthy subjects.

4.6 Pregnancy and lactation

Ubenzole-400 is contraindicated during pregnancy, and for one month prior to conception. In order to avoid administering albendazole during early pregnancy, women of child bearing age should initiate treatment during the first week of menstruation or after a negative pregnancy test. The use of Ubenzole-400 in human pregnancy has not been studied, but in animal studies it is teratogenic in more than one species. In animal studies oral treatment with maternotoxic doses of albendazole (30mg/kg/day) during the period of organogenesis was associated with multiple malformations in rats and ectrodactyly in rabbits. In one study in rats, an oral dose (10mg/kg/day) similar to the human therapeutic dose was not maternotoxic, but was associated with microphthalmia and microfetalis. The latter occurred alone and together with multiple malformations including cranioschisis, talipes and renal agenesis. There is no information on the possible effect of albendazole on the human foetus.
Lactation: Adequate human and animal data on use during lactation are not available. Therefore breast feeding should be discontinued during and for a minimum of 5 days after treatment.

4.7 Effects on ability to drive and use machines

There have been no studies to investigate the effect of albendazole 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 albendazole.

4.8 Undesirable effects

The adverse event profile of albendazole differs between hydatid disease and neurocysticercosis. Adverse events occurring with a frequency of ≥1% in either disease are described in the table below. These symptoms were usually mild and resolved without treatment. Treatment discontinuations were predominantly due to leukopenia (0.7%) or hepatic abnormalities (3.8% in hydatid disease). The following incidence reflects events that were reported by investigators to be at least possibly or probably related to albendazole.

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Adverse Event	Hydatid Disease	Neurocysticercosis
Abnormal Liver Function Tests	15.6	< 1.0
Abdominal Pain	6.0	0
Nausea/Vomiting	3.7	6.2
Headache	1.3	11.0
Dizziness/Vertigo	1.2	< 1.0
Raised Intracranial Pressure	0	1.5
Meningeal Signs	0	1.0
Reversible Alopecia	1.6	< 1.0
Fever	1.0	0

Blood and Lymphatic System Disorders: Aplastic anemia, bone marrow suppression, neutropenia.

Hepatobiliary Disorders: Elevations of hepatic enzymes, hepatitis, acute liver failure.

Skin and Subcutaneous Tissue Disorders: Erythema multiforme, Stevens-Johnson syndrome.

Renal and Urinary Disorders: Acute renal failure.

4.9 Overdose

Significant toxicity and mortality were seen in male and female mice at doses exceeding 5,000 mg /kg; in rats, at estimated doses between 1,300 and 2,400 mg /kg; in hamster, at doses exceeding 10,000 mg /kg. In animals, symptoms were demonstrated in a dose- response relationship and included diarrhea, vomiting, tachycardia and respiratory distress.

No untoward effects were reported in case of overdose symptomatic therapy e.g. gastric lavage and activated charcoal and general supportive measurs are recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: P02CA03.
Mechanism of Action Albendazole is a benzimidazole carbamate with antiprotozoal and anthelmintic effects against intestinal and tissue parasites. 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.

Systemic Helminth Infections
Albendazole is effective in the treatment of tissue parasites, including cystic echinococcosis and alveolar echinococcosis caused by infestation of Echinococcus granulosus and Echinococcus multilocularis, respectively. Albendazole is also effective in the treatment of neurocysticercosis caused by larval infestation of Taenia solium.
Albendazole has been shown (in clinical trials) to eradicate cysts or significantly reduce cyst size in up to 80% of patients with Echinococcus granulosus cysts who were treated. Where cysts have been investigated for viability following treatment with albendazole, 90% have been non-viable in laboratory or animal studies compared to only 10% of untreated cysts.
In the treatment of cysts due to Echinococcus multilocularis, a minority of patients were considered to be cured and a majority had an improvement or stabilisation of disease due to albendazole therapy.

5.2 Pharmacokinetic properties

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. Elimination from cysts has been shown to occur over several weeks following high and prolonged dosing.

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 relevant information.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on studies of safety pharmacology, genotoxicity and toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

AC-DI-SOL (Crosscarmellose Sodium NF)
Mannitol
Colloidal Silicon Dioxide
Crospovidone
Colour sunset yellow supra
Lactose
Maize Starch (Dry mix)*
Purified Water**
Isopropyl Alcohol**
P.V.P.K. 30
Tween 80 (Sorbox 80)
Magnesium Stearate
Sodium Lauryl Sulphate
Sodium Saccharin
Strawberry DC 109 C
Sodium Carboxy Methyl Cellulose
Talcum

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30° C.

6.5 Nature and contents of container

Blister pack of 1 Tablets

Alu PVC blister of 1 Tablets. 1 such blisters are packed in one printed carton with pack insert.

6.6 Instructions for use and handling and disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

Certificate No: 07740/09573/NMR/2022

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/09/2022

10. DATE OF REVISION OF THE TEXT

July 2023