SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

Nubend-200 (Albendazole Tablets 200mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sr. No.	Ingredient
1	Albendazole
2	Maize starch
3	Mannitol
4	Lactose
5	Saccharin Sodium
6	Sodium Citrate
7	Color Sunset yellow FCF
8	Magnesium Stearate
9	Colloidal Silicon Dioxide
10	Essence DC Capsaroma Orange

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Albendazole is active against most nematode and some cestode worms. It is used in the treatment of single or mixed intestinal nematode infections. It is indicated in ascariasis, hookworm infections, trichuriasis, strongyloidiasis, taeniasis when mixed with other infections.It is also used in enterobiasis, capillariasis. Albendazole has also been given in higher doses in the treatment of hydatid diseases.

4.2 Posology and method of administration

Albendazole is given by mouth, usually as a single dose, in the treatment of single or mixed intestinal nematode infections. The usual dose for adults or children aged 2 years or over the ascariasis, hookworm infections or trichuriasis is 400mg as a single dose. In strongyloidiasis, 400mg is given daily for 3 consecutive days; this may be repeated after 3 weeks if necessary; a similar schedule is used for taeniasis when mixed with other worm infections. In enterobiasis, children aged 2 years or more have been given a single dose of 100mg repeated after 7 days; the adult dose is 400mg repeated after 7 days. More prolonged treatment has been used in capillariasis.

4.3 Contraindications

Albendazole is contraindicated in pregnant women. If it is used in the pregnancy, especially during the first trimester, then such use should be where the potential benefits justify the risk to the fetus.

4.4 Special warnings and precautions for use

Warnings:

Rare fatalities associated with the use of Albendazole 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 28day 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.

Precautions:

Patients receiving high doses of Albendazole, such as those with hydatid disease, should be supervised closely with blood counts and liver function being monitored.

4.5 Interaction with other FPPs 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:

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.

Lactation:

Albendazole is excreted in animal milk. It is not known whether it is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when albendazole is administered to a nursing woman.

4.7 Effects on ability to drive and use machines

None has been reported so far.

4.8 Undesirable effects

Albendazole is generally well tolerated. The side effects produced are comparable to that of placebo. The commonly reported side effects include dizziness, headache, epigastric pain, dry mouth, fever, pruritus, vomiting and diarrhoea. Albendazole should only be used in the treatment of hydatid disease if there is constant medical supervision with regular monitoring of serum-

transaminase concentrations and of leucocytes and platelet counts. Patients with liver damage should be treated with reduced doses of 2- benzimidazolecarbamates, if at all.

4.9 Overdose

Significant toxicity and mortality were shown 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 hamsters, at doses exceeding 10,000 mg/kg; and in rabbits, at estimated doses between 500 and 1,250 mg/kg. In the animals, symptoms were demonstrated in a dose-response relationship and included diarrhea, vomiting, tachycardia, and respiratory distress.

One overdosage has been reported with Albendazole in a patient who took at least 16 grams over 12 hours. No untoward effects were reported. In case of overdosage, symptomatic therapy and general supportive measures are recommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthelmintic

ATC code: P02CA03

Mechanism of action

Albendazole's anthelmintic activity is considered to be dependent on the inhibition or destruction of cytoplasmic microtubules in the worm's intestinal or absorptive cells. Inhibition of glucose uptake and depletion of glycogen stores follow as do other inhibitory effects leading to death of the worm within several days.

Microbiology (when applicable)
Not Applicable

Drug resistance (when applicable)
Not Applicable

Cross resistance (when applicable)
Not Applicable

Pharmacodynamic effects

Albendazole, a benzimidazole carbamate derivative is an anthemintic with activity against most nematodes and some cestode worms; activity against some larval stages and ova has also been demonstrated.

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Inhibition of glucose uptake and depletion of glycogen stores follow as do other inhibitory effects leading to death of the worm within several days.

5.2 Pharmacokinetic properties

Absorption

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 coadministered 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 neurocysticercosis 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.

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.

Biliary Effects

In patients with evidence of extrahepatic obstruction (n = 5), the systemic availability of albendazole sulfoxide was increased, as indicated by a 2-fold increase in maximum serum concentration and a 7-fold increase in area under the curve. The rate of absorption/conversion and elimination of albendazole sulfoxide appeared to be prolonged with mean Tmax and serum elimination half-life values of 10 hours and 31.7 hours, respectively. Plasma concentrations of parent albendazole were measurable in only 1 of 5 patients.

Pediatrics

Following single-dose administration of 200 mg to 300 mg (approximately 10 mg/kg) albendazole to 3 fasted and 2 fed pediatric patients with hydatid cyst disease (age range 6 to 13 years), albendazole sulfoxide pharmacokinetics were similar to those observed in fed adults.

Elderly Patients

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.

5.3 Preclinical safety data

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch, Mannitol, Lactose, Saccharin Sodium, Sodium Citrate, Color Sunset yellow, Magnesium Stearate, Colloidal Silicon Dioxide, Ess. DC Capsaroma Orange.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months (3 Years)

6.4 Special precautions for storage

Store below 30ºC in a dry place. Protect from light.

6.5 Nature and contents of container

ALU/ALU Strip

6.6 Instructions for use and handling

The tablet should be chewed before swallowing.

7. MARKETING AUTHORISATION HOLDER

Kopran Limited

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

KOP/IND/006

04332/06824/REN/2018

9. DATE OF FIRST AUTHORISATION/RENEWALOF THE AUTHORISATION

26/03/2009

Jun 19, 2023

10. DATE OF REVISION OF THE TEXT

Jun 19, 2023