SUMMARY OFPRODUCTCHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICALPRODUCT

Albendazole Tablets USP 400mg (ALBEZOLE)

2. QUALITATIVE AND QUANTITATIVECOMPOSITION:

Each chewable tablet contains:

Albendazole USP 400 mg

Approved colour(s) as mentioned in Rule 127 of D and C Rules

For a full list of excipients, see section 6.1

3. PHARMACEUTICALFORM

Orange coloured, circular, flat tablets with bevelled edges having a breakline on oneface and plain on the other face of thetablet.

4. Clinicalparticulars

4.1 Therapeuticindications

- Albendazole is a member of the benzimidazole compounds used as a drug indicated forthe treatmentofavarietyofworminfestations.Itisabroadspectrumanthelmintic,effective against: roundworms, tapeworms, and flukes of domestic animals andhumans.
- As a vermicidal, albendazole causes degenerative alterations in the tegument andintestinal cellsofthewormbybindingtothecolchicine-sensitivesiteoftubulin,thusinhibitingits polymerizationorassemblyintomicrotubules.Thelossofthecytoplasmicmicrotubules leads to impaired uptake of glucose by the larval and adult stages of thesusceptible parasites, and depletes their glycogen stores. Degenerative changes in theendoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release oflysosomes result in decreased production of adenosine triphosphate (ATP), which is theenergy required for the survival of the helminth. Due to diminished energy production, the parasite is immobilized and eventuallydies.

4.2 Posology and method of administration

Posology

- Dosages are dependent on the parasite involved, the weight of the patient, and theseverity of theinfection:

CysticEchinococcosisPatients weighing >60kg

- Total daily dose: 800 mg given in two divided doses of 200 mg for a total of 28days.

Patients weighing <60kg

- Total daily dose: 12 mg/kg given in two equally divided doses (maximum dose800 mg/day) as above.

- This 28-day treatment period may be repeated after a 14-day period without treatment for a total of threecycles.

AlveolarEchinococcosis

- Patients weighing >60kg
- Total daily dose: 800 mg given in two equally divided doses for cycles of 28 days with14 days betweencycles.

Patients weighing <60kg

- Total daily dose: 12 mg/kg given in two equally divided doses (maximum dose800 mg/day) as above.
- Treatmentmayneedtobeprolongedformonthsoryears.Continuoustreatmentatthe same dose has been used for periods of up to 20months.

SpecialPopulationsChildren

- There has been limited experience to date with the use of albendazole in children undersix yearsofage;therefore,usageinchildrenlessthansixyearsisnotrecommended.The recommended dose for older children is 12 mg/kg body weight/day in divideddoses.

Elderly

- Experience in patients 65 years of age or older is limited. Reports indicate that nodosage adjustment is required; however, albendazole should be used with caution inelderly patients with evidence of hepaticdysfunction.

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 thesepatients. No dosage adjustment is required; however, patients with evidence of renal impairment should be carefully monitored.

4.3 Contraindications

Albendazole is contraindicated in patients with known hypersensitivity to the benzimidazole.

4.4 Special warnings and precautions for use

- Albendazole has been associated with mild to moderate elevations of hepaticenzymes. Hepatic enzymes generally normalise on discontinuation of treatment. Case reportsof hepatitishavealsobeenreceived.Liverfunctiontestsshouldbeobtainedbeforethestart of each treatment cycle and at least every two weeks during treatment. If hepaticenzymesare significantly increased (greater than twice the upper limit of normal),albendazole should be discontinued. Treatment may be

restarted when hepatic enzymes havereturned tonormallimits,butpatientsshouldbemonitoredforrecurrence.Albendazolehasbeenshown to cause bone marrow suppression and therefore blood counts should beperformed atthestartandeverytwoweeksduringeach28-daycycle.Patientswithliverdisease, including hepatic echinococcosis, appear to be more susceptible to bonemarrow suppression leading to pancytopenia, aplastic anaemia, agranulocytosis and leucopeniaand therefore warrant closer monitoring of blood counts. Albendazole should be discontinued if clinically significant decreases in blood cell countsoccur

Precautions:

In order to avoid administering albendazole during early pregnancy, womenof childbearingageshould:-initiatetreatmentonlyafteranegativepregnancytest.These testsshouldberepeatedatleastoncebeforeinitiatingthenextcycle.-beadvisedtotake effectiveprecautionsagainstconceptionduringandwithinonemonthofcompletionof treatment with albendazole for a systemic infection. Symptoms associated withan inflammatory reaction following death of the parasite may occur in patientsreceiving albendazoletreatmentforneurocysticercosis(e.g.seizures,raisedintracranialpressure,focal signs). These should be treated with appropriate steroid and anticonvulsanttherapy. Oral or intravenous corticosteroids are recommended to prevent cerebralhypertensive episodesduringthefirstweekoftreatment.Pre-existingneurocysticercosismayalsobe uncoveredinpatientstreatedwithalbendazoleforotherconditions,particularlyinareas with high taenosis infection. Patients may experience neurological symptoms e.g.seizures, increasedintracranialpressureandfocalsignsasaresultofaninflammatoryreaction caused by death of the parasite within the brain. Symptoms may occur soon after treatment, appropriate steroid and anticonvulsant therapy should be startedimmediately.

4.5 Interaction with other medicinal products and other forms of interaction

Dexamethasone

- Steady-state trough concentrations of albendazole sulfoxide were about 56% higher when 8 mg dexamethasone was co-administered with each dose of albendazole (15mg/kg/day) in 8 neurocysticercosispatients.

Praziquantel

- In the fed state, praziquantel (40 mg/kg) increased mean maximum plasmaconcentration andareaunderthecurveofalbendazolesulfoxidebyabout50%inhealthysubjects(n=

10)comparedwithaseparategroupofsubjects(n=6)givenalbendazolealone.Mean Tmax and mean plasma elimination half-life of albendazole sulfoxide wereunchanged. Thepharmacokineticsofpraziquantelwereunchangedfollowingco-administrationwith albendazole (400mg).

Cimetidine

- Albendazole sulfoxide concentrations in bile and cystic fluid were increased (about2-fold) inhydatidcystpatientstreatedwithcimetidine(10mg/kg/day)(n=7)comparedwith albendazole (20 mg/kg/day) alone (n = 12). Albendazole sulfoxide plasmaconcentrations were unchanged 4 hours afterdosing.

Theophylline

- Followingasingledoseofalbendazole(400mg),thepharmacokineticsoftheophylline (aminophylline 5.8 mg/kg infused over 20 minutes) were unchanged. Albendazoleinduces cytochromeP4501Ainhumanhepatomacells;therefore,itisrecommendedthatplasma concentrations of theophylline be monitored during and aftertreatment.

4.6 Fertility, pregnancy andlactation

- Long-term carcinogenicity studies were conducted in mice and rats. In the mousestudy, albendazole was administered in the diet at doses of 25, 100, and 200 mg/kg/day (0.1,0.5, and 2 times the recommended human dose based on body surface area inmg/m2, respectively)for108weeks.Intheratstudy,albendazolewasadministeredinthedietat doses of 3.5, 7, and 20 mg/kg/day (0.04, 0.08, and 0.21 times the recommendedhuman dosebasedonbodysurfaceareainmg/m2,respectively)for117weeks.Therewasno evidenceofincreasedincidenceoftumorsinthetreatedmiceandratswhencomparedto the controlgroup.
- In genotoxicity tests, albendazole was found negative in an AmesSalmonella/Microsome Plate mutation assay with and without metabolic activation or with andwithout preincubation, cell-mediated Chinese Hamster Ovary chromosomal aberration test andin vivo mouse micronucleus test. In the in vitro BALB/3T3 cells transformationassay, albendazole produced weak activity in the presence of metabolic activation whileno activitywasfoundintheabsenceofmetabolicactivation.Albendazoledidnotadversely affectmaleorfemalefertilityintheratatanoraldoseof30mg/kg/day(0.32timesthe recommended human dose based on body surface area inmg/m2).

<u>Pregnancy</u>

- Pregnancy Category C. Albendazole has been shown to be teratogenic (tocause embryotoxicityandskeletalmalformations)inpregnantratsandrabbits.Theteratogenic responseintheratwasshownatoraldosesof10and30mg/kg/day(0.10timesand0.32 timestherecommendedhumandosebasedonbodysurfaceareainmg/m2,respectively) duringgestationdays6to15andinpregnantrabbitsatoraldosesof30mg/kg/day(0.60 timestherecommendedhumandosebasedonbodysurfaceareainmg/m2)administered duringgestationdays7to19.Intherabbitstudy,maternaltoxicity(33%mortality)was noted at 30 mg/kg/day. In mice, no teratogenic effects were observed at oral doses up to30 mg/kg/day (0.16 times the recommended human dose based on body surface areain mg/m2),administeredduringgestationdays6to15.Therearenoadequateandwell- controlled studies of albendazole administration in pregnant women. Albendazoleshould be used during pregnancy only if the potential benefit justifies the potential risk tothe fetus.

4.7 Effects on ability to drive and usemachines

- Nostudiesontheeffectsontheabilitytodriveandusemachineshavebeenperformed. However, undesirable effects may occur (e.g. allergic reactions,dizziness, convulsions),which may influence the ability to drive and usemachines.

4.8 Undesirable effects

- The following adverse events were observed during clinical studies. It should howeverbe noted that causality has not necessarily been established for theseevents.

Common(≥1%)

- Abdominal pain was the most frequently reported symptom (1%) during short termdosing, however this frequency was not significantly different from that inplacebo-treatedpatients.

Uncommon (>0.1% and <0.1%)

- Rarely reported events included bone pain, proteinuria, and low red cell count.Leucopenia and transiently raised hepatic enzymes were reported in studies with laboratory monitoring, however no definite relationship to the drug was shown.Hypersensitivity reactionsincludingrash,pruritisandurticariahavebeenreportedveryrarely.During prolonged higher dose albendazole therapy of hydatid disease there have also beenreports of severe hepatic abnormalities, including jaundice and hepatocellular damage whichmay beirreversible.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinalproduct is important. It allows continued monitoring of the benefit/risk balanceof the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme (www.mhra.gov.uk/yellowcard) or search for MHRA Yellow Card in theGooglePlay or Apple App Store.

4.9 Overdose

- Significant toxicity and mortality were shown in male and female mice at dosesexceeding 5,000mg/kg;inrats,atestimateddosesbetween1,300and2,200mg/kg;inhamsters,at dosesexceeding10,000mg/kg;andinrabbits,atestimateddosesbetween500and1,250 mg/kg.Intheanimals,symptomsweredemonstratedinadose-responserelationshipand includeddiarrhoea,vomiting,tachycardia,andrespiratorydistress.Oneoverdosagehas 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 (e.g.,gastric lavage and activated charcoal) and general supportive measures arerecommended.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

Albendazole is a member of the benzimidazole compounds used as a drug indicated forthe treatmentofavarietyofworminfestations.Itisabroadspectrumanthelmintic,effective against: roundworms, tapeworms, and flukes of domestic animals andhumans.

ATC code: P02CA03

5.2Pharmacokineticproperties

Absorption andMetabolism

- Albendazole is poorly absorbed from the gastrointestinal tract due to its lowaqueous solubility.Albendazoleconcentrationsarenegligibleorundetectableinplasmaasitis rapidlyconvertedtothesulfoxidemetabolitepriortoreachingthesystemiccirculation. The systemic anthelmintic activity has been attributed to the primarymetabolite, albendazolesulfoxide.
- Oralbioavailabilityappearstobeenhancedwhenalbendazoleiscoadministeredwitha fattymeal(estimatedfatcontent40g)asevidencedbyhigher(upto5-foldonaverage) plasma concentrations of albendazole sulfoxide as compared to the fastedstate.

- Maximalplasmaconcentrationsofalbendazolesulfoxidearetypicallyachieved2to5 hours after dosing and are on average 1.31 mcg/mL (range 0.46 to 1.58mcg/mL) following oral doses of albendazole (200 mg) in 6 hydatid disease patients,when administered with a fatty meal. Plasma concentrations of albendazole sulfoxide increasein a dose-proportional manner over the therapeutic dose range following ingestion of afatty meal (fat content 43.1 g). The mean apparent terminal elimination half-life ofalbendazole sulfoxidetypicallyrangesfrom8to12hoursin25normalsubjects,aswellasin14 hydatid and 8 neurocysticercosispatients.
- Following 4 weeks of treatment with albendazole (200 mg three times daily), 12patients' plasma concentrations of albendazole sulfoxide were approximately 20% lower thanthose observedduringthefirsthalfofthetreatmentperiod,suggestingthatalbendazolemay induce its ownmetabolism.

Distribution

- Albendazolesulfoxideis70%boundtoplasmaproteinandiswidelydistributed throughoutthebody;ithasbeendetectedinurine,bile,liver,cystwall,cystfluid,and cerebralspinalfluid(CSF).Concentrationsinplasmawere3-to10-foldand2-to4-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 fromcysts at a slower rate than observed inplasma.

Metabolism andExcretion

- Albendazole is rapidly converted in the liver to the primary metabolite,albendazole sulfoxide, which is further metabolized to albendazole sulfone and other primaryoxidative metabolites that have been identified in human urine. Following oraladministration, albendazole has not been detected in human urine. Urinary excretion ofalbendazole sulfoxideisaminoreliminationpathwaywithlessthan1%ofthedoserecoveredinthe urine. Biliary elimination presumably accounts for a portion of the eliminationas evidenced by biliary concentrations of albendazole sulfoxide similar to those achievedin plasma.

5.3 Preclinical safety data

- Nonclinicaldatarevealnospecialhazardforhumansbasedonstudiesofsafety pharmacology, genotoxicity and toxicity toreproduction..

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Microcrystalline Cellulose (101) BP
- Anhydrous Calcium Hydrogen Phosphate BP
- Sodium Chloride BP
- Maize Starch BP
- Sodium Starch Glycolate BP
- Lactose BP
- Colloidal Silicon Dioxide NF
- Sodium Lauryl Sulphate BP
- Maize Starch BP
- Sodium Saccharin BP
- Sunset Yellow Supra INH
- Magnesium Stearate BP
- Stearic Acid BP
- Colloidal Silicon Dioxide NF
- Sodium Bicarbonate BP
- Doshion-P-544-D
- Croscarmellose Sodium NF
- Beta Cyclo Dextrin
- Crospovidone NF (PVP XL 10)
- Maize Starch (Q.S. to Kgs.)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months from the Date ofManufacturing

6.4 Special precautions for storage

Store in a dry place below 30°C. Protect from light.

6.5 Nature and contents ofcontainer

Presentation: Albendazole tablets USP 400mg (ALBEZOLE) is available as , 10x10's & 100x10's blister pack and 1000’s Bulk pack

Primary Container (s):

Albendazole tablets USP 400mg (ALBEZOLE) is available as Blister pack.

10x10's & 100x 10’s- Each blister contains 10 tablets

Secondary packing:

Such blisters are packed in cartons of GSM 300, made of ITC cyber XL board with aqua varnish.Carton is printed in Multicolor.

Leaflet: leaflet made with 70 GSM Map Lithopaper.

Outer Container:

Such cartons are packed in Export Worthy 5/7 Ply Shippers. These shippers are labelled with product name and relevant batch details and sealed with BOPP tape. Shippers are then strapped with Polypropylene tapes.

Transportation: Should be transported with precautions.

The Cautions Like- This Side Up

- Not For Loose Handling
- Protect from Water
- Avoid Vigorous Transportation Not all pack sizes may be marketed.

6.6 Special precautions for disposal and otherhandling

None

7. MARKETING AUTHORIZATIONHOLDER

Name and Permanent address of the Marketing authorization holder: Medopharm,

“MEDO HOUSE”

25, Puliyur II Main road, Trustpuram, Chennai-600 024, Tamil Nadu, India.

PH: +91 44-30149992/30149955

Fax: 260211 286283

Manufacturing Site address:

Medopharm

No. 13-B Industrial area, Malur 563160, Karnataka, India.

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

0838/09887/NMR/2022

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION:

13.01.2023

10. DATE OF REVISION OF THE TEXT

13.07.2023