SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICALPRODUCT

Zestaval 200 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains albendazole 200 mg.

Excipient(s) with known effect:
This product contains 150 mg lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

White, round, film-coated tablets with star embossed on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Zestaval is indicated in the treatment of hydatid cysts caused by *Echinococcus granulosus* or *Echinococcus multilocularis*. Zestaval may be used as first-line medical therapy in patients with hydatid disease where surgery is not possible or as an adjunct to surgery, either pre- or post-operatively.

4.2 Posology and method of administration

Posology

Adults and elderly
Echinococcus granulosus: Zestaval is normally given at a dose of 800 mg/day in divided doses for 28 days. This 28-day treatment period may be repeated after a 14-day period without treatment, for a total of 3 cycles. Zestaval shows greatest efficacy in the treatment of liver, lung and peritoneal cysts. More prolonged treatment may be required for sites such as bones and brain.

Pre-surgery: Dosage is 800 mg/day in divided doses for 28 days followed by a period of 14 drug-free days. Two 28-day cycles should be given where possible prior to surgery. Where surgical intervention is necessary before completion of two cycles of treatment, Zestaval should be given for as long as possible before surgery, but for not more than 28 days at a time.

Pre- and post-surgery: Where only a short pre-operative course of Zestaval has been given, and in cases where emergency surgery is required, Zestaval should be given post-surgically for two 28-day cycles separated by 14 days drug free. In addition, where cysts are found to be viable after pre-surgical treatment or where spillage has occurred, a full two-cycle course should be given.

Echinococcus multilocularis: 800 mg/day in divided doses for cycles of 28 days with 14 days between cycles. Long treatment with regular monitoring may be required.

Paediatric population
There is limited experience to date with the use of Albendazole in children under 6 years of age. Therefore usage in children less than 6 years old is not recommended.

Method of administration
Oral administration. Zestaval should be taken with meals.

4.3 Contraindications

Zestaval is contra-indicated in patients hypersensitive to albendazole or to any other of the ingredients of the product, in pregnant women and in children under 6 years of age.

4.4 Special warnings and precautions for use

Albendazole has not been studied in children under six years of age.

Albendazole has been shown to cause elevations in hepatic enzyme levels which are reversible on discontinuation of treatment. Liver function tests should be obtained before the start of each treatment cycle and at least every two weeks during treatment. If enzymes are significantly increased (greater than twice the upper limit of normal), Zestaval should be discontinued. Zestaval treatment may be instituted when liver enzymes have returned to normal limits, but laboratory tests should be more frequently obtained during repeat therapy.

Reversible reduction in total white cell count has also been occasionally reported. Blood counts should be performed at the start and every two weeks during each 28-day cycle.

In order to avoid administering albendazole during early pregnancy, women of childbearing age should initiate treatment only after a negative pregnancy test. These tests should be repeated at least once before initiating the next cycle. Women of childbearing age should be advised to take effective precautions, with non-hormonal contraceptive measures, against conception during and within one month of completion of treatment with Zestaval.

Zestaval contains lactose
Patients with rarehereditary problems of galactoseintolerance, the Lapp lactasedeficiency or glucose-galactosemalabsorption should not takethis medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Albendazole has been shown to induce liver enzymes of the P450 system responsible of its own metabolism. There is a theoretical risk of interaction with theophylline, anticonvulsants, anticoagulants, oral contraceptives and oral hypoglycaemics. Cimetidine and praziquantel have been reported to increase the plasma levels of the albendazole active metabolite.

4.6 Fertility,pregnancy and lactation

Pregnancy
Albendazole is teratogenic in rats. It is therefore contra-indicated in pregnant women.

Lactation

It is not known whether albendazole or its metabolites are excreted in human breast milk. Therefore, Zestaval should not be used during lactation unless the potential benefits are considered to out-weigh the potential risks associated with treatment.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Gastro-intestinal disturbances abdominal pain, nausea, vomiting, headaches and dizziness have been reported during treatment. These symptoms are usually mild and resolve without treatment. Alopecia, (thinning of hair and moderate hair loss) has been reported and is reversible on cessation of treatment. Rash and fever have been reported, especially during the first few days of treatment. Allergic shock has been observed where cyst leakage has occurred during treatment. In patients where there is cerebral involvement, convulsions and meningism may occur during treatment.
Also leucopenia and pancytopenia have been reported.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product isimportant. Itallows continued monitoring of the benefit/risk balance of the medicinalproduct. Healthcareprofessionals are asked to report any suspected adverse reactionsvia the national reporting system.

4.9 Overdose

No cases of over-dosage with Zestaval have been reported.

In case of overdose, gastric lavage and general supportive measures should be taken.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthelmintics, Antinematodal agents, ATC code: P02CA03

Albendazole is a benzimidazole carbamate with anthelmintic effects against tissue parasites. Albndazole inhibits larvicidal, ovicidal and vermicidal activity and it is thought to exert its anthelmintic effect by inhibiting tubulin polymerisation. This causes the distribution of the helminth metabolism, including energy depletion, which immobilises and then kills the susceptible helminth. 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. In the treatment of cysts due to E. multilocularis a minority of patients were considered to be cured and a majority had an improvement or stabilisation of disease due to albendazole.

5.2 Pharmacokinetic properties
Albendazole is poorly absorbed from the gastro-intestinal tract, but rapidly undergoes extensive first-pass metabolism. Its principal metabolite Albendazole Sulfoxide has anthelmintic activity and a plasma half-life of about 8,5 hours. The metabolite is mainly excreted in bile with only a small proportion appearing in the urine.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core
Lactose
Maize starch
Povidone
Microcrystalline cellulose
Sodium starch glycollate
Colloidal silicon dioxide
Magnesium stearate
Talc

Coating
Hypromellose
Polyethylene glycol 400
Titanium dioxide E171
Talc

6.2 Incompatibilities

None.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

Do not storeabove30°C.Protect from light and moisture.

6.5 Nature and contents of container

PVC/Aluminium blisters. Pack-size of 100 film-coated tablets.

6.6 Special precautions for disposal and other handling

No special precautions.

7. MARKETING AUTHORISATION HOLDER

Remedica Ltd
Aharnon Str., Limassol Industrial Estate,

3056 Limassol, Cyprus

8. MARKETING AUTHORISATION NUMBER(S)

3466/4641/REN/2017

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 28 August2008
Date of latest renewal: 05 October 2017

10. DATE OF REVISION OF THE TEXT

05/07/2023