Summary of Product Characteristics

1. Name of the medicinal product

1.1 (Invented) name of the medicinal product

Trade/Proprietary Name: G-Abzole™
Approved/Inn/Generic Name: Albendazole Chewable Tablets

1.2 Strength

400mg

1.3 Pharmaceutical form

Tablet

2. Qualitative and quantitative composition

No.	Name of ingredient	Qty (SI units)
1	Albendazole	400mg
2	Sucrose	100mg
3	Corn starch	120mg
4	Croscarmellose sodium	20mg
5	Povidone K30	10mg
6	Sodium lauryl sulfate	10mg
7	Polysorbate 80	10mg
8	Saccharin sodium	1mg
9	Tartrazine	0. 24mg
10	Carmine	0. 36mg
11	Micro-crystalline cellulose	40mg
12	Hyprolose	10mg
13	Orange oil essence	2mg
14	Magnesium stearate	6mg
15	Sodium bicarbonate	30mg

3. Pharmaceutical form

Pink tablet.

4. Clinical particulars

4.1 Therapeutic indications

G-Abzole is a broad spectrum anthelmintic for the treatment of:
Enterobius vermicularis - Pinworm or threadworm
Trichuris trichiura - Whipworm
Ascaris lumbricoides - Large roundworm

Necator americanus - Hookworm
Strongyloides stercorals
Taenia spp. - Tapeworm
In single or mixed infestations of any of the above

4.2 Posology and method of administration

Under medical prescription

Usual dose in both adults and children over 2 years of age: 400mg as a single dose in cases of Enterobius vermicularis, Trichures trichiura, Ascaris lumbricoides, Ancylostoma duodenale and Necator americanus. In cases of Strongyloidiasis or Taeniasis G-Abzole 400mg as a single dose should be given for 3 consecutive days.

If the patient is not cured on follow-up after three weeks, a second course of treatment is indicated.

The tablets may be chewed, swallowed or crushed and mixed with food.

No specific procedures such as fasting or purging are required.

4.3 Contraindications

G-Abzole is contraindicated in patients with known hypersensitivity to the benzimidazole class of compounds or any components of G-Abzole.

4.4 Special warnings and special precautions for use：

WARNINGS

Rare fatalities associated with the use of G-Abzole have been reported due to granulocytopenia or pancytopenia (see PRECAUTIONS). 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

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.

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.

Information for Patients

Patients should be advised that:

- Some people, particularly young children, may experience difficulties swallowing the tablets whole. In young children, the tablets should be crushed or chewed and swallowed with a drink of water.
- Albendazole may cause fetal harm, therefore, women of childbearing age should begin treatment after a negative pregnancy test.
- Women of childbearing age should be cautioned against becoming pregnant while on albendazole or within 1 month of completing treatment.
- During albendazole therapy, because of the possibility of harm to the liver or bone marrow, routine (every 2 weeks) monitoring of blood counts and liver function tests should take place.
- Albendazole should be taken with food.

Laboratory Tests

White Blood Cell Count

Albendazole has been shown to cause occasional (less than 1% of treated patients) reversible reductions in total white blood cell count. Rarely, more significant reductions may be encountered including granulocytopenia, agranulocytosis, or pancytopenia. Blood counts should be performed at the start of each 28-day treatment cycle and every 2 weeks during each 28-day cycle in all patients. Patients with liver disease, including hepatic echinococcosis, appear to be more at risk of bone marrow suppression and warrant closer monitoring of blood counts (see WARNINGS). Albendazole should be discontinued in all patients if clinically significant decreases in blood cell counts occur.

Liver Function

In clinical trials, treatment with albendazole has been associated with mild to moderate elevations of hepatic enzymes in approximately 16% of patients. These elevations have generally returned to normal upon discontinuation of therapy. There have also been case reports of acute liver failure of uncertain causality and hepatitis (see ADVERSE REACTIONS).

Liver function tests (transaminases) should be performed before the start of each treatment cycle and at least every 2 weeks during treatment. If hepatic enzymes exceed twice the upper limit of normal, consideration should be given to discontinuing albendazole therapy based on individual patient circumstances. Restarting albendazole treatment in patients whose hepatic enzymes have normalized off treatment is an individual decision that should take into account the risk/benefit of further albendazole usage. Laboratory tests should be performed frequently if albendazole treatment is restarted.

Patients with abnormal liver function test results are at increased risk for hepatotoxicity and bone marrow suppression (see WARNINGS). Therapy should be discontinued if liver

enzymes are significantly increased or if clinically significant decreases in blood cell counts occur.

Theophylline

Although single doses of albendazole have been shown not to inhibit theophylline metabolism (see Drug Interactions), albendazole does induce cytochrome P450 1A in human hepatoma cells. Therefore, it is recommended that plasma concentrations of theophylline be monitored during and after treatment with G-Abzole.

4.5 Interactions 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 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

Teratogenic Effects

Pregnancy Category C. Albendazole has been shown to be teratogenic (to cause embryotoxicity and skeletal malformations) in pregnant rats and rabbits. The teratogenic response in the rat was shown at oral doses of 10 and 30 mg/kg/day (0.10 times and 0.32 times the recommended human dose based on body surface area in mg/m2, respectively) during gestation days 6 to 15 and in pregnant rabbits at oral doses of 30 mg/kg/day (0.60 times the recommended human dose based on body surface area in mg/m2) administered during gestation days 7 to 19. In the rabbit study, maternal toxicity (33% mortality) was noted at 30 mg/kg/day. In mice, no teratogenic effects were observed at oral doses up to 30 mg/kg/day (0.16 times the recommended human dose based on body surface area in mg/m2), administered during gestation days 6 to 15.

There are no adequate and well-controlled studies of albendazole administration in pregnant women. Albendazole should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus (see WARNINGS).

Nursing Mothers

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

Nonexistence or can be ignored.

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.

Adverse Event Incidence ≥1% in Hydatid Disease and Neurocysticercosis

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

The following adverse events were observed at an incidence of <1%:

Blood and Lymphatic System Disorders

Leukopenia. There have been rare reports of granulocytopenia, pancytopenia, agranulocytosis, or thrombocytopenia (see WARNINGS). Patients with liver disease, including hepatic echinococcosis, appear to be more at risk of bone marrow suppression (see WARNINGS and PRECAUTIONS).

Immune System Disorders

Hypersensitivity reactions, including rash and urticaria.

Postmarketing Adverse Reactions

In addition to adverse events reported from clinical trials, the following events have been identified during world-wide post-approval use of G-Abzole. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. These events have been chosen for inclusion due to a combination of their seriousness, frequency of reporting, or potential causal connection to G-Abzole.

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 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 G-Abzole 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 are recommended.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Albendazole belongs to the benzimidazole class f anthelmintics.

Benzimidazoles bind to nematode tubulin, a protein necessary for the formation and viability of microtubules. This occurs primarily in absorptive intestinal cells resulting in the absence of microtubules in the intestinal cells of the nematode, with the result that these cells can't absorb nutrients, thus causing a consequent reduction in glycogen and effective starvation of the parasites. Structural differences have been shown to exist between tubulin from mammalian and helminth sources, resulting in the preferential toxicity of albendazole to the helminth and not to the host.

Benzimidazoles have also been shown to inhibit the fumarate reductase system of helminthes and impair energy production.

The selenium and cobalt are trace elements of use as nutritional supplements and are not intended to be used therapeutically.

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 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.

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.

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

Sucrose, Corn starch, Croscarmellose sodium, Povidone K30, Sodium lauryl sulfate, Polysorbate 80, Saccharin sodium, Tartrazine, Carmine, Micro-crystalline cellulose, Hyprolose, Orange oil essence, Magnesium stearate, Sodium bicarbonate

6.2 Incompatibilities

In the absence of compatibility study, this pharmaceutical product must not be mixed with other pharmaceutical products.

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6.3 Shelf life

3 years

6.4 Special precaution for storage

Stored below 30℃, protected from light.

6.5 Nature and contents of container
Aluminiun foil-PVC blister, box, and carton

6.6 Instructions for use and handling <and disposal>
No special requirement.

7. MARKETING AUTHORISATION HOLDER
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9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
N/A

10. DATE OF REVISION OF THE TEXT
09/2013