WHO-PQ RECOMMENDED SUMMARY OF PRODUCT CHARACTERISTICS

This summary of product characteristics focuses on uses of the medicine covered by WHO's Prequalification Team - Medicines. The recommendations for use are based on WHO guidelines and on information from stringent regulatory authorities.[*]

The medicine may be authorised for additional or different uses by national medicines regulatory authorities.

[*]https://extranet.who.int/prequal/sites/default/files/document_files/75%20SRA%20clarification_Feb2017_newtempl.pdf

1. NAME OF THE MEDICINAL PRODUCT

[NT014 trade name]†

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains albendazole 400 mg.

Excipients with potential clinical effect

Each tablet contains 8 mg of aspartame.

The tablet also contains 3.12 mg of lactose and 0.2 mg of benzyl alcohol (both from the flavour).

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Chewable tablets

White to off-white, oblong, uncoated tablets. They are biconvex (rounded on top and bottom) with a flat edge. The tablets have a break line on one side and are plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[NT014 trade name] is a broad-spectrum anthelmintic used for the treatment of the following infections:

Cestode infections (tapeworms)

[NT014 trade name] is indicated for the treatment of *Echinococcus multilocularis* and *E. granulosus* infections before or after surgery or where surgery is not suitable.

[NT014 trade name] is further indicated for the treatment of neurocysticercosis caused by larval forms of the pork tapeworm, *Taenia solium*. It may also be given for preventive chemotherapy of *Taenia solium* taeniasis in endemic populations, where other alternatives are not available.

Lymphatic filariasis

[NT014 trade name] is indicated together with ivermectin and/or diethylcarbamazine for the elimination of lymphatic filariasis.

Treatment is given to the entire eligible population in endemic areas through a mass drug administration programme.

Other nematode infections (roundworms)

Albendazole is effective for the treatment of various nematode infections. [NT014 trade name] can be used, alone or in combination with other medicines, for the control of soil-transmitted helminthiasis (ascariasis, trichuriasis and hookworm infections) through mass drug administration programmes.

† Trade names are not prequalified by WHO. This is the national medicines regulatory agency's responsibility.

4.2 Posology and method of administration

Posology

Cestode infections (tapeworms)

Adults

In adults over 60 kg, the usual dose for treatment of echinococcosis or *Taenia solium* neurocysticercosis is 400 mg twice a day. In adults up to 60 kg, the dose is 15 mg/kg daily in 2 divided doses (maximum 800 mg daily).

For *cystic echinococcosis*, [NT014 trade name] treatment is continued for 3 to 6 months or longer.

For *alveolar echinococcosis* treatment should be given for at least 2 years and may be continued for many years, reviewed at 2-year intervals.

For *neurocysticercosis*, treatment with [NT014 trade name] is usually for 10–14 days but can be increased to up to 30 days or more for extraparenchymal cysts (e.g. in the ventricles or subarachnoid space).

Children

Only limited data are available on the use of [NT014 trade name] in children for cestode infections.

Mass drug administration

In mass drug administration programmes for preventive chemotherapy of *taeniasis* where other alternatives are not available, [NT014 trade name] may be given to endemic populations from 2 years of age in a dose of 400 mg daily for 3 consecutive days. Because of the risk of triggering latent neurocysticercosis, a reporting system must be in place with active surveillance and referral of any neurological adverse events.

Nematode infections

For the elimination of *lymphatic filariasis* and the control of *soil-transmitted helminthiasis* (ascariasis, trichuriasis, or hookworm disease), a single oral dose of [NT014 trade name] is normally given once a year in mass treatment programmes. The dose may be given twice a year at 6-monthly intervals, if required, in line with national treatment plans. For lymphatic filariasis, [NT014 trade name] is given together with diethylcarbamazine, or ivermectin, or both.

Adults and children aged over 2 years

In adults and children aged over 2 years, the dose of [NT014 trade name] for mass drug administration is 400 mg.

Children aged 1–2 years

In children aged 1–2 years, the dose of [NT014 trade name] for the control of soil-transmitted helminthiasis is 200 mg (half a tablet).

[NT014 trade name] is not used in children below 2 years for the elimination of lymphatic filariasis.

Special populations

Renal impairment

No dose adjustment is required.

Hepatic impairment

Caution should be used if [NT014 trade name] is given to patients with liver disease, since albendazole is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

Method of administration

Oral use.

The tablet can be chewed before swallowing

[NT014 trade name] should be taken with a meal for the prevention and treatment of tissue infections such as echinococcosis, neurocysticercosis and lymphatic filariasis. Taking albendazole with a fatty meal improves its bioavailability and leads to higher blood levels (see section 5.2).

For treatment of intestinal infections such as taeniasis or soil-based helminth infections, [NT014 trade name] should be taken at least 2 hours after a meal and 30 minutes before the next meal. This leads to higher intestinal and lower systemic albendazole levels, which is desirable in these conditions.

4.3 Contraindications

Hypersensitivity to the active substance, other benzimidazoles or to any excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Pre-existing neurocysticercosis

Treatment with albendazole may uncover pre-existing neurocysticercosis, particularly in areas where taeniasis is common.

Patients may experience neurological symptoms such as 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 develop rapidly after treatment, and appropriate corticosteroid and anticonvulsant therapy should be given straight away.

Risk of retinal damage in patients with retinal neurocysticercosis

Cysticercosis may, in rare cases, involve the retina. Before starting therapy for neurocysticercosis, the patient should be examined for the presence of retinal lesions. If such lesions are present, the need for anticysticeral therapy should be weighed against the possibility of retinal damage caused by albendazole-induced changes to the retinal lesion.

Hepatic effects

Patients undergoing treatment for echinococcosis should have their liver function tested before the start of treatment and regularly (ideally every 2 weeks) during treatment. Patients with disturbed liver function tests before starting albendazole should be carefully evaluated, since the medicine is metabolised by the liver and has been associated with idiosyncratic hepatotoxicity.

Mild to moderate elevations of liver enzymes have been reported frequently with prolonged albendazole treatment. Enzyme abnormalities are usually reversible on discontinuation of treatment. In prolonged higher-dose albendazole therapy for echinococcosis there have been rare reports of severe hepatic abnormalities such as jaundice and histological hepatocellular damage, which may be irreversible.

If enzymes are significantly increased (greater than twice the upper limit of normal) during treatment, [NT014 trade name] should be discontinued. [NT014 trade name] treatment may be reinstituted when levels have returned to normal limits, but liver function should be monitored frequently during repeat therapy.

Bone marrow suppression

Albendazole can cause bone marrow suppression and therefore blood counts are needed at the start and ideally every two weeks thereaftery during treatment for echinococcosis. Patients with liver disease, including hepatic echinococcosis, may be more susceptible to bone marrow suppression leading to pancytopenia, aplastic anaemia, agranulocytosis and leucopenia and therefore warrant closer monitoring of blood counts. Albendazole should be discontinued if clinically significant decreases in blood cell counts occur.

Excipients

This medicine contains benzyl alcohol which has been linked with the risk of severe side effects including breathing problems (called “gasping syndrome”) in young children. Medicine containing benzyl alcohol should not be given to a newborn baby (up to 4 weeks old), unless recommended by the health care provider. See section 4.2 for information on which children can be given [NT014 trade name].

[NT014 trade name] should not be used for more than a week in young children (less than 3 years old), unless advised by the health care provider.

[NT014 trade name] should be used with caution, under the health care provider's advice, in pregnant women, breast-feeding women, and patients with liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in the body, resulting in metabolic acidosis.

[NT014 trade name] contains lactose. Patients with congenital lactase deficiency, galactosaemia or glucose-galactose intolerance must not be given this medicine unless strictly necessary. The small amount of lactose in each dose is unlikely to cause symptoms of lactose intolerance in other patients.

This medicine contains aspartame. Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. One of the major hydrolysis products is phenylalanine. It may be harmful if the patient has phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age.

It is important to consider the contribution of excipients from all the medicines that the patient is taking.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine, dexamethasone and praziquantel may all increase the plasma concentration of the active metabolite of albendazole, albendazole sulfoxide.

Carbamazepine, phenobarbital, phenytoin and ritonavir may reduce plasma concentrations of the active metabolite of albendazole. The clinical relevance of this is unknown, but may result in decreased efficacy, especially in the treatment of systemic helminth infections. Patients should be monitored for efficacy and may require alternative dose regimens or therapies.

4.6 Fertility, pregnancy and breastfeeding

Women of childbearing potential

Pregnancy should be avoided in women treated with albendazole. Adequate contraceptive measures should be taken, particularly with prolonged treatment.

Pregnancy

There are no adequate and well-controlled studies of [NT014 trade name] administration in pregnant women. Limited data from inadvertent single-dose administration of albendazole during the first trimester have not demonstrated an increased incidence of congenital anomalies. However, animal studies with albendazole have revealed evidence of teratogenicity in rats and rabbits (see section 5.3), and therefore preventive chemotherapy with [NT014 trade name] is not recommended in the first trimester of pregnancy.

In general, [NT014 trade name] should be used in pregnant women only if there are no alternatives and the potential benefit justifies the potential risk to the fetus.

Breast-feeding

Albendazole and its active metabolite pass into breast milk in very small amounts; it is generally considered compatible with breast-feeding, particularly in single doses.

Fertility

There are no data on the effects of [NT014 trade name] on human male or female fertility.

Animal studies indicate no effects of albendazole on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

[NT014 trade name] is unlikely to affect the ability to drive or operate machinery.

However, patients should be advised to consider if their clinical status, including any undesirable effects of the medicine, allows them to perform skilled tasks safely.

4.8 Undesirable effects

Data from clinical trials and post-marketing surveillance were used to estimate the frequency of adverse events linked to albendazole.

The adverse reactions considered related to albendazole are listed below by body system, organ class and absolute frequency. Frequencies are defined as very common (≥ 1/10), common (1/100 to 1/10), uncommon (1/1000 to 1/100), rare (1/10 000 to 1/1000), and very rare (< 1/10 000).

Short duration of treatment

Blood and lymphatic system disorders

Rare	Low red cell count

Immune system disorders

Rare	Hypersensitivity reactions including rash, pruritus and urticaria

Nervous system disorders

Uncommon	Headache, dizziness

Gastrointestinal disorders

Common	Upper gastrointestinal symptoms (e.g. epigastric or abdominal pain, nausea, vomiting)
Uncommon	Diarrhoea

Hepatobiliary disorders

Rare	Elevations of hepatic enzymes

Skin and subcutaneous tissue disorders

Uncommon	Itchiness, skin rashes
Very rare	Erythema multiforme, Stevens-Johnson syndrome

Musculoskeletal and connective tissue disorders

Rare	Bone pain

Renal and urinary disorders

Rare	Proteinuria

Longer duration of treatment

Blood and lymphatic system disorders

Uncommon	Leucopenia
Rare	Low red cell count
Very rare	Pancytopenia, aplastic anaemia, agranulocytosis

Immune system disorders

Uncommon	Hypersensitivity reactions including rash, pruritus and urticaria

Nervous system disorders

Very common	Headache
Common	dizziness

Gastrointestinal disorders

Common	Gastrointestinal disturbances (abdominal pain, nausea, vomiting)

Hepatobiliary disorders

Very common	Mild to moderate elevations of hepatic enzymes
Uncommon	Hepatitis[1]

Skin and subcutaneous tissue disorders

Common	Reversible alopecia (thinning of hair, and moderate hair loss)
Very rare	Erythema multiforme, Stevens-Johnson syndrome

Musculoskeletal and connective tissue disorders

Rare	Bone pain

Renal and urinary disorders

Rare	Proteinuria

General disorders

Common	Fever

[1] With prolonged albendazole treatment for echinococcosis there have also been reports of severe hepatic abnormalities, including jaundice and hepatocellular damage which may be irreversible

Reporting of suspected adverse reactions

Health care providers are asked to report adverse reactions that may be linked to a medicine, to the marketing authorisation holder, or, if available, to the national reporting system. Reports of suspected adverse reactions to a medicine are important for the monitoring of the medicine's benefits and risks.

4.9 Overdose

In case of overdosage, symptomatic therapy and general supportive measures are recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthelmintics, benzimidazole derivatives, ATC code: P02CA03.

Mechanism of action

Albendazole is a benzimidazole derivative that causes degenerative alterations in the tegument and intestinal cells of the parasite and blocks their energy production, ultimately leading to immobilisation and death of the parasite. It works by binding to the colchicine-sensitive site of tubulin, thus inhibiting its assembly into microtubules. As cytoplasmic microtubules are critical in promoting glucose uptake, the glycogen stores of the parasites are depleted.

Albendazole exhibits larvicidal, ovicidal and vermicidal activity against helminth parasites. At lower doses the anthelminthic action of albendazole is thought to be mainly intra-intestinal. However, at higher doses, sufficient is absorbed and metabolised to the active sulfoxide metabolite to have a therapeutic effect against tissue parasites.

A number of studies have suggested that therapeutic doses of benzimidazoles are only parasitostatic against *E. multilocularis*. Nonetheless, after several years of albendazole treatment, treatment interruption may be considered, in the absence of progression of the lesions assessed by conventional imaging, and indirect assessment of viability using PET/CT. Although it does not provide direct evidence of *E. multilocularis* viability, and recurrence may occur, this technique, together with the follow-up of specific serum antibodies, may support decision-making and follow-up after albendazole withdrawal in highly selected patients.

5.2 Pharmacokinetic properties

The absorption characteristics of [NT014 trade name] have been determined in healthy subjects under fed conditions as follows:

Characteristic	**Arithmetic mean ± standard deviation**
Maximum concentration (C_{max})	116 ± 95 ng/mL
Area under the curve ($AUC_{0-\infty}$), a measure of the extent of absorption	420 ± 347 ng·h/mL
Time to attain maximum concentration (T_{max}) #	4.33 (0.67 – 6.00) hours

#median (range)

Pharmacokinetics of albendazole

General	
	Albendazole concentrations are negligible or undetectable in plasma as it is rapidly converted into the sulfoxide metabolite prior to reaching the systemic circulation. The systemic anthelmintic activity has been attributed to this primary metabolite, albendazole sulfoxide.

	Maximal plasma concentrations of albendazole sulfoxide are typically achieved 2 to 5 hours after dosing.
Absorption	
Absolute bioavailability	Not available
Oral bioavailability	Albendazole is poorly absorbed from the gastrointestinal tract (< 5%) due to its low aqueous solubility.
Food effect	Absorption is significantly enhanced (approximately 5-fold) if albendazole is taken with a fatty meal. Following a single 400-mg oral dose of albendazole, the maximum plasma concentration of albendazole sulfoxide was 0.4–1.6 μmol/L in fasting patients and 1.8–6.0 μmol/L when taken with breakfast (estimated fat content 40 g).
Distribution	
Volume of distribution (mean)	Not available
Plasma protein binding *in vitro*	Albendazole sulfoxide is 70% bound to plasma protein.
Tissue distribution	Albendazole sulfoxide is widely distributed throughout the body; it has been detected in urine, bile, liver, cyst wall, cyst fluid, and cerebral spinal fluid.
Metabolism	
	Albendazole rapidly undergoes extensive first-pass metabolism in the liver to albendazole sulfoxide, and is generally not detected in plasma. Albendazole sulfoxide is further metabolised to albendazole sulfone and other primary oxidative metabolites.
Active metabolite(s)	Albendazole sulfoxide
Elimination	
Elimination half life	The terminal elimination half-life of albendazole sulfoxide typically ranges from 8 to 12 hours.
Mean systemic clearance (Cl/F)	
Excretion	Following oral administration, albendazole has not been detected in human urine. Albendazole sulfoxide and its metabolites appear to be principally eliminated in bile, with only a small proportion appearing in the urine.
Pharmacokinetic linearity	
	Plasma concentrations of albendazole sulfoxide increase in a dose-proportional manner over the therapeutic dose range following ingestion of a fatty meal.
Drug interactions *(in vitro*)	
Transporters	Not available
Metabolising enzymes	Not available

Special populations

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 these patients.

Liver impairment

In patients with evidence of extrahepatic obstruction, the systemic availability of albendazole sulfoxide was increased 7-fold.

Elderly patients

Although no studies have investigated the effect of age on albendazole sulfoxide pharmacokinetics, data suggest that the pharmacokinetics are similar to those in young healthy subjects.

Children

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

5.3 Preclinical safety data

General toxicity

Studies of up to 6 months in mice, rats and dogs recognised the haematopoietic system and the liver as target organs of toxicity.

Genotoxicity

In genotoxicity tests, albendazole was found negative in an Ames Salmonella/microsome plate mutation assay, Chinese hamster ovary chromosomal aberration test, and *in vivo* mouse micronucleus test. In the *in vitro* BALB/3T3 cells transformation assay, albendazole produced weak activity in the presence of metabolic activation while no activity was found in the absence of metabolic activation.

Carcinogenicity

Long-term carcinogenicity studies in mice and rats found no evidence of increased incidence of tumours was found in the mice or rats at up to 400 mg/kg/day and 20 mg/kg/day, respectively.

Effects on reproduction

Albendazole did not affect male or female fertility in the rat at an oral dose level of 30 mg/kg/day.

Albendazole was teratogenic (embryotoxicity and skeletal malformations) in pregnant rats and rabbits. The teratogenic response in the rat occurred at oral doses of 10 and 30 mg/kg/day during gestation days 6 to 15, and in pregnant rabbits at oral doses of 30 mg/kg/day during gestation days 7 to 19. In the rabbit study, maternal toxicity (33% mortality) ocurred at 30 mg/kg/day. In mice, no teratogenic effects were observed at oral doses up to 30 mg/kg/day administered during gestation days 6 to 15.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium starch glycolate

Microcrystalline cellulose

Sodium lauryl sulphate

Maize starch

Colloidal anhydrous silica

Aspartame

Mixed fruit flavour

Purified talc

Magnesium stearate

This medicine is essentially ‘sodium-free’. It contains less than 1 mmol sodium (23 mg) per tablet.

6.2 Incompatibilities

Not applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30ºC. Avoid excursions above 30ºC. Protect from moisture.

Discard the product 60 days after initial opening.

6.5 Nature and contents of container

Round, white plastic (HDPE) bottle containing 100 tablets. The bottle has an aluminium tagger seal and a round, white childproof plastic (polypropylene) cap.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. SUPPLIER

Mepro Pharmaceuticals Pvt. Ltd.
Unit-II, Q Road, Phase-IV,
G.I.D.C, Wadhwan
Dist: Surendranagar,
Gujarat 363 035,
India
Tel.: +91-22 61477171
Fax: +91-22 66385339
Email: dipesh@mepro.in

8. WHO REFERENCE NUMBER (WHO Prequalification Programme)

NT014

9. DATE OF PREQUALIFICATION

16 August 2024

10. DATE OF REVISION OF THE TEXT

November 2024

References

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Albendazole. Drugs and lactation database [online database]. Bethesda: National Institute of Child Health and Human Development; 2024 (https://www.ncbi.nlm.nih.gov/books/NBK501368/, accessed 15 September 2024)

Detailed information on this medicine is available on the World Health Organization (WHO) website: https://extranet.who.int/prequal/medicines/prequalified/finished-pharmaceutical-products