SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ZEBEN® 200mg, tablet
ZEBEN® 400mg and 200mg, chewable tablet
ZEBEN® 2% w/v oral suspension 100mg/5ml bottle of 20ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Zeben 200 mg tablet contains Albendazole 200 mg.
Each Zeben 200 mg chewable tablet contains Albendazole 200mg.
Each Zeben 400 mg chewable tablet contains Albendazole 400mg.
Each ml of Zeben 2% oral suspension contains 20 mg of Albendazole, i.e., 0.4 g in 20 ml

For full list of excipients, see section 6.1.
Excipients with known effect:
Zeben 200 mg tablet: Lactose, Propylene Glycol.
Zeben 200 mg chewable tablet: Lactose.
Zeben 400 mg chewable tablet: Lactose, Sunset Yellow Supra.
Zeben 2% oral suspension: Sorbitol, Glycerol, Benzoate.

3. PHARMACEUTICAL FORM

Tablet, chewable tablet and oral suspension.

Zeben 200 mg tablet.
Zeben 200 mg chewable tablet.
Zeben 400 mg chewable tablet.
Zeben 2% oral suspension.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Intestinal and skin infections
• pinworm infection (Enterobius vermicularis),
• ascariasis (Ascaris lumbricoides),
• hookworm infection (Ancylostoma duodenale, Necator americanus),
• whipworm infection (Trichuris trichiura),
• strongyloidiasis (Strongyloides stercoralis),
• tapeworm infection (Taenia saginata, Taenia solium), treatment with albendazole should only be considered in the event of combined parasitic infections susceptible to albendazole,
• giardiasis (Giardia intestinalis or duodenalis) in children.

Systemic infection
• trichinosis (Trichinella spiralis).

4.2. Posology and method of administration

Indication	Daily dose	Duration of treatment
Intestinal and skin infections (short-term low-dose treatment)		
Pinworm infection	Children from 1 to 2 years: 200 mg, i.e. 10 ml of 2% oral suspension (half a 20 ml bottle) Adults and children over 2 years: 400 mg, i.e. one 400 mg tablet or two 200mg tablets or i.e. one 20 ml bottle of 2% oral suspension. Strict hygiene measures should be followed and family and friends in contact with you should also be treated	A single dose to be repeated 7 days later
Ascariasis Hookworm infection Whipworm infection	Children from 1 to 2 years: 200 mg, i.e. 10 ml of 2% oral suspension (half a 20 ml bottle) Adults and children over 2 years: 400 mg, i.e. one 400 mg tablet or two 200mg tablets or i.e. one 20 ml bottle of 2% oral suspension.	A single dose*
Strongyloidiasis Tapeworm infection (combined with other parasitic infections)	Adults and children over 2 years: 400mg, i.e. one 400 mg tablet or two 200mg tablets or i.e. one 20 ml bottle of 2% oral suspension.	Single daily dose to be repeated 3 days in succession*
Giardiasis	Children aged over 2 years: 400 mg, i.e. one 400 mg tablet or two 200mg tablets or i.e. one 20 ml bottle of 2% oral suspension.	A single daily dose to be repeated 5 days in succession
Systemic infection (long-term high-dose treatment)		
Trichinosis (parasitic infection caused by Trichinella)	Children: 15 mg/kg/day, divided into 2 daily doses, without exceeding 800 mg/day Adults: 800 mg, i.e. one 400 mg tablet twice a day or i.e. one 20 ml bottle of 2% oral suspension twice a day.	One dose morning and evening for 10 to 15 days, depending on the severity of symptoms and the stage at which treatment is initiated

* Particularly in case of strongyloidiasis, whipworm and tapeworm infestation, if the parasitological examination of the stool specimen performed 3 weeks after treatment is positive, a second treatment course should be administered.

Special populations

Elderly subjects:

There are limited data on patients aged 65 years and over. According to reports, no dose adjustment is necessary in elderly subjects. However, albendazole should be used with caution in elderly subjects with impaired liver function.

Patients with liver failure:
Albendazole is rapidly metabolized by the liver, with the main metabolite, albendazole sulfoxide, being pharmacologically active. As a result, the pharmacokinetics of albendazole sulfoxide in patients with liver failure is likely to be significantly affected.
Patients with abnormal liver function test results (transaminases) before initiation of treatment with albendazole should be closely monitored. Treatment should be discontinued in the event of significant elevation of liver enzymes or a clinically significant decrease in complete blood count (see section 4.4).

Patients with kidney failure:
As the renal elimination of albendazole and its main active metabolite, albendazole sulfoxide, is negligible, it is unlikely that the clearance of these compounds will be changed in patients with kidney failure. No dose adjustment is necessary; however, patients with impaired renal function should be closely monitored.

Method of administration
Oral use.
No purgatives or fasting conditions are necessary prior to treatment.
In the treatment of trichinosis, albendazole should be administered at mealtime.
Some people, especially young children and the elderly, may have difficulty swallowing the tablets whole. In this case, the tablet should be chewed with a small amount of water, or crushed.
An oral suspension form may also be used, in this case shake the suspension before use.

4.3. Contraindications

Known hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4. Special warnings and precautions for use

Neurological symptoms
Treatment with albendazole may reveal pre-existing neurocysticercosis, particularly in regions with a high prevalence of tapeworm infestation. Patients may experience neurological symptoms such as seizures, increased intracranial pressure, and focal signs resulting from the inflammatory reaction caused by the death of the parasite within the brain. Symptoms may occur shortly after treatment; appropriate corticosteroid and anticonvulsant therapy should be initiated immediately.

Precautions for use when albendazole is administered in systemic infections (long-term high-dose treatment):
• Hepatic disorders
Albendazole may cause a mild to moderate elevation of liver enzymes, which generally return to normal when treatment is stopped. Serious cases of hepatitis have also been reported during treatment of systemic helminth infections (longterm high-dose treatment) (see section 4.8). Liver function tests should be performed before initiation of treatment, then at least every two weeks during treatment. Albendazole should be discontinued in the event of elevated liver enzymes (more than twice the upper limit of normal). If reintroduction of treatment is essential, this should take place after liver enzymes have returned to normal limits. Furthermore, patients should be closely monitored due to possible recurrence, as an allergic mechanism cannot be ruled out.

• Bone marrow suppression

Cases of bone marrow suppression have been reported during treatment of systemic helminth infections (long-term highdose treatment) (see section 4.8). Complete blood counts should be performed at the start of treatment and after two weeks of albendazole treatment .
Patients with liver disease, including hepatic echinococcosis, appear to be more susceptible to bone marrow suppression leading to pancytopenia, bone marrow aplasia, agranulocytosis and leukopenia and therefore warrant closer monitoring of blood counts.
Albendazole should be discontinued if a major decrease in blood cell count occurs (see sections 4.2 and 4.8).
Limited data are available for albendazole in the treatment of trichinosis in children under 6 years of age.
In the treatment of trichinosis, due to the activity particularly on intestinal forms and larvae at the start of tissue migration, albendazole should be administered as soon as possible at the start of infestation to reduce symptoms and complications. This treatment has no effect on encysted larvae in chronic forms and when started late.

Excipients with known effect
Zeben 200mg tablet contains propylene glycol
This medicine contains 0.73mg propylene glycol in each tablet. Co-administration with any substrate for alcohol dehydrogenase such as ethanol may induce serious adverse effects in neonates and children less than 5 years old.

While propylene glycol has not been shown to cause reproductive or developmental toxicity in animals or humans, it may reach the foetus and was found in milk. As a consequence, administration of propylene glycol to pregnant or lactating patients should be considered on a case by case basis.

Medical monitoring is required in patients with impaired renal or hepatic functions because various adverse events attributed to propylene glycol have been reported such as renal dysfunction (acute tubular necrosis), acute renal failure and liver dysfunction.

Zeben 200mg tablet and Zeben 200mg/400mg chewable tablet contain lactose
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Zeben 400mg chewable tablet contains an azo coloring agent
This medicine contains an azo coloring agent (E110 yellow sunset) and may cause allergic reactions.

Zeben oral suspension contains:
- Sorbitol

This medicine contains 1000mg sorbitol in each 5ml of suspension. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.
The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly. Patients with hereditary fructose intolerance (HFI) should not take/be given this medicinal product.

- Benzoates

May cause allergic reactions (possibly delayed). Increase in bilirubinaemia following its displacement from albumin may increase neonatal jaundice which may develop into kernicterus (non-conjugated bilirubin deposits in the brain tissue).

4.5. Interactions with other medicinal products and other forms of interaction

Precautions for use
+ritonavir

+enzyme-inducing anticonvulsants
+rifampicin
A marked reduction in plasma concentrations of albendazole and its active metabolite may occur, due to phenobarbital and may result in decreased efficacy.
Clinical monitoring of response to treatment should be performed and albendazole dose adjustment may be required during and after treatment with the enzyme inducer.

4.6. Pregnancy and lactation

Pregnancy
Animal studies have demonstrated teratogenic effects.
In a clinical context, sufficiently relevant data are not yet available to evaluate the possible teratogenic or fetotoxic effect of albendazole when administered during pregnancy.
Therefore, use of this treatment is not recommended in pregnant women or women of child-bearing potential not using birth control, particularly since therapeutic alternatives exist which have undergone more in-depth assessment in terms of safety in pregnant women.

Breast-feeding
It is not known whether this drug is excreted into breast milk. Use of this medicine is not recommended while breastfeeding.

4.7. Effects on ability to drive and use machines

Patients who drive or use machines should note that dizzy sensations have been reported after using albendazole (see section 4.8).

4.8. Undesirable effects

The frequency of adverse reactions (very common to rare) was determined based on clinical trial data. The frequency of other adverse reactions was mainly determined based on post-marketing data and refers to frequency of cases reported rather than actual frequency.
The following adverse reactions are presented by system organ class and frequency, according to the following convention:

Very common ≥1/10
Common ≥1/100 to < 1/10
Uncommon ≥1/1,000 to < 1/100
Rare ≥1/10,000 to < 1/1,000
Very rare < 1/10,000
Frequency not known (cannot be estimated from the available data)

Intestinal and skin infections (short-term low-dose treatment)

System organ class	**Uncommon**	**Frequency not known**
Immune system disorders		*Hypersensitivity reactions, including skin rash, pruritus, and urticaria*
Nervous system disorders	*Headache* *Dizziness (see section 4.7)*	

Gastrointestinal disorders	*Gastrointestinal symptoms (epigastric or abdominal pain, nausea, vomiting) and diarrhea*	
Hepatobiliary disorders		*Elevated liver enzymes (see section 4.4)*
Skin and subcutaneous tissue disorders		*Erythema multiforme* *Stevens-Johnson syndrome*

Systemic infection (long-term high-dose treatment)

System organ class	**Very common**	**Common**	**Uncommon**	**Frequency not known**
Blood and lymphatic system disorders				Bone marrow aplasia Leukopenia Pancytopenia Agranulocytosis (see section 4.4)
Immune system disorders			Hypersensitivity reactions, including skin rash, pruritus, and urticaria	
Nervous system disorders	Headache	Dizziness (see section 4.7)		
Gastrointestinal disorders		Gastrointestinal disorders (abdominal pain, nausea, vomiting)		
Hepatobiliary disorders	Mild to moderately elevated liver enzymes (see section 4.4)		Hepatitis (see section 4.4)	
Skin and subcutaneous tissue disorders		Reversible alopecia. (thinning of hair, moderate hair loss)		Erythema multiforme, Stevens-Johnson syndrome
General disorders and administration site conditions		Fever		

Reporting of side effects

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.

4.9. Overdose

In the event of overdose, symptomatic treatment and medical surveillance are recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: ANTIPARASITIC PRODUCTS-ANTHELMINTICS
ATC code: **P02CA03 (P. Parasitology)**
Albendazole is a benzimidazole carbamate. It acts on nematodes, cestodes and certain protozoa.
Albendazole acts on the cytoskeleton of helminths by inhibiting tubulin polymerization and its incorporation into the microtubules, thus blocking glucose absorption by the parasites and resulting in death.
Albendazole also acts on Giardia intestinalis (or duodenalis). It has a targeted irreversible action on the ventral disk of the trophozoite due to an effect on the polymerization of tubulin and giardin, resulting in disorganization of the cytoskeleton and microstrips. The ability to adhere to enterocytes is reduced, which inhibits parasite growth and multiplication.

5.2. Pharmacokinetic properties

Absorption and metabolism
Following oral administration, the small proportion of albendazole absorbed (< 5%) is metabolized into albendazole sulfoxide and sulfone. The plasma concentration of sulfoxide, the predominant circulating active metabolite, reaches its peak approximately two and a half hours after administration.
The systemic pharmacological effect of albendazole is increased if the dose is administered with a high-fat meal, which gives rise to an approximately five-fold improvement in absorption.

Elimination
The plasma half-life of albendazole sulfoxide is 8 hours and 30 minutes.
Albendazole sulfoxide and its metabolites appear to be mainly eliminated in the bile, and a small proportion in the urine.

Special populations:
Patients with kidney failure: The pharmacokinetics of albendazole in patients with kidney failure have not been studied.
Patients with liver failure: The pharmacokinetics of albendazole in patients with liver failure have not been studied.

5.3. Preclinical safety data

No carcinogenic potential was evidenced during carcinogenicity studies conducted in rats (20 mg/kg/day) and in mice (400 mg/kg/day). Albendazole did not have a genotoxic effect in in vitro studies on bacteria and mammalian cell cultures, or in an in vivo study on the micronucleus in rodents.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Zeben 200mg tablet contains Lactose monohydrate; Maize Starch; Maize Starch (additional 10%); Povidone (K-30); Sodium Lauryl Sulphate; Microcrystalline Cellulose; Sodium Starch Glycolate; Trusil Vanilla Special; Trusil Orange Special; Magnesium Stearate; Purified Water; Hypromellose (E-5); Hypromellose (E-15); Propylene Glycol.
The excipients with known effect are: Lactose; Propylene Glycol.

Zeben 200mg chewable tablet contains Lactose monohydrate ; Maize Starch ; Povidone (K-30) ; Sodium Lauryl Sulphate ; Microcrystalline Cellulose ; Sodium Starch Glycolate ; Trusil Vanilla Special ; Trusil Orange Special ; Magnesium Stearate ; Menthol ; Sucralose NF.
The excipient with known effect is: Lactose.

Zeben 400mg chewable tablet contains Lactose ; Maize Starch ; Polysorbate 80 (Tween 80) ; Povidone (Polyvinyl Pyrrolidone) K-30 ; Sodium Lauryl Sulphate ; Saccharin Sodium ; Sunset Yellow Supra ; Microcrystalline Cellulose ; Sodium Starch Glycollate ; Trusil Vanilla Special ; Trusil Orange Special ; Magnesium Stearate ; Purified Water.
The excipients with known effect are: Lactose, Sunset Yellow Supra.

Zeben oral suspension contains Sodium Lauryl sulphate , Glycerol , Methyl Hydroxy Benzoate , Propyl Hydroxy Benzoate , Sodium Carboxy Methylcellulose , Sorbitol Solution 70%, Orange Flavour (S 2598) , Passion Fruit Flavour , Vanilla Extra Strong , Purified Water.
The excipients with known effect are: Sorbitol, Glycerol, Benzoate.

6.2. Incompatibilities

Not applicable.

6.3. Shelf-life

Do not use this medicine after the expiry date which is stated on the packaging. The expiry date refers to the last day of that month.

6.4. Special precautions for storage

- **Zeben 200mg /400mg chewable tablet and Zeben oral suspension**
  Store below 30°C and protect from light.
- **Zeben 200mg tablet**
  Store in dry place below 25°C and protect from light.

6.5. Nature and contents of container

ZEBEN 200 mg, tablet and ZEBEN 200 mg, chewable tablet:
Two tablets in blister packs (PVC/Aluminium)

ZEBEN 400 mg, chewable tablet:
1 tablet in a blister pack (Aluminium/PVC)
500 tablets in a HDPE vial

ZEBEN 2% w/v oral suspension:
20ml in PVC bottle

Not all pack size may be marketed in your country.

6.6. Special precautions for disposal and handling

ZEBEN 2% w/v oral suspension:
Shake before use.

7. NAMES AND ADDRESSES OF THE MANUFACTURERS

- **Zeben tablets**

Medreich Limited
4/3,
Avalahalli, Anjanapura Post,
Off Kanakapura Road,
Bangalore
560 062
Karnataka
INDIA
For: SANOFI

- **Zeben 2% w/v oral suspension**

Medreich Limited
Madras Pharmaceuticals
137-B, Old Mahabalipuram Road,
Karapakkam, Chennai - 600 096,
INDIA.
For: SANOFI

8. CONDITIONS FOR PRESCRIPTION AND RELEASE

LIST II

9. DATE OF REVISION OF THE TEXT

August 2017

NAFDAC REG No. ZEBEN® 2% w/v, oral suspension: 04-2779
NAFDAC REG No. ZEBEN® 200mg, chewable tablet: 04-2728