1.3 Product information

1.3.1 Summary of Product Characteristics (SmPC)

1. Name of the medicinal product

NEROZETEL CAPLET

2. Qualitative and quantitative composition

Each hard capsule contains Albendazole BP 200mg.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

An Orange oblong, film coated caplet with “NEROS” inscription on one side and plain on the other side. For oral administration.

4. Clinical particulars

4.1 Therapeutic indications

Albendazole is an anthelmintic (an-thel-MIN-tik) or anti- worm medication. It prevents newly hatched insectlarvae (worms) from growing or multiplying in your body. Albendazole is used to treat certain infections caused by worms such as pork tapeworm and dog tapeworm.

4.2 Posology and method of administration

Posology

Special populations

Elderly and paediatric population

Some people, particularly young children, may experience difficulties swallowing the Capletwhole and should be encouraged to chew the Capletwith a little water, alternatively Capletmay be crushed.

Hepatic impairment

Patients with abnormal liver function test results (transaminases) prior to commencing albendazole therapy should be carefully evaluated and therapy should be discontinued if liver enzymes are significantly increased or full blood count decreased by a clinically significant level.

4.3 Contraindications

Albendazole should not be administered during pregnancy or in women thought to be pregnant. Albendazole is contraindicated in patients with a known history of hypersensitivity to albendazole or other constituents of the dose forms.

4.4 Special warnings and precautions for use

Use in Intestinal Infections and Cutaneous Larva Migrans (short duration treatment at lower dose):

Pregnancy

In order to avoid administering albendazole during early pregnancy, women of childbearing age should initiate treatment during the first week of menstruation or after a negative pregnancy test.

Neurological symptoms

Treatment with albendazole may uncover pre-existing neurocysticercosis, particularly in areas with high taenosis infection. Patients may experience neurological symptoms e g. 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 occur soon after treatment, appropriate steroid and anticonvulsant therapy should be started immediately.

Hypersensitivity reactions

Albendazole suspension contains benzoic acid which is a mild irritant to the skin, eyes and mucous membrane. It may increase the risk of jaundice in newborn babies.

Use in Systemic Helminth Infections (longer duration of treatment at higher doses):

Hepatobiliary disorders

Albendazole treatment has been associated with mild to moderate elevations of hepatic enzymes .Hepatic enzymes generally normalize on discontinuation of treatment. Case reports of hepatitis have also been received (see Adverse Reactions) Liver function tests should be obtained before the start of each treatment cycle and at least every two weeks during treatment If hepatic enzymes are significantly increased (greater than twice the upper limit of normal), albendazole should be discontinued. Albendazole treatment may be restarted when hepatic enzymes have returned to normal limits, but patients should be carefully monitored for a recurrence.

Bone marrow suppression

Albendazole has been shown to cause bone marrow suppression and therefore blood counts should be performed at the start and every two weeks during each 28 day cycle. Patients with liver disease, including hepatic echinococcosis, appear to be more susceptible to bone marrow suppression leading to pancytopenia, aplastic anaemia, agranulocytosis and leukopenia and therefore warrant closer monitoring of blood counts. Albendazole should be discontinued if clinically significant decreases in blood cell counts occur.

Pregnancy

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

-be advised to take effective precautions against conception during and within one month of completion of treatment with albendazole for a systemic infection

Neurological symptoms

Symptoms associated with an inflammatory reaction following death of the parasite may occur in patients receiving albendazole treatment for neurocysticercosis (e. g seizures, raised intracranial pressure, focal signs). These should be treated with appropriate steroidand anticonvulsant therapy. Oral or intravenous corticosteroids are recommended to prevent cerebral hypertensive episodes during the first week of treatment. Pre-existing neurocysticercosis may also be uncovered in patients treated with albendazole for other conditions, particular in areas with high taenosis infection. Patients may experience neurological symptoms e g. seizures, increased intracranial pressure and focal signs as a result of an inflammatory reactio caused by death of the parasite within the brain. Symptoms may occur soon after treatment, appropriate steroid and anticonvulsant therapy should be started immediately.

Hypersensitivity reactions

Albendazole suspension contains benzoic acid which is a mild initant to the skin, eyes and mucous membrane. It may increase the risk of jaundice in newborn babies.

4.5 Interaction with other medicinal products and other forms of interaction

Cimetidine, praziquantel and dexamethasone have been reported to increase the plasma levels of the albendazole metabolite responsible for the systemic efficacy of the product Ritonavir,

phenytoin, carbamazepine and phenobarbital may have the potential to reduce plasma concentrations of the active metabolite of albendazole; albendazole sulfoxide. 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 lactation

Pregnancy

There are no adequate data from the use of albendazole in pregnant women. Data from studies with animals have shown reproductive toxicity. The potential risk to humans is unknown. Albendazole should not be used during pregnancy unless clearly necessary. In order to rule out pregnancy, women of childbearing age should undergo a pregnancy test before the start of treatment and regularly during treatment with albendazole. In view of the teratogenic effects of benzimidazole derivatives, women of childbearing age should be advised to take effective contraceptive measures. Owing to uncertain interactions with hormonal ovulation inhibitors, use of an oral contraceptive alone is unsuitable for this purpose. Contraception must be ensured shortly before, during and for one month after treatment with albendazole.

Lactation

Adequate human and animal data on use during lactation are not available. Albendazole should only be administered during lactation if the potential benefit justifies the potential risk to the infant.

4.7 Effects on ability to drive and use machines

There have been no studies to investigate the effect of albendazole on driving performance or the ability to operate machinery. However, when driving vehicles or operating machinery, it should be taken into account that dizziness has been reported after using albendazole.

4.8 Undesirable effects

Intestinal Infections and Cutaneous Larva Migrans

The most common adverse reactions are headache, dizziness and upper gastrointestinal symptoms and diarrhoea, particularly in patients with intestinal infections and cutaneous larva migrans. Data from large clinical studies were used to determine the frequency of very common to rare undesirable reactions. The frequencies assigned to all other undesirable reactions (i.e. those occurring at < 1/1000) were mainly determined using post-marketing data

as frequency cannot be estimated from this data a frequency category of "Not known" is assigned. Treatment related adverse reactions, all grades, are listed below by MedDRA body system organ class and frequency. The following convention has been utilised for the classification of frequency: 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

System Organ Class	**Unknown**	**Not known**
Immune system disorders, including hypersensitivity		Hypersensitivity reactions including rash, pruritus and urticaria
Nervous system disorders	Upper gastrointestinal symptoms (e.g. epigastric or abdominal pain, nausea, vomiting) and diarrhoea.	
Hepatobiliary disorders		Elevations of hepatic enzymes
Skin and subcutaneous tissue disorders		Erythema multiforme, Stevens-Johnson syndrome

Systemic helminth infections

The most common adverse reactions are headache, mild to moderate elevations of hepatic enzymes, dizziness, gastrointestinal disturbances, reversible alopecia and fever, particularly in patients with systemic helminth infections. Patients with liver disease, including hepatic echinococcosis, appear to be more susceptible to bone marrow suppresssion. Gastrointestinal disturbances have been associated with albendazole when treating patients with echinococcosis. Data from large clinical studies were used to determine the frequency of very common to rare undesirable reactions. The frequencies assigned to all other undesirable reactions (i.e. those occurring at < 1/1000) were mainly determined using post-marketing data as frequency cannot be estimated from this data a frequency category of "Not known" is assigned. Treatment related adverse reactions, all grades, are listed below by MedDRA body system organ class, frequency and grade of severity. The following convention has been utilised for the classification of frequency: very common ≥ 1/10; common ≥ 1/100 to < 1/100; rare ≥ 1/10,000 to < 1/1,000; very rare < 1/10,000.

System Organ Class	Very common	Common	Unknown	Not known
Blood and lymphatic system disorders				Leukopenia Pancytopenia, aplastic anaemia, agranulocytosis
Immune system disorders, including hypersensitivity reactions			Hypersensitivity reactions including rash, pruritus and urticaria	
Nervous system disorders	Headache	Dizziness		
Gastrointestinal disorder		Gastrointestinal disturbances (abdominal pain, nausea, vomiting)		
Hepatobiliary disorders	Mild to moderate elevations of hepatic enzymes		Hepatitis	
Skin and subcutaneous tissue disorders		Reversible alopecia (thinning of hair, and moderate hair loss)		Erythema multiforme, Stevens-Johnson syndrome
General disorders and administration site conditions		Fever		

4.9 Overdose

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

Immediate medical advice should be sought in the event of overdosage because of the risk of irreversible liver damage.

Symptoms of paracetamol overdosage in the first 24 hours are pallor, nausea, vomiting, anorexia and abdominal pain. Liver damage may become apparent 12 to 48 hours after ingestion and this may be manifested in increasing pro-thrombin time, which is a reliable indicator of deteriorating liver function. Abnormalities of glucose metabolism and metabolic acidosis may occur. In severe poisoning, hepatic failure may progress to encephalopathy, coma and death. Acute renal failure with acute tubular necrosis may develop even in the absence of severe liver damage. Cardiac arrhythmias and pancreatitis have been reported.

Liver damage is likely in adults who have taken 10g or more of paracetamol. It is considered that excess quantities of toxic metabolite (usually adequately detoxified by glutathione when normal doses of paracetamol are ingested), become irreversibly bound to liver tissue. Ingestion of 5g or more of paracetamol may lead to liver damage if the patient has risk factors (see below)

Risk Factors:
If the patient;
a. Is on long-term treatment with carbamazepine, phenobarbitone, phenytoin, primidone, rifampicin, St John's Wort or other drugs that induce liver enzymes.
Or
b. Regularly consumes ethanol in excess of recommended amounts
Or
c. Is likely to be glutathione depleted due to e.g. eating disorders, cystic fibrosis, HIV infection, starvation, cachexia.

Treatment

Immediate treatment is essential in the management of paracetamol overdose. Despite lack of significant early symptoms, patients should be referred to hospital urgently for immediate medical attention and any patient who has ingested around 7.5g
or more of paracetamol in the preceding 4 hours should undergo gastric lavage. Intravenous N-Acetylcysteine or oral methionine protects the liver if administered within 8 to 12 hours of ingesting the overdose. N-Acetylcysteine is effective up to and possibly beyond 24 hours, but expert advice is essential. General supportive measures must be available.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anthelmintics

ATC code: P02CA03

Albendazole is a broad-spectrum anthelmintic. The principal mode of action for albendazole is by its inhibitory effect on tubulin polymerization which results in the loss of cytoplasmic microtubules.

Albendazole causes degenerative alterations in the tegument and intestinal cells of the worm by diminishing its energy production, ultimately leading to immobilization and death of the parasite. It works by binding to the colchicine-sensitive site of tubulin, thus inhibiting its

polymerization or assembly into microtubules. As cytoplasmic microtubules are critical in promoting glucose uptake in larval and adult stages of the susceptible parasites, the glycogen stores of the parasites are depleted. Degenerative changes in the endoplasmic reticulum, the mitochondria of the germinal layer, and the subsequent release of lysosomes result in decreased production of adenosine triphosphate (ATP), which is the energy required for the survival of the helminth.

5.2 Pharmacokinetic properties

Absorption: Albendazole is Poorly absorbed from the gastrointestinal tract due to its low aqueous solubility.

Oral bioavailability appears to be enhanced when co-administered with a fatty meal

Metabolism: Hepatic. 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.

Elimination: 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. 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

Conventional studies using the currently accepted standards for the evaluation of toxicity to reproduction and development are not available

6. Pharmaceutical particulars

6.1 List of excipients

Lactose Monohydrate
Corn starch
Methyl paraben
Propyl paraben
Pvp k-
IPA
Crorcarmellose sodium
PVP XL-10
Talcum powder
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Blisters pack of 2 Tablets.

6.6 Special precautions for disposal and other handling

None

7. Applicant

NEROS Pharmaceuticals Ltd.

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Km 38, Lagos-Abeokuta Expressway

By Singer Bus Stop

Sango, Ota

Ogun State

Nigeria

8. Reference/Authorisation number(s)
Not applicable

9. Date of first authorisation/renewal of the authorisation

Not applicable

10. Date of revision of the text

20 June 2020.