For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

UNICARBAZAN FORTE

1. Generic Name

Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets

2. Qualitative and quantitative composition

Each film coated tablet contains:
Diethylcarbamazine Citrate I.P…….250mg
Chlorpheniramine Maleate I.P…..5mg
Colour: Tartrazine

The excipients used are Dibasic Calcium Phosphate Dihydrate, Starch, Lake of Tartrazine Yellow, Colloidal Silicon Dioxide, Povidone, Isopropyl Alcohol, Talc, Magnesium Stearate, Hydroxy Propyl Methyl Cellulose, Diethyl Phthalate, Methylene Chloride.

3. Dosage form and strength

Dosage Form: Tablets
Strength:
Diethylcarbamazine Citrate…250 mg
Chlorpheniramine Maleate….5 mg

4. Clinical particulars

4.1 Therapeutic indication

Unicarbazan Forte Tablets are indicated for:

- Filariasis
- Tropical Pulmonary Eosinophilia
- Loa-loa

4.2 Posology and method of administration

To be taken as directed by the physician.

4.3 Contraindications

- Hypersensitivity to active ingredients or to any of the excipients.
- The anticholinergic properties of Chlorpheniramine maleate are intensified by Monoamine Oxidase Inhibitors (MAOIs). The tablets are therefore, contraindicated in patients who have been treated with MAOIs within the last fourteen days.
- Co-infection with onchocerciasis. Serious ocular damage may occur.

4.4 Special warnings and precautions for use

Diethylcarbamazine

Use of diethylcarbamazine citrate in patients without underlying filarial infestation

Diethylcarbamazine citrate must be used with care in patients who have a history of convulsions or who show factors that predispose them to convulsions.

Severely ill persons

Use of diethylcarbamazine citrate should be avoided in the frail, elderly and debilitated, especially those with cardiac or renal disease. In the event of a concomitant disorder, the patient should be allowed to recover before taking diethylcarbamazine citrate.

Children
Diethylcarbamazine citrate should not be used in children under the age of 2 years.

Use of diethylcarbamazine citrate in patients with underlying filarial infestation

Lymphatic filariasis
Patients with symptoms suggesting lymphatic filariasis (swelling of legs, arms, female breast or male genitalia) should be managed according to the relevant local or international treatment guidelines.

Loa-loa
The intensity and the severity of the undesirable effects that appear after administration of diethylcarbamazine citrate are associated with the level of microfilariae in the blood prior to treatment. In the event of *Loa-loa* infestation, the level of microfilariae present in the blood is often very high, which predisposes the treated patients to an increased risk of serious side effects. Serious central nervous system problems such as encephalopathy and coma have been observed in patients with *Loa-loa* infections that have been treated with diethylcarbamazine citrate, in particular.

Onchocerciasis
Diethylcarbamazine must not be administered in patients co-infected with onchocerciasis. Skin and/or systemic reactions of variable severity (Mazzotti reaction) and eye reactions have been observed after administration of drugs with rapid microfilariacidal action such as diethylcarbamazine citrate. If there is evidence of hypersensitivity to the eye, administration must be stopped due to potential sight loss. These manifestations are probably associated with an inflammatory process that is triggered following the death of microfilariae and the release of decomposition products.

Chlorpheniramine

- Chlorpheniramine maleate, in common with other drugs having anticholinergic effects, should be used with caution in epilepsy; raised intra-ocular pressure including glaucoma; prostatic; hypertrophy; severe hypertension or cardiovascular disease; bronchitis, bronchiectasis or asthma; hepatic impairment. Children and the elderly are more likely to experience the neurological anticholinergic effects and paradoxical excitation (e.g. increased energy, restlessness, nervousness).
- The effects of alcohol may be increased and therefore concurrent use should be avoided.
- Should not be used with other antihistamine containing products, including antihistamine containing cough and cold medicines.
- Keep out of sight and reach of children

4.5 Drugs interactions

Diethylcarbamazine
No known interactions.

Chlorpheniramine

Concurrent use of Chlorpheniramine maleate and hypnotics or anxiolytics may cause an increase in sedative effects; therefore, medical advice should be sought before taking Chlorpheniramine maleate concurrently with these medicines.

Chlorpheniramine maleate inhibits phenytoin metabolism and can lead to phenytoin toxicity.

The anticholinergic effects of Chlorpheniramine maleate are intensified by MAOIs (see Contra-indications).

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Diethylcarbamazine

Pregnancy
The potential risk to the fetus in humans is unknown.
Diethylcarbamazine Citrate should not be used in pregnancy.

Breastfeeding
It is unknown whether diethylcarbamazine citrate or its metabolites are excreted in human milk. As a risk to the new-born or infant cannot be excluded, the product should not be given to breastfeeding women.

Fertility
The potential risk for humans is unknown. No specific studies with diethylcarbamazine in humans have been conducted to evaluate effects on fertility.

Chlorpheniramine

Pregnancy
There are no adequate data from the use of Chlorpheniramine maleate in pregnant women. The potential risk for humans is unknown. Use during the third trimester may result in reactions in the newborn or premature neonates. Not to be used during pregnancy unless considered essential by a physician.

Lactation
Chlorpheniramine maleate and other antihistamine may inhibit lactation and may be secreted in breast milk. Not to be used during lactation unless considered essential by a physician.

4.7 Effects on ability to drive and use machines

Diethylcarbamazine

Diethylcarbamazine Citrate may cause short-term drowsiness, which may affect the ability to drive, and use machines. Vehicle drivers and machine users should be informed of the risk of drowsiness related to using this medicinal product.

Chlorpheniramine

The anticholinergic properties of Chlorpheniramine maleate may cause drowsiness, dizziness, blurred vision and psychomotor impairment, which can seriously hamper the patients' ability to drive and use machinery.

4.8 Undesirable effects

Diethylcarbamazine

Summary of the safety profile

There is no clear information on the frequency of adverse reactions occurring as a result of diethylcarbamazine citrate administration. Mild to moderate adverse reactions are common,but the incidence of serious adverse reactions is considered to be very low.

In the absence of circulating microfilaraemia, the administration of diethylcarbamazine citrate, when given at the recommended dosage, may cause nausea, vomiting, abdominal pain, diarrhoea, loss of appetite, muscle pain, dizziness, drowsiness, fatigue and headache. These begin within one to two hours and may persist for several hours.

In patients with circulating microfilaraemia adverse reactions may be more common and severe, particularly in patients with a high parasite burden. Adverse reactions vary with the infecting filarial species, may be local and/or systemic, and may occur with or without fever. These are considered allergic reactions due to antigen-antibody reaction caused by dead microfilariae or adult filarial worms, and the intensity and the severity of adverse reactions are usually associated with the level of microfilariae in the blood prior to treatment. Usually such symptoms are transient and self-limiting, but when the symptoms are significant enough to interfere with daily life, the patient needs to be observed carefully and given clinically appropriate treatment. Steroids have been used. If there is evidence of hypersensitivity involving the eye, administration must be stopped due to potential sight loss.

System Organ Class	**Reactions attributable to DEC (may be seen in subjects without microfilariae)**	**Reactions attributable to death of microfilariae (may be seen in subjects with microfilariae and/or adult worm infections)**
Blood and lymphatic system disorders		Lymphadenitis, lymphangitis, lymph node abscess, lymph node pain, lymphoedema
Gastrointestinal disorders	Nausea, vomiting, abdominal pain, diarrhoea	Abdominal pain, nausea, vomiting, diarrhoea
General disorders and administration site conditions		Pyrexia, chills, weakness, malaise
Metabolism and nutrition disorders	Decreased appetite	Decreased appetite

Musculoskeletal and connective tissue disorders	Myalgia	Myalgia, arthralgia, chest pain
Nervous system disorders	Dizziness, somnolence, lethargy, headache	Dizziness, headache, lethargy
Renal and urinary disorders		Haematuria
Reproductive system and breast disorders		Epididymitis, spermatic cord inflammation, hydrocele, scrotal mass
Respiratory disorders		Dyspnoea, cough
Skin and subcutaneous tissue disorders		Pruritus, papular rash
Vascular disorders		Circulatory collapse, orthostatic hypotension

Reactions only observed in subjects with loaisis or onchocerciasis infection	
Cardiac disorders	Tachycardia
Eye disorders	Optic neuritis, punctate keratitis, iridocyclitis, conjunctivitis, visual field defect, eye pain, lacrimation, photophobia, corneal oedema
Immune system disorders	Mazotti reaction
Infections and infestations	Meningoencephalitis helminthic
Investigations	Increased intraocular pressure
Nervous system disorders	Coma, allergic encephalitis, encephalopathy, vertigo, convulsion (isolated cases in patients with a history of epilepsy)
Renal and urinary disorders	Proteinuria

NOTE: frequency of all reactions is unknown (cannot be estimated from the available data).
DEC = diethylcarbamazine citrate.

Children

Frequency, type and severity of adverse reactions in children are expected to be the same as in adults

Chlorpheniramine

Specific estimation of the frequency of adverse events for OTC products is inherently difficult (particularly numerator data). Adverse reactions which have been observed in clinical trials and which are considered to be common (occurring in ≥1% to <10% of subjects) or very common (occurring in ≥10% of subjects) are listed below by MedDRA System Organ Class. The frequency of other adverse events identified during postmarketing use is unknown.

Blood and lymphatic system disorders:
Unknown: haemolytic anaemia, blood dyscrasias

Immune system disorders:

Unknown: allergic reaction, angioedema, anaphylactic reactions

Metabolism and nutritional disorders:
Unknown: anorexia

Psychiatric disorders:
Unknown: confusion*, excitation*, irritability*, nightmares*, depression
Nervous system disorders*:
Very common: sedation, somnolence
Common: disturbance in attention, abnormal coordination, dizziness, headache

Eye disorders:
Common: blurred vision

Ear and labyrinth disorders:
Unknown: tinnitus

Cardiac disorders:
Unknown: palpitations, tachycardia, arrhythmias

Vascular disorders:
Unknown: Hypotension

Respiratory, thoracic and Mediastinal disorders:
Unknown: thickening of bronchial secretions

Gastrointestinal disorders:
Common: nausea, dry mouth
Unknown: vomiting, abdominal pain, diarrhoea, dyspepsia

Hepatobiliary disorders:
Unknown: hepatitis including jaundice

Skin and subcutaneous disorders:
Unknown: exfoliative dermatitis, rash, urticaria, photosensitivity,
Musculoskeletal and connective tissue disorders:
Unknown: muscular twitching, muscle weakness.

Renal and Urinary disorders:
Unknown: Urinary retention

General disorders and administration site conditions:
Common: fatigue
Unknown: chest tightness

*Children and the elderly are more susceptible to neurological anticholinergic effects and paradoxical excitation (eg increased energy, restlessness, nervousness).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

4.9 Overdose

Diethylcarbamazine

Symptoms
Overdose may cause nausea, vomiting, headache, vertigo, drowsiness and, in rare but serious cases, convulsions.

Management
Administration of activated charcoal may be of value. Monitor for adverse reactions, with symptomatic treatment and hospitalisation if necessary.

Chlorpheniramine

Symptoms and signs

The estimated lethal dose of Chlorpheniramine maleate is 25 to 50mg/kg body weight. Symptoms and signs include sedation, paradoxical excitation of the CNS, toxic psychosis, convulsions, apnoea, anticholinergic effects, dystonic reactions and cardiovascular collapse including arrhythmias.

Treatment
Symptomatic and supportive measures should be provided with special attention to cardiac, respiratory, renal and hepatic functions and fluid and electrolyte balance. If overdosage is by the oral route, treatment with activated charcoal should be considered provided there are no contraindications for use and the overdose has been taken recently (treatment is most effective if given within an hour of ingestion). Treat hypotension and arrhythmias vigorously. CNS convulsions may be treated with i.v. diazepam. Haemoperfusion may be used in severe cases.

5. Pharmacological properties

5.1 Mechanism of Action

Diethylcarbamazine

Pharmacotherapeutic group: Antihelmintics, ATC code: P02CB02

Mechanism of action
Diethylcarbamazine citrate is a synthetic piperazine derivative with an antihelmintic action.

The mode of action of diethylcarbamazine citrate is not clearly known. Diethylcarbamazine citrate can be best described as a potent anti-microfilaraemic agent with variable macrofilaricidal properties. The drug is known to exert its effect directly

on the parasite and also achieve parasite killing by activating the host immune response. Several potential modes of action of diethylcarbamazine citrate leading to microfilariae killing have been identified:

• Overstimulation of the neuromuscular system of the parasites and increased motility, inhibition of vital parasite metabolic enzymes, activation of surface membrane complement, activation of eosinophils and release of eosinophil-derived cationic proteins, enhanced eosinophil-dependent antibody mediated destruction of parasites and increased adhesion of parasites to phagocytic and antibody producing cells.
• Inhibition of acetylcholinesterase production by parasites, leading to increased levels of lysosomal enzymes β-glucuronidase and acid phosphatase that are involved in phagocytosis.
• Release of nitric oxide as evidenced by increased levels of nitrite and nitrates.
• Changes in arachidonic acid metabolism in the parasite and the host that alter adhesiveness of the parasite.

The mode of action of diethylcarbamazine citrate on adult worms is less well documented. However, there is sufficient evidence to suggest that diethylcarbamazine is macrofilaricidal. Degenerating adult worms have been demonstrated in lymph nodes post-treatment. It is also well known that the macrofilaricidal effects are inconsistent.

Chlorpheniramine

ATC Code R06AB04 Antihistamines for systemic use

Chlorpheniramine maleate is a potent antihistamine (H1-antagonist).
Antihistamines diminish or abolish the actions of histamine in the body by competitive reversible blockade of histamine H1-receptor sites on tissues. Chlorpheniramine maleate also has anticholinergic activity.

5.2 Pharmacodynamic properties

Diethylcarbamazine
Diethylcarbamazine citrate has potential to interrupt the parasitic life cycle by destruction of microfilariae which are essential for host to vector transmission of the parasite.

Diethylcarbamazine citrate was found to have effects on the arachidonic acid and cyclooxygenase metabolic pathways and COX-1 pathway of filaria. It has also been determined that inducible nitric oxide is essential for the rapid sequestration of microfilariae by diethylcarbamazine citrate. It has been suggested that as diethylcarbamazine citrate alters arachidonic acid metabolism in microfilariae (and in host endothelial cells), these changes may result in vasoconstriction and amplified endothelial adhesion, leading to immobilization of microfilarial parasites, enhanced adherence, and cytotoxic activity by host platelets and granulocytes. This would represent activation of the innate, nonspecific immune system, independent of the adaptive, antigen-specific, immune response.

Chlorpheniramine

Chlorpheniramine maleate act to prevent the release of histamine, prostaglandins and leukotrienes and have been shown to prevent the migration of inflammatory mediators. The actions of Chlorpheniramine maleate include inhibition of histamine on smooth muscle, capillary permeability and hence reduction of oedema and wheal in hypersensitivity reactions such as allergy and anaphylaxis.

5.3 Pharmacokinetic properties

Diethylcarbamazine

Absorption and bioavailability
Diethylcarbamazepine is readily absorbed following oral administration. Bioavailability is between 80 and 85%. Following single dose administration of one diethylcarbamazine tablet in healthy volunteers in the fed state, the mean (±SD) diethylcarbamazepine Cmax value was 598 (±84) ng/ml and the corresponding value for AUC was 7950 (±1660) ng.h/ml. The mean (±SD) diethylcarbamazepine Tmax value was 2.25 (± 1.17) hours.

Distribution
Diethylcarbamazine is widely distributed in tissues and is mainly excreted in the urine unchanged and as the metabolite, diethylcarbamazine N-oxide. Urinary excretion, and hence plasma half–life, is dependent on urinary pH. About 5% of a dose is excreted in the faeces.

Metabolism
In rats and monkeys after an intravenous dose, 10-20% is excreted in the urine as unchanged drug, most of which is excreted in the first 3 hours. Metabolites more slowly eliminated include N-ethyl-4-methyl-1-piperazine-carboxamide (MEC) and their N-oxides, 4-methyl-piperazine-carboxamide and N,N-diethyl-1-piperazine-carboxamide. In vivo most of the metabolites are active on microfilariae and both N-oxides active on adults and infective larvae. The antifilarial action of DEC is swift and of short duration. This action is prolonged by the activity of metabolites, especially the N-oxides.

Elimination
Diethylcarbamazine elimination is primarily through renal clearance, which accounts for around 50% of the total plasma clearance. The remaining clearance is via metabolism, leading to a number of metabolites, which are also renally cleared. Given that the major elimination pathway is renal clearance and that metabolic clearance is via several routes, genetic polymorphisms of drug metabolizing enzymes are very unlikely to have any clinically relevant consequences. This is borne out by the fact that there are no reported significant drug-drug interactions with diethylcarbamazine citrate which would likely be evident if modulation of metabolic clearance was an important factor in determining systemic exposure.

The PK of diethylcarbamazine citrate was not altered by timing of administration (morning versus evening).

The elimination half-life and area under the plasma concentration-time curve of diethylcarbamazine citrate were significantly increased when an alkaline urinary pH was

maintained compared with the values of these parameters obtained on a second occasion when an acidic urinary pH was maintained.

Renal impairment
Results in patients with chronic renal impairment and in healthy subjects given a single 50 mg oral dose of diethylcarbamazine citrate indicated that the plasma half–life of diethylcarbamazine citrate is prolonged and its 24-hour urinary excretion is considerably reduced in those with moderate to severe renal impairment. No significant correlations were observed between age, sex or weight and renal function, but diethylcarbamazine citrate excretion did appear to decrease with increasing urinary pH.

Chlorpheniramine

Chlorpheniramine maleate is well absorbed from the gastro-intestinal tract, following oral administration. The effects develop within 30 minutes, are maximal within 1 to 2 hours and last 4 to 6 hours. The plasma half-life has been estimated to be 12 to 15 hours. Chlorpheniramine maleate is metabolised to the monodesmethyl and didesmethyl derivatives. About 22% of an oral dose is excreted unchanged in the urine. Only trace amounts have been found in the faeces.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Diethylcarbamazine
Nonclinical studies have not been performed with Diethylcarbamazine Citrate. However, diethycarbamazine citrate is a well-established drug with an extensive record of clinical use.

Chlorpheniramine
There is no pre-clinical safety data that could be of relevance to the prescriber, which are not already included in other sections of the SPC

7. Description

Diethylcarbamazine Citrate is N,N-diethyl-4-methylpiperazine-1-carboxamide dihydrogen citrate. The empirical formula of Diethylcarbamazine Citrate is $C_{10}H_{21}N_3O,C_6H_8O_7$ and its molecular weight is 391.4. Diethylcarbamazine Citrate is white, crystalline powder; odourless; slightly hygroscopic.

Chlorpheniramine Maleate is (RS)-3-(4-chlorophenyl)-3-(pyrid-2-yl)propyldimethylamine hydrogen maleate. The empirical formula is $C_{16}H_{19}ClN_2,C_4H_4O_4$ and its molecular weight is 390.9. Chlorpheniramine Maleate is white, crystalline powder; odourless.

Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets are yellow coloured coated capsule shaped (caplet) tablets plain on both sides. The excipients used are Dibasic Calcium Phosphate Dihydrate, Starch, Lake of Tartrazine Yellow, Colloidal Silicon Dioxide, Povidone, Isopropyl Alcohol, Talc, Magnesium Stearate, Hydroxy Propyl Methyl Cellulose, Diethyl Phthalate, Methylene Chloride.

8. Pharmaceutical particulars

8.1 Incompatibilities
None Stated.

8.2 Shelf-life
Do not use later than the date of expiry.

8.3 Packaging information
Unicarbazan Forte is available in Blister strip of 8 tablets and Jar of 100 tablets.

8.4 Storage and handing instructions
Store in a cool and dry place, protect from light and moisture.

Dosage: As directed by the Physician
Keep all medicine out of reach of children

9. Patient Counselling Information

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

• Keep this leaflet. You may need to read it again.

• If you have any further questions, ask your doctor or pharmacist.

• This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.

• If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

9.1 What Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets are and what they are used for.
Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets are combination of a antihelmintic (diethylcarbamazine) and an antihistamine (chlorpheniramine).

This combination product is used for the treatment of Filariasis, Tropical Pulmonary Eosinophilia and Loa-loa.

9.2 What you need to know before you use Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets

Do not use Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets:

- If you are allergic (hypersensitive) to diethylcarbamazine citrate, chlorpheniramine maleate or to any of the other ingredients in this medicine.
- If you have previously had river blindness (onchocerciasis) involving your eyes.
- If you have had monoamine oxidase inhibitor (MAOI) antidepressive treatment within the past 14 days.

Take special care with Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets:

- If you think you may have an underlying worm infection, such as loaisis (African eye worm), onchocerciasis (river blindness) or lymphatic filariasis (elephantiasis). With an underlying worm infection, depending on the type of underlying infection, side effects may occur more frequently and may be more serious.
- if you have a history of epilepsy or suffer from convulsions (fits), raised blood pressure within the eye or glaucoma, very high blood pressure, liver, asthma or other chest diseases.
- if you are elderly or have heart or kidney problems you should not normally take these tablets.

Children and the elderly are more likely to experience certain side effects.

Taking other medicines

Please tell your healthcare provider if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

The following affect the way Chlorpheniramine maleate works:

- MAOIs – these must not be given with Chlorpheniramine maleate.

Chlorpheniramine maleate may increase the effects of the following:

- drugs that treat anxiety or help you to sleep
- psychotropic drugs (that change perception or behaviour)
- atropine (used as eye drops to dilate the pupils, or given as an injection to treat low heart rate in emergencies)
- phenytoin (used to treat epilepsy).

Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets with alcohol

Do not consume alcohol whilst being treated with these tablets. It may cause the effects of the medicine to be increased, making you drowsier. It may also cause the effect of the alcohol to be increased.

Pregnancy and breast-feeding

You will not normally be given these tablets if you are pregnant or breast-feeding. This is because it is not known how the tablets affect a developing baby (fetus) and it is not known if diethylcarbamazine citrate passes into a nursing mother's breast milk.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, you should not take these tablets. Ask your healthcare provider for advice before taking any medicine.

Driving and using machines
These tablets may cause drowsiness and make you sleepy. Do not drive or operate machinery until you know how this product affects you.

9.3 How to use Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets

Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets will be given to you by a health care provider.

- Always use these tablets exactly as your health care provider has told you.
- You should check with your health care provider if you are unsure of the instructions.
- These tablets should preferably be taken after meals.

How much will be given
Your health care provider will decide how much to give you.

If you take more tablets than you should
You may experience the following effects: nausea (feeling sick), vomiting, headache, vertigo (feeling dizzy), drowsiness, and, in rare but serious cases, convulsions (fits).

You should contact your health care provider if you experience any of these effects and you may be admitted to hospital for appropriate treatment, if necessary.

If you have any further questions on the use of this product, ask your health care provider.

9.4 Possible side effects

Like all medicines, these tablets can cause side effects, although not everybody gets them. They may happen hours or days after you have taken the tablets.

There is no clear information on how often side effects occur after taking this medicine.

When no underlying worm infection is present, side effects generally occur within one or two hours of taking the medicine and may last for a few hours. Such side effects include nausea (feeling sick), vomiting, abdominal pain, diarrhoea, loss of appetite, muscle pain, dizziness, drowsiness, fatigue and headache.

In patients with an underlying worm infection including African eye worm (loaisis), river blindness (onchocerciasis) and elephantiasis (lymphatic filariasis), side effects may be more common and serious, in particular when there is a high number of parasites in the blood. Such side effects can vary depending on the type of worm infection, may affect your whole body and may occur with or without fever. These are considered to be allergic reactions to the dead worms following treatment and are particularly common in patients with river blindness infection.

When an underlying worm infection is present, side effects include irritation and swelling of the lymph nodes, abdominal pain, nausea (feeling sick), vomitting, diarrhoea, fever, chills, weakness, feeling unwell, loss of appetite, muscle pain, joint pain, chest pain, cough, dizzinesss, headache, fatigue, blood in the urine, irritation and swelling in and around the testicles, swelling or painful lumps developing under the skin in the scrotum, difficulty in breathing, itchiness, rash, failure of the circulation and low blood pressure upon standing.

The following side effects are associated only when an underlying African eye worm (loaisis) or river blindness (onchocerciasis) infection is present: fast heart beat, irritation or inflammation of the eye, blurred vision, eye pain, watery eyes, intolerance to light, swelling of the eye, coma, swelling of the brain, convulsions (fits), vertigo (feeling dizzy) and protein in the urine.

The following side effects have been reported:
Frequency Not Known (cannot be estimated from the available data)

- allergic reactions (skin reactions, including redness and scaling of the skin, itching of raised bumps on the skin, sensitivity to light)
- a stinging or burning feeling at the site of injection
- giddiness or drowsiness if the drug is injected too quickly into a vein (this usually passes)
- dryness of the mouth, thickening of the phlegm in the airways (this may make it more difficult to cough up phlegm), headache, indigestion, liver problems including jaundice (this can cause yellowing of the skin and whites of the eyes), difficulty passing urine
- muscular twitching, weakness and incoordination, ringing in the ears, blurred vision, irritability, depression, nightmares
- blood abnormalities
- Collapse
- Skin peeling, itchy rash and sensitivity to sun.
- Ringing in ears

Children and the elderly are more likely to experience the side effects which relate to the nervous system (these may affect the mind, nerves, muscles, and the senses). Elderly people may become confused and children may become agitated or excitable.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your health care provider.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at: http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting.

By reporting side effects, you can help provide more information on the safety of this medicine.

9.5 How to store Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets
Store in a cool and dry place, protect from light and moisture.

9.6 Contents of the pack and other information

What Diethylcarbamazine Citrate and Chlorpheniramine Maleate Tablets contains:

The active ingredients are Diethylcarbamazine and Chlorpheniramine Maleate Tablets. The excipients used are Dibasic Calcium Phosphate Dihydrate, Starch, Lake of Tartrazine Yellow, Colloidal Silicon Dioxide, Povidone, Isopropyl Alcohol, Talc, Magnesium Stearate, Hydroxy Propyl Methyl Cellulose, Diethyl Phthalate, Methylene Chloride.

10. Details of manufacturer

Manufactured by:
Torrent Pharmaceuticals Ltd.
32 No. Middle Camp, NH-10, East District, Gangtok. Sikkim-737 135

11. Details of permission or licence number with date

Mfg Licence No.: M/563/2010 issued on 08.12.2017

12. Date of revision

June 2019

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/UNICARBAZAN FORTE 250, 5 mg /JUN-19/01/PI