Summary of products characteristics (SmPC):

1. Name of the Medicinal Product: REZEPINE TABLETS
Carbamazepine 200mg

2. Qualitative and Quantitative composition:
Each uncoated tablet contains Carbamazepine BP 200mg.
For the full list of excipients, See section 6.1

3. Pharmaceutical form: Tablet
White coloured round shaped tablet plain on one side and break line on another side.

4. Clinical particular's:

4.1 Therapeutic indication:
Partial seizures with complex symptoms (psychomotor, temporal lobe); Generalized tonic-clonic seizures (grand mal); Mixed seizure patterns or other partial or generalized seizures; pain associated with true trigeminal neuralgia; glossopharyngeal neuralgia; for prophylaxis of manic depressive psychosis in patients unresponsive to lithium therapy.

4.2 Posology and method of administration:
Epilepsy: Adults and children (over 12 years): Initially 100mg twice daily. Increase at weekly intervals by 200mg in divided dosage regimen until best response is obtained. Do not exceed 1000mg/day in children 12-15 years or 1200mg/day in patients over 15 years. In rare instances, doses upto 1600 mg/day have been used in adults. Maintenance: usually 800- 1200mg daily.

Children (6-12 years): 20-30mg/kg/day, in divided doses 3-4 times a day.

Maintenance: Usually 400-800 daily.

Trigeminal neuralgia: Initial: 100mg twice daily on the first day. May increase by 200mg/day using 100mg increments every 12 hours as needed. Do not exceed 1200mg daily. Maintenance: 400 - 800mg daily.

Prophylaxis of manic-depressive psychosis: Initially 400mg daily in divided doses, increasing gradually until symptoms are controlled or total 1600mg daily dose, is reached. Usual range 400-600 mg in divided dosage.

Method of Administration: Oral route.

4.3 Contraindication:
History of bone marrow depression; hypersensitivity to carbamazepine and tricyclic antidepressants; concomitant use of MAO inhibitors.

4.4 Special warning and precaution for use:
Restrict treatment of epilepsy to those classifications listed under indications. Discontinue, if the patient exhibits evidence of marrow suppression. Use with caution in patients with increased intraocular pressure. Discontinue MAO inhibitors for a minimum of 14 days before carbamazepine administration. Patients should observe caution while driving or performing other tasks requiring alertness, as it may produce drowsiness, dizziness. Prescribe Rezepine, only after benefit –risk appraisal is done in patients with a history of cardiac, hepatic or renal damage. Perform baseline liver function tests at regular intervals. Safety for use during pregnancy, lactation and in children below 6 years has not been established.

4.5 Interactions with other medicinal products and other forms of interactions:
Erythromycin may increase serum levels of carbamazepine. Breakthrough bleeding has been reported in women receiving concomitant oral contraceptives. Simultaneous administration of phenobarbital, phenytoin or primidone, or combination, may lower serum levels of carbamazepine with no loss of the seizure control. Half-life of doxycycline was reduced when administered with carbamazepine. Cimetidine, isoniazid and propoxyphene may inhibit the metabolism of carbamazepine. Carbamazepine may potentiate the antidiuretic effects of vasopressin, or desmopressin.
Additional information on special populations:
Not Applicable

Paediatric population:
Not Applicable

4.6 Fertility, pregnancy and lactation:
Pregnancy
Offspring of epileptic mothers with untreated epilepsy are known to be more prone to developmental disorders, including malformations. Developmental disorders and malformations, including spina bifida, and also other congenital anomalies e.g. craniofacial defects such as clept lip/palate, cardiovascular malformations, hypospadias and anomalies involving various body systems, have been reported in association with the use of Carbamazepine tablets. Patients should be counselled regarding the possibility of an increased risk of malformations and given the opportunity of antenatal screening. Based on data in a North American pregnancy registry, the rate of major congenital malformations, defined as a structural abnormality with surgical, medical, or cosmetic importance, diagnosed within 12 weeks of birth was 3.0% (95% CI 2.1 to 4.2%) among mothers exposed to carbamazepine monotherapy in the first trimester and 1.1% (95% CI 0.35 to 2.5%) among pregnant women not taking any antiepileptic drug (relative risk 2.7, 95% CI 1.1 to 7.0).
Taking these data into consideration:
- Pregnant women with epilepsy should be treated with special care.

- If women receiving Carbamazepine tablets become pregnant or plan to become pregnant, or if the problem of initiating treatment with Carbamazepine tablets arises during pregnancy, the drug's expected benefits must be carefully weighed against its possible hazards, particularly in the first 3 months of pregnancy.
- In women of childbearing potential Carbamazepine tablets should, wherever possible, be prescribed as monotherapy, because the incidence of congenital abnormalities in the offspring of women treated with a combination of antiepileptic drugs is greater than in those of mothers receiving the individual drugs as monotherapy. The risk of malformations following exposure to carbamazepine as polytherapy may vary depending on the specific drugs used and may be higher in polytherapy combinations that include valproate.
- Minimum effective doses should be given and monitoring of plasma levels is recommended. The plasma concentration could be maintained in the lower side of the therapeutic range 4 to 12 micrograms/mL provided seizure control is maintained. There is evidence to suggest that the risk of malformation with carbamazepine may be dose-dependent i.e. at a dose < 400mg per day, the rates of malformation were lower than with higher doses of carbamazepine.
- Patients should be counseled regarding the possibility of an increased risk of malformations and given the opportunity of antenatal screening.
- During pregnancy, an effective antiepileptic treatment should not be interrupted, since the aggravation of the illness is detrimental to both the mother and the fetus.

Monitoring and prevention

Folic acid deficiency is known to occur in pregnancy. Antiepileptic drugs have been reported to aggravate deficiency. This deficiency may contribute to the increased incidence of birth defects in the offspring of treated epileptic women. Folic acid supplementation has therefore been recommended before and during pregnancy.

In the neonate

In order to prevent bleeding disorders in the offspring, it has also been recommended that vitamin K_1 be given to the mother during the last weeks of pregnancy as well as to the neonate.

There have been a few cases of neonatal seizures and/or respiratory depression associated with maternal Carbamazepine tablets and other concomitant antiepileptic drug use. A few cases of neonatal vomiting, diarrhoea and/or decreased feeding have also been reported in association with maternal Carbamazepine tablets use. These reactions may represent a neonatal withdrawal syndrome.

Women of child-bearing potential and contraceptive measures

Due to enzyme induction, Carbamazepine tablets may result in a failure of the therapeutic effect of oral contraceptive drugs containing oestrogen and/or progesterone. Women of child bearing potential should be advised to use alternative contraceptive methods while on treatment with Carbamazepine tablets.

Breast-feeding:
Carbamazepine passes into the breast milk (about 25-60% of the plasma concentrations). The benefits of breast-feeding should be weighed against the remote possibility of adverse effects occurring in the infant. Mothers taking Carbamazepine tablets may breast-feed their infants, provided the infant is observed for possible adverse reactions (e.g. excessive somnolence, allergic skin reaction). There have been some reports of cholestatic hepatitis in neonates exposed to carbamazepine during antenatal and or during breast feeding. Therefore breast-fed infants of mothers treated with carbamazepine should be carefully observed for adverse hepatobiliary effects.
Fertility:
There have been very rare reports of impaired male fertility and/or abnormal spermatogenesis.

4.7 Effects on ability to drive and use machines:
The patient's ability to react may be impaired by the medical condition resulting in seizures and adverse reactions including dizziness, drowsiness, ataxia, diplopia, impaired accommodation and blurred vision reported with carbamazepine tablets, especially at the start of treatment or in connection with dose adjustments. Patients should therefore exercise due caution when driving a vehicle or operating machinery.

4.8 Undesirable effects:
Dizziness, drowsiness, unsteadiness, nausea and vomiting are reported frequently. Less frequently aplastic anaemia, leukopenia, agranulocytosis, eosinophilia, leukocytosis thrombocytopenia, abnormal liver function tests, have been reported in some patients.

4.9 Overdose and Treatment:
Symptoms include neuromuscular disturbances, cardiovascular complications, irregular breathing, respiratory depression, impaired consciousness ranging to deep coma, convulsions, especially in small children, motor restlessness, muscular twitching, and tremors. Irrigate stomach repeatedly. There is no specific antidote. Dialysis is indicated only in severe poisoning associated with renal failure. Replacement transfusion is indicated in severe poisoning in small children.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties:
Pharmacotherapeutic group: Anti-epileptic; ATC Code: N03AF01.

As an antiepileptic agent its spectrum of activity embraces: partial seizures (simple and complex) with and without secondary generalisation; generalised tonic-clonic seizures, as well as combinations of these types of seizures.
Carbamazepine stabilises hyperexcited nerve membranes, inhibits repetitive neuronal discharges, and reduces synaptic propagation of excitatory impulses. It is conceivable that prevention of repetitive firing of sodium-dependent action potentials in depolarised neurons via use- and voltage-dependent blockade of sodium channels may be its main mechanism of action.

Whereas reduction of glutamate release and stabilisation of neuronal membranes may account for the antiepileptic effects, the depressant effect on dopamine and noradrenaline turnover could be responsible for the antimanic properties of carbamazepine.

5.2 Pharmacokinetic properties:

Carbamazepine is slowly and irregularly absorbed from the gastrointestinal tract and has a bioavailability of 85 to 100%. It is extensively metabolised in the liver,
notably by the cytochrome P450 isoenzymes CYP3A4 and CYP2C8. One of its primary metabolites, carbamazepine- 10,11-epoxide, is also active. Carbamazepine is excreted in the urine almost entirely in the form of its metabolites; some are also excreted in
faeces. Elimination of carbamazepine is reported to be more rapid in children and accumulation of the active metabolite may often be higher than in adults.
Carbamazepine is widely distributed throughout the body and is about 70 to 80% bound to plasma proteins.
It induces its own metabolism so that the plasma halflife may be considerably reduced after repeated dosage.
The mean plasma half-life of carbamazepine on repeated dosage is about 12 to 24 hours; it appears to be considerably shorter in children than in adults. Moreover, the metabolism of carbamazepine is readily induced by drugs that induce hepatic microsomal enzymes Monitoring of plasma concentrations may be performed when clinically indicated and the therapeutic range of total plasma-carbamazepine is usually quoted as being about 4 to 12 micrograms/mL (17 to 50 micromoles/litre), although this is subject to considerable
variation. It has been suggested by some, but not all investigators, that measurement of free carbamazepine concentrations in plasma may prove more reliable, and concentrations in saliva or tears, which contain only free carbamazepine, have also been measured.
Carbamazepine crosses the placental barrier and is distributed into breast milk.
The pharmacokinetics of carbamazepine are affected by use with other antiepileptics

5.3 Preclinical safety data:

No further relevant information.

6. Pharmaceutical Particulars:

6.1 List of excipients

Rezepine tablet contains the following excipients:
Maize starch, Microcrystalline cellulose, colloidal silicon dioxide, Povidone K30, Sodium methyl paraben, sodium propyl paraben, Sodium Starch Glycolate and magnesium stearate,

6.2 Incompatibilities

None known

6.3 Shelf life
24 months

6.4 Special precaution for storage
Do not store above 30°C. Protect from light. Keep out of reach of children.

6.5 Nature and contents of container
10 tablets are packed in Aluminium/PVC blister; such ten blisters are packed in a unit carton along with literature insert.
1000 Tablets packed in polythene bag and contained in HDPE Container with leaflet.

6.6 Special precautions for disposal
No special precaution.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES:

Marketing Authorization Holder:
Rene Industries Ltd
Address: PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

Manufactured by:
Rene Industries Ltd
Address: PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

8. MARKETING AUTHORISATION NUMBER:
Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION:
Not Applicable

10. DATE OF REVISION OF THE TEXT:
Not Applicable

11. DOSIMETRY (IF APPLICABLE):
Not Applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):
Not Applicable