Prescribing information (Summary of products characteristics):

1. Name of the medicinal product

Labtol-200 Tablets.

2. Qualitative and quantitative composition.

Each tablet contains: Carbamazepine BP 200mg and excipients provided in section 6.1

3. Pharmaceutical form.

Tablet

White, circular, biconvex tablets scored on one side and plain on reverse, packed in blisters of 10 x 10's in a unit box, 1000's in HDPE container with literature insert.

4. Clinical Particulars.

4.1 Therapeutic Indications

4.2 Dosage and method of administration.

Dosage should be adjusted to the need of the individual patient. A low initial daily dosage with a gradual increase is advised to minimize side effects. As soon as adequate control is achieved, the dosage may be reduced very gradually to the minimum effective level. Medication should be taken with meals.

Epilepsy

Adults and Children over 12 years of age:

Initial 200mg b.i.d. the dosage may be increased up to 200mg a day at weekly intervals until the best response is obtained.

Maintenance: Adjust dosage to the minimum effective level, visually 800mg - 1200mg a day. (Rarely 600mg -1600mg a day).

Children 6 - 12 Years of age:

Initial: 100mg b.i.d. increase at weekly intervals by adding to 100mg a day until the optimal response is obtained.

Dosage generally should not exceed 100mg daily.

Maintenance: Adjust dosage to the minimum effective level usually 400mg - 800mg daily.

Combination Therapy

Carbamazepine may be used alone or with other anticonvulsants. When added to existing anticonvulsants therapy, the drug should be added gradually while the other anticonvulsants are maintained and gradually decreased except phenytoin, which may have to be increased.

Trigeminal Neuralgia

Initial: 100mg b.i.d. on the first day, the dosage being increased by up to 200mg a day, using increments of 100mg every 12 hours only as needed until pain is relieved.

Maintenance: 200mg to 1200mg a day (average 400mg-800mg a day) in divided doses.

4.3 Contraindications

- Known hypersensitivity to the active substance or structurally related drugs (e.g., tricyclic antidepressants) or any of the excipients listed in section 6.1
- Patients with atrioventricular block.
- Patients with a history of bone-marrow depression.
- Patients with a history of hepatic porphyrias (e.g., acute intermittent porphyria, variegate porphyria, porphyria cutanea tarda)
- The use of carbamazepine is not recommended in combination with monoamine oxidase inhibitors (MAOIs).

4.4 Special warnings and precautions for use.

Carbamazepine should be avoided in patients with atrioventricular conduction abnormalities and in patients with history of bone marrow depression.

It should be given with caution to patients with history of blood disorders or haematological reaction to other drugs of cardiac, hepatic or renal disease.

Caution should be observed in patients with glaucoma or raised intraocular pressure due to its mild antimuscarinic properties.

Care is required when withdrawing Carbamazepine. Clinical monitoring is of primary importance throughout treatment. It may produce dizziness and drowsiness, which could impair a patient's ability to drive or operate machinery.

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

There are complex interactions between antiepileptics and toxicity may be enhanced without a corresponding increase in antiepileptic activity. Plasma monitoring is often advisable with combination therapy. Carbamazepine is a hepatic enzyme inducer and induces its own metabolism as well as that of a number of other drugs (doxycycline, anticoagulants, oral contraceptives). CYP3A4 inhibitors such as cimetidine and ketoconazole inhibit Carbamazepine metabolism leading to raised plasma concentrations and associated toxicity. Enzyme inducers such as Phenobarbital can enhance the metabolism of Carbamazepine leading to reduced plasma levels.

4.6 Fertility, pregnancy and lactation

Pregnancy

Offspring of epileptic mothers are known to be more prone to developmental disorders, including malformations.

Although conclusive evidence from controlled studies with carbamazepine monotherapy is lacking, developmental disorders and malformations, including spinal bifida and also other congenital anomalies, e.g. craniofacial defects, cardiovascular malformations, hypospadias and anomalies involving various body systems, have been reported in association with the use of carbamazepine. Based on data from several pregnancy registries and meta- analyses the rate of major congenital malformations, defined as a structural abnormality with surgical, medical, or cosmetic importance, was 2-3 times increased among mothers exposed to carbamazepine monotherapy in the first trimester. Taking these data into consideration: - Pregnant women with epilepsy should be treated with special care. - If women receiving carbamazepine become pregnant or plan to become pregnant, or if the problem of initiating treatment with carbamazepine 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 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 < 400 mg 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 folic acid 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 K1 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 and other concomitant anticonvulsant drug use. A few cases of neonatal vomiting, diarrhoea and/or decreased feeding have also been reported in association with maternal carbamazepine use. These reactions may represent a neonatal withdrawal syndrome.

Breast-feeding

Carbamazepine passes into the breast milk (about 25 to 60% of plasma concentrations). The benefits of breast-feeding should be weighed against the remote possibility of adverse effects occurring in the infant. Mothers taking carbamazepine 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.
Women of child-bearing potential and contraceptive measures
Due to enzyme induction, carbamazepine 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.

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 have been reported with Carbamazepine, 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:
Fairly common side effects of Carbamazepine, particularly in the initial stages of therapy, include: dizziness, drowsiness and ataxia. The effects may be minimized by starting therapy with a low dose.
Gastrointestinal symptoms are less common and include; dry mouth, abdominal pain, nausea and vomiting, anorexia, and diarrhoea or constipation. Generalized erythematous rashes may be severe and may necessitate withdrawal of treatment. Other adverse effects include: photosensitivity reactions, blood disorders, hypersensitivity reactions, hyponatreamia and sometimes oedema. Overdosage may result in stupor, coma, convulsion, respiratory depression and death.
Treatment of Adverse Effects
In case of overdosage, repeated doses of activated charcoal may be given orally to prevent absorption and also aid elimination. Gastric lavage may be considered if undertaken within 1 hour of ingestion. Supportive and symptomatic therapy may then suffice, with a particular attention to correcting hypoxia and hypotension.

4.9 Overdose:
Signs and symptoms
The presenting signs and symptoms of overdosage involve the central nervous, cardiovascular of respiratory systems.
Metabolism and nutrition disorders
Hyponatraemia, possibly metabolic acidosis, possibly hyperglycaemia, water intoxication due to an ADH-like effect of carbamazepine.
Psychiatric disorders
Disorientation, agitation, hallucination
Nervous system disorders
CNS depression; somnolence, depressed level of consciousness, coma; slurred speech, dysarthria, nystagmus, ataxia, dyskinesia, initially hyper-reflexia, later hyporeflexia; convulsions, psychomotor disturbances, myoclonus, psychomotor disturbances.
Eye disorders
Blurred vision, mydriasis. Cardiac disorders
Tachycardia, hypotension, at times hypertension, conduction disturbance with widening of QRS complex; syncope in association with cardiac arrest.
Vascular disorders
Hypotension, at times hypertension. Respiratory thoracic and mediastinal disorders Respiratory depression, pulmonary oedema.
Gastrointestinal disorders
Vomiting, delayed gastric emptying, reduced bowel motility. Renal and urinary disorders
Retention of urine, oliguria or anuria, fluid retention. General disorders and administration site conditions Hypothermia
Musculoskeletal system
There have been some cases which reported rhabdomyolysis in association with carbamazepine toxicity. **Investigations**
Increased muscle creatinine phosphokinase.

Management
There is no specific antidote.
Management should initially be guided by the patient's clinical condition; admission to hospital may be necessary. Measurement of the plasma level is desirable to confirm carbamazepine poisoning and may be helpful to ascertain the size of the overdose. Absorption inhibiting therapy can exist of repeated administration of activated charcoal in combination with osmotic laxative, if necessary. In case of severe carbamazepine intoxication there is a risk on decrease of the peristalsis of the colon to ileas due to anticholinergic characteristics of carbamazepine. Repeated administration could lead to complications in such situations. When peristalsis is recovered a dose activated charcoal may be administered. In cases of potential severe intoxications and within 1 hour of intake gastric lavage may be considered. Total intestinal lavage may be considered in case of preparations with regulated release (provided that peristalsis is well and no other contraindications exist). Further treatment is supportive and symptomatic: inclusion in an intensive care unit with cardiac monitoring and careful correction of electrolyte imbalance, treatment of hypotension with fluid and vasopressors, treatment of convulsions with benzodiazepines. Special recommendations
Activated charcoal haemoperfusion may be considered. Haemodialysis is the effective treatment method with carbamazepine's overdose. High-flux haemodialysis could be considered. Relapse and aggravation of symptomatology on the 2nd and 3rd day after overdose, due to delayed absorption, should be anticipated.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

Therapeutic class: Nervous System, Antiepileptics, Carboxamide derivatives.
ATC Code: N03AF01.
Carbamazepine is a dibenzazepine derivative used as an anticonvulsant and in the treatment of trigeminal neuralgia.
It appears to act on seizures reducing polysynaptic responses and blocking the post-tetanic potentiation. The mechanism of action in controlling trigeminal pain of neuralgia is unknown.

5.2 Pharmacokinetic properties

Carbamazepine is slowly and irregularly absorbed from the gastrointestinal tract. It is extensively metabolized in the liver, notably by the cytochrome P 450 isoenzymenes CYP3A4 and CYP2C8. One of the primary metabolites, Carbamazepine -10, 11-epoxide is also active. Carbamazepine is excreted in the urine almost ent1rely m the form of 1ts metabolites, some is also excreted in feaces. Elimination is 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 extensively bound (about 75%) to plasma proteins. It induces its own metabolism so that the plasma half-life may be considerably reduced after repeated administration. The mean plasma half-life of Carbamazepine on repeated administration is about 10-20 hours; it appears to be considerably shorter in children than in adults. It crosses the placental barrier and is distributed into breast milk.

5.3 Preclinical safety data

Not Applicable

6. Pharmaceutical Particulars

6.1 List of Excipients White Corn Starch Microcrystalline Cellulose pH 101

- White Corn Starch
- Microcrystalline Cellulose pH 101
- Docusate Sodium Sulfate (Doss)
- Potassium Sorbate
- Sodium Benzoate
- Povidone (PVP) K-30
- Purified Water
- METHOCEL™ K100 LV
- Purified Talc
- Magnesium Stearate

6.2 Incompatibilities:
None.

6.3 Shelf Life:
36 months

6.4 Special Precautions for Storage:
Store in a dry place, below 30°C,
Protect from light,
Keep all medicines out of reach of children.

6.5 Nature and Contents of Container:
White, circular, biconvex tablets scored on one side and plain on reverse, packed in blisters of 10 x 10's in a unit box, 1000's in HDPE container with literature insert.

6.6 Special precaution for disposal and other handling:
No special requirements.

7. Marketing Authorization Holder and Manufacturing Site Addresses:
Marketing Authorization Holder:
Company Name: Laboratory & Allied Limited.
Address: Plot No. 209/10349, Opposite Sameer Business Park, Next to Libra House, Mombasa Road, P.O. Box 42875 GPO 00100, Nairobi
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8. Marketing Authorization Number:
Kenya: H2008/18885/792.

9. Date of first Registration/ Renewal of the Registration:
Registration: 14/04/2009.
Renewal: Retained Annually.

10. Date of revision of the text:
August, 2023.