| MICRO LABS LIMITED, BANGALORE, INDIA | | | |
|---|---|---|---|
| 1 | Product Name | Carbox | Colours Used |
| 2 | Strength | 300 mg and 600 mg | |
| 3 | Component | Leaflet | ■ BLACK |
| 4 | Category | Export - Philippines | |
| 5 | Dimension | 120 (L) x 240 (H) mm | |
| 6 | Artwork Code | EXG-ML01C-1491/A | |
| 7 | Pharma Code | N/A | |
| 8 | Reason for Change | Size and New Regulation | |

| | Prepared by (DTP) | Checked by (PD) | Approved by | | | |
|---|---|---|---|---|---|---|
| | | | Head CQA | Head Production/ Packing (Site) | Head QC (Site) | Head QA (Site) |
| Sign | Kantharaju L. | | | | | |
| Date | 14-01--2022 | | | | | |

Front

Back

240 mm

# OXCARBAZEPINE

## CARBOX™

300 / 600 mg FILM COATED TABLET
ANTIEPILEPTIC

**PRODUCT NAME:**
CARBOX

**NAME AND STRENGTH:**
Oxcarbazepine 300 / 600 mg

**PHARMACOLOGIC CATEGORY:** Antiepileptic

**PRODUCT DESCRIPTION:**
Carbox 300: Yellow colored, circular, biconvex, film-coated tablets with a break line on one surface and plain on other.
Carbox 600: Yellow colored, oblong shaped, film-coated tablets, plain on both surfaces.

**FORMULATION/COMPOSITION:**
Each film coated tablet contains:
Oxcarbazepine .....300 mg
Oxcarbazepine..... 600 mg

**PHARMACODYNAMICS/PHARMACOKINETICS:**
The pharmacological activity of Oxcarbazepine is primary exerted through the 10-monohydroxy metabolite (MHD) of oxcarbazepine. The precise mechanism by which oxcarbazepine and MHD exert their antiseizure effect is unknown: however, in vitro electrophysiological studies indicate that they produce blockade of voltage sensitive sodium channels, resulting in stabilization of hyper excited neural membranes, inhibition of repetitive neuronal firing, and diminution of propagation of synaptic impulses. These actions are thought to be important in the prevention of seizure spread in the intact brain. In addition, increased potassium conductance and modulation of high voltage activated calcium channels may contribute to the anticonvulsant effect of the drug . No significant interaction of oxcarbazepine or MHD with brain neurotransmitter or modulator receptor sites has been demonstrated.

**Pharmacokinetics**
Absorption: Following oral administration of oxcarbazepine is completely absorbed and extensively metabolized to its pharmacologically active 10-monohydroxy metabolite (MHD). The half life of the parent is about 2 hours while the half - life of MHD is about 9 hours, so that MHD is responsible for most antiepileptic activity.
***Distribution:*** The apparent volume of distribution of MHD is 49L. Approximately 40% of MHD is bound to serum proteins, predominantly to albumin. Binding is independent of the serum concentration within the therapeutically relevant range. Oxcarbazepine and MHD do not bind to alpha-1-acid glycoprotein.
***Metabolism and Excretion:*** Oxcarbazepine is rapidly reduced by cytosolic enzymes in the liver to its 10-monohydroxy metabolite MHD , which is primarily responsible for the pharmacological effect of Oxcarbazepine MHD is metabolized further by conjugation with glucuronic acid. Minor amounts (4% of the dose) are oxidized to the pharmacologically inactive 10, 11-dihydroxy metabolite ( DHD).Oxcarbazepine is cleared from the body mostly in the form of metabolites which are predominantly excreted by the kidneys . More than 95% of the dose appears in the urine, with less than 1% as unchanged oxcarbazepine Fecal Excretion accounts for less than 4% of the administered dose. Approximately 80% of the dose is excreted in the urine either as glucuronides of MHD(49%) or as unchanged MHD(27%); the inactive DHD accounts for approximately 3% and conjugated of MHD and oxcarbazepine account for 13% of the dose.

**INDICATIONS:**
Oxcarbazepine is use as monotherapy or adjunctive therapy in the treatment of partial seizures in adult and children aged 4 years old and above.

**DOSAGE AND MODEL ROUTE OF ADMINISTRATION:**
The initial adult dose for monotherapy and adjunctive therapy in adult is 600 mg daily by mouth given in 2 divided doses. The dose may be increased thereafter, if necessary, in maximum increments of 600 mg daily at approximately weekly intervals until the desired clinical response has been achieved Maintenance dose are usually in the range of 600 mg to 1200 mg daily or up to 2,400 mg daily if given as adjunctive therapy or in refractory patient s switched from other antiepileptics.
The recommended initial dose for children over 6 years of age is 8 to 10 mg per kg body-weight by mouth daily; given in 2 divided doses. This may be increased as necessary in maximum increments of 10 mg per kg daily at approximately weekly intervals to a maximum dose of 46 mg per kg daily: usual maintenance doses are around 30 mg per kg daily. Initial doses for patients with renal impairment with a creatine clearance of less than 30 mL per minute should be half the usual starting dose, increased a weekly intervals or longer.

**CONTRAINDICATIONS &PRECAUTION(S), WARNING(S)**
Hypersensitivity to the active substance, to Eslicarbazepine or to any of the excipients

**PRECAUTIONS & WARNINGS:**
Clinically significant hyponatremia (sodium<125mmol/L), can develop during oxcarbazepine use. In the 14 controlled epilepsy studies 2.5% of oxcarbazepine treated patients (38/1524) had a sodium of less than 125 mmol/L at some point during treatment, compared to no such patients assigned placebo or active control ( carbamazepine and phenobarbital for adjunctive and monotherapy substitution studies, and phenytoin and valproate for the monotherapy initiation studies).
Clinically significant hyponatremia generally occurred during the first 3 months of treatment with Oxcarbazepine, although there were patients who first developed a serum sodium < 125mmol/L more than 1 year initiation of therapy. Most patients who developed hyponatremia were frequently monitored and some had their oxcarbazepine dose reduced, discontinued or had their intake restricted for hyponatremia. Whether or not these maneuvers prevented the occurrence of more severe events is unknown. Cases of symptomatic hyperemia have been reported during post marketing use. In clinical trials, patients whose treatment with oxcarbazepine was discontinued due to hyperemia generally experienced normalization of serum sodium within a few days without additional treatment.

**PREGNANCY AND LACTATION:**
There are no adequate and well -controlled clinical studies of Oxcarbazepine in pregnant women;; however ,Oxcarbazepine is closely related structurally to carbamazepine, which is considered to be teratogenic in humans. Given this fact, and the result of the animal studies described, it is likely that Oxcarbazepine is a human teratogen. Oxcarbazepine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Oxcarbazepine and its active metabolite (MHD) are excreted in human breast milk. A milk-to-plasma concentration ratio of 0.5 was found for both. Because of the potential for serious adverse reactions to oxcarbazepine in nursing infants, a decision should be made about whether to discontinue nursing or to discontinue the drug in nursing women, taking into account the importance of the drug to the mother.

**INTERACTIONS:**
Oxcarbazepine can inhibit CYP2C19 and induce CYP3A4/5 with potentially important effect on plasma concentration of other drugs. In addition, several AEDs that are cytochrome P450 inducers can decrease plasma concentrations of oxcarbazepine and MHD. Oxcarbazepine was evaluated in human liver microsomes to determine its capacity to inhibit the major cytochrome P450 enzymes responsible for the metabolism of the other drugs. Results demonstrate that oxcarbazepine and its pharmacological active 10-monohydroxy metabolite (MHD) have little or no capacity to function as inhibitors for most of the human cytochrome P450 enzymes evaluated (CYPIA2, CYP2A6, CYP2C9,CYP2D6,CYP2EI,CYP4A9 and CYP4A11)with the exception of CYP2C19 and CYP3A4/5. Although inhibition of CYP3A4/5 by oxcarbazepine and MHD did occur at high concentration, it is not likely to be of clinical significance. The inhibition of CYP2C19 by oxcarbazepine and MHD, however, is clinically relevant.
***Calcium Antagonist:***
After repeated co-administration of oxcarbazepine the AUC of felodipine was lowered by 28% [ 90%CI: 20-33}. Verapamil produced a decrease of 20% [90%CI:18-27] of the plasma level of MHD.
***Hormonal Contraceptives:***
Co-administration of Oxcarbazepine with an oral contraceptive has been shown to influence the plasma concentration of the two hormonal components, ethinylestradiol (EE) and levonorgestrel (LNG).
***Other Drug Interaction:***
Cimetidine, erythromycin and dextropropoxyphene had no effect on the pharmacokinetics of MHD. Results with warfarin show no evidence of interaction with either single or repeated doses of oxcarbazepine.

**ADVERSE EFFECTS:**
The most commonly observed adverse effects experiences seen in association with oxcarbazepine and substantially more frequent than in placebo -treated patients were: dizziness, somnolence, fatigue, diplopia, nausea, vomiting, ataxia, abnormal vision, abdominal pain, tremor, dyspepsia, abnormal gait.

**OVERDOSAGE AND TREATMENT:**
Isolated cases of overdose with oxcarbazepine have been reported. The maximum dose taken was approximately 24,000mg. All patients recovered with symptomatic treatment. There is no specific antidote. Symptomatic and supportive treatment should be administered as appropriate. Removal of the drug by gastric lavage and /or inactivation by administering charcoal should be considered.

**STORAGE CONDITION:**
STORE AT TEMPERATURES NOT EXCEEDING 30°C.

**DOSAGE FORMS AND PACKAGING AVAILABLE:**
Film Coated Tablets
Oxcarbazepine 300 mg (Carbox-300)
Alu / Orange PVC blister Pack x10's (Box of 50's)
Oxcarbazepine 600 mg (Carbox-600)
Alu / PVC blister Pack x 10's (Box of 50's) Tablet

**INSTRUCTIONS AND SPECIAL PRECAUTIONS FOR HANDLING AND DISPOSAL (IF APPLICABLE):**
Not Applicable

**NAME AND ADDRESS OF MARKETING AUTHORIZATION HOLDER:**
**Marketing Authorization Holder**
Brown & Burk Philippines Inc
U-501, 5/F SEDCCO 1 Bldg., 120 Rada cor.
Legaspi Sts., Legaspi Village, Makati, Metro Manila

**NAME AND ADDRESS OF MANUFACTURER:**
**MICRO LABS LIMITED**
92, Sipcot, Hosur-635 126,
Tamil Nadu, India

**CAUTION STATEMENT:**
FOODS, DRUGS, DEVICES, AND COSMETICS ACT PROHIBITS DISPENSING WITHOUT PRESCRIPTION.

**ADR REPORTING STATEMENT**:
FOR SUSPECTED ADVERSE DRUG REACTION, REPORT TO THE FDA: www.fda.gov.ph
Seek medical attention immediately at the first sign of Adverse Drug Reaction.

**REGISTRATION NUMBER:**
Carbox 300: DR-XY38694
Carbox 600: DR-XY39197

**DATE OF FIRST AUTHORIZATION:**
Carbox 300: 27 OCT. 2010
Carbox 600: 17 MAR. 2011

**DATE OF REVISION OF PACKAGE INSERT:**
Mar. 2021

EXG-ML01I-1491/A

120 mm

120 mm

**Size: 120 (L) x 240 (H) mm**
Folding size: 30 x 60 mm
Carton size: 45 x 36 x 100 mm
85 x 40 x 60 mm (Lock Bottom)