

**Mazemal**  
Carbamazepine 200 mg  
tablets

**DESCRIPTION:**

Carbamazepine USP is an anticonvulsant and specific analgesic for trigeminal neuralgia, its chemical name is 5H-dibenz (b, f) azepine-5- carboxamide.

**CLINICAL PHARMACOLOGY:**

Mazemal® has been shown to be effective in the treatment of psychomotor and grand mal seizures, as well as trigeminal neuralgia.

**Mechanism of Action:**

Carbamazepine appears to act by reducing polysynaptic response and blocking the post-tetanic potentiation.

Carbamazepine greatly reduces or abolishes pain induced by stimulation of the infraorbital nerve .

The principal metabolite of carbamazepine-10, **11-epoxide**, has anticonvulsant activity as demonstrated in several in vivo animal models of seizures.

**Pharmacokinetics:**

The bioavailability of the tablet was 89% compared to suspension. Following a twice a day dosage regimen, the suspension provides higher peak levels and lower trough levels than those obtained from the conventional tablet for the same dosage regimen. Carbamazepine in blood is 76% bound to plasma proteins. Plasma levels of Carbamazepine are variable and may range from 0.5-25 mcg/ml. The CSF/serum ratio is 0.22, similar to the 22% unbound. **Indications and dosage:**

**1- Epilepsy**

*Adults And Children Over 12 Years Of Age* Initial: Either 200 mg twice a day .increase at weekly intervals by adding up to 200 mg per day using a twice a day regimen or three times a day or four times a day regimen until the optimal response is obtained. Dosage generally should not exceed 1000 mg daily in children 12 to 15 years of age, and 1200 mg daily in patients above 15 years of age. Doses up to 1600 mg daily have been used in adults in rare instances. Maintenance: Adjust dosage to the minimum effective level, usually 800-1200mg daily.

### *Children 6 -12 Years Of Age*

**Initial:** Either 100 mg twice a day, Increase at weekly intervals by adding up to 100 mg per day using a three times a day or four times a day regimen until the optimal response is obtained. Dosage generally should not exceed 1000 mg daily.

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

**Combination Therapy:** Mazemal ® may be used alone or with other anticonvulsants. When added to existing anticonvulsant therapy, the drug should be added gradually while the other anticonvulsants are maintained or gradually decreased, except phenytoin, which may have to be increased.

### **2-Trigeminal Neuralgia**

**Initial:** On the first day, either 100 mg twice .This daily dose may be increased by up to 200 mg a day using increments of 100 mg every 12 hours, only as needed to achieve freedom from pain. Do not exceed 1200 mg/daily.

**Maintenance: Control** of pain can be maintained **in most patients with** 400 mg to 800 mg daily. At least once every 3 months throughout **the** treatment period, attempts should be made to reduce the dose to the minimum effective level or even to discontinue the drug.

### **SIDE EFFECTS:**

If adverse reactions are of such severity that the drug must be discontinued, the physician must be aware that abrupt discontinuation of any anticonvulsant drug in a responsive epileptic patient may lead to seizures or even status epilepticus with its life-threatening hazards. The most severe adverse reactions have been observed in the hemopoietic system To minimize the possibility of such reactions, therapy should be initiated at the low dosage recommended. The following additional adverse reactions have been reported:

**Hemopoietic System:** Aplastic anemia, agranulocytosis, pancytopenia, bone marrow depression, thrombocytopenia, leukopenia, leukocytosis, eosinophilia, acute intermittent porphyria

**Skin:** Pruritic and erythematous rashes, urticaria, toxic epidermal necrolysis (Lyell's Syndrome) ,photosensitivity reactions, alterations **In** skin pigmentation, exfoliative dermatitis, erythema multiforme and nodosum, purpura, aggravation of disseminated lupus erythematosus, alopecia, and diaphoresis. In certain cases, discontinuation of therapy may be necessary. Isolated cases of hirsutism have been reported, but a causal relationship is not clear.

**Cardiovascular System:** Congestive heart failure, edema, aggravation of hypertension, hypotension, syncope and collapse, aggravation of coronary artery disease, arrhythmias and AV block, primary thrombophlebitis, recurrence of thrombophlebitis, and adenopathy or lymphadenopathy. Some of these cardiovascular complications have resulted in fatalities. Myocardial infarction has been associated with other tricyclic compounds.

**Liver:** Abnormalities in liver function tests, cholestatic and hepatocellular jaundice, hepatitis.

**Respiratory System:** Pulmonary hypersensitivity characterized by fever, dyspnea, pneumonitis or pneumonia.

**Genitourinary System:** Urinary frequency, acute urinary retention, oliguria with elevated blood pressure, azotemia, renal failure, and impotence

**Nervous System:** Dizziness, drowsiness, disturbances of coordination, confusion, headache, fatigue, blurred vision, visual hallucinations, and transient diplopia.

**Digestive System:** Nausea, vomiting, gastric distress and abdominal pain, diarrhea, constipation, anorexia, and dryness of the mouth and pharynx, including glossitis and stomatitis.

**Eyes:** Scattered punctate cortical lens opacities, as well as conjunctivitis, have been reported

**Musculoskeletal System:** Aching joints and muscles, and leg cramps.

Metabolism: Fever and chills. Inappropriate antidiuretic hormone (ADH) secretion syndrome has been reported.

Drug Abuse and Dependence

No evidence of abuse potential has been associated with carbamazepine, nor is there evidence of psychological or physical dependence in humans.

## **DRUG INTERACTIONS:**

The simultaneous administration of phenobarbital, phenytoin, or primidone, or a combination of two, produces a marked lowering of serum levels of carbamazepine. The effect of valproic acid on carbamazepine blood levels is not clearly established, although an increase in the ratio of active 10, 11-epoxide metabolite to parent compound is a consistent finding.

The half-lives of phenytoin, warfarin, doxycycline, and theophylline were significantly shortened when administered concurrently with carbamazepine. Haloperidol and valproic acid serum levels

may be reduced when these drugs are administered with carbamazepine. The doses of these drugs may therefore have to be increased when carbamazepine is added to the therapeutic regimen. Concomitant administration of carbamazepine with erythromycin, cimetidine, propoxyphene, isoniazid, fluoxetine or calcium channel blockers has been reported to result in elevated plasma levels of carbamazepine resulting in toxicity in some cases. Also concomitant administration of carbamazepine and lithium may increase the risk of neurotoxic side effects.

Alterations of thyroid function have been **reported in** combination therapy with other anticonvulsant medications. Breakthrough bleeding has been reported among patients receiving concomitant oral contraceptives and their reliability may be adversely affected.

### **WARNINGS:**

Patients with a history of adverse hematological reaction to any drug may be particularly at risk.

Carbamazepine has shown mild anticholinergic activity: therefore, patients with increased intraocular pressure should be closely observed during therapy.

Because of the relationship of the drug to other tricyclic compounds, the possibility of activation of a latent psychosis and in elderly patients of confusion or agitation should be borne in mind.

### **PRECAUTIONS:**

#### General

Before initiating therapy, a detailed **history and physical examination** should be made.

Carcinogenesis, Mutagenesis and Impairment of Fertility Carbamazepine, when administered to Sprague-Dawley rats for **two years** in the diet at doses of 25, 75, and 250 mg/kg/day, resulted in a dose-related increase in the incidence of hepatocellular tumors in females and of benign interstitial cell adenomas in the testes of males. Bacterial and mammalian mutagenicity studies using carbamazepine produce negative results. The significance of these findings relative to the use of carbamazepine in humans is at present, unknown.

#### **Pregnancy Category C**

There are no adequate and well-controlled studies in pregnant women. Epidemiological data suggest that there may be an association between the use of carbamazepine during pregnancy and congenital malformations, including spina bifida. Carbamazepine should **be used** during pregnancy only if the potential benefit justifies the potential **risk to** the fetus.

#### Labor and Delivery

The effect of carbamazepine on human labor and **delivery is unknown.**

## **Nursing Mothers**

During lactation, concentration of carbamazepine in milk is approximately 60% of the maternal plasma concentration. Because of the potential of serious adverse reactions in nursing infants from carbamazepine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use**

Safety and **effectiveness in children below the age of 6 years have not** been established.

## **OVERDOSE Acute Toxicity**

Lowest known lethal dose: adults, >60 g (39 year-old man). Highest known doses survived: adults, 30 g (31 year-old woman); children, 10 g (6 year-old boy); small children, 5 g (3 year-old girl). Oral LD50 in animals (mg/kg): mice, 1100-3750; rats, 3850-4025; rabbits, 1500-2680; guinea pigs, 920.

## **CONTRAINDICATIONS**

Carbamazepine should not be used in patients with a history of **previous bone** marrow depression, hypersensitivity to the drug, or known sensitivity to any of the tricyclic compounds such as amitriptyline, desipramine, imipramine, protriptyline, nortriptyline, etc. Likewise, **on** theoretical grounds its use with monoamine oxidase inhibitors is not recommended. Before administration of carbamazepine, MAO inhibitors should be discontinued **for a** minimum of fourteen days, or longer if the clinical situation permits.

## **HOW SUPPLIED**

Box contains 2 strips, **each strip contains 10 tablet Storage**

Do not store above **30°C**.

## **Produced by:**

UNI PHARMA

EL OBOUR CITY. CAIRO - EGYPT