

Carbazin[®]

Carbamazepine Tablet

DESCRIPTION

Carbazin[®] is a preparation of carbamazepine, a dibenzazepine derivative with anti-epileptic, neurotropic and psychotropic properties. It is used to control generalised tonic-clonic (grand mal) and partial (focal) seizures. It is also used in neuralgias and the treatment of manic depression.

INDICATIONS

- Epilepsy-generalised tonic-clonic and partial seizures
Note: Carbamazepine is not usually effective in absences (petit mal). Moreover, anecdotal evidence suggests that seizure exacerbation may occur in patients with a typical absences
- The paroxysmal pain of trigeminal neuralgia
- For the prophylaxis of manic-depressive psychosis in patients unresponsive to lithium therapy.

DOSAGE AND ADMINISTRATION

Carbazin[®] is given orally, usually in two or three divided doses. Carbazin tablets may be taken during, after or between meals.

Epilepsy

ADULTS : Initially, 100-200 mg 1-2 times daily, increased slowly to usual dose of 800-1200 mg daily in divided doses; in some cases 1600-2000 mg daily may be needed;

ELDERLY: Reduce initial dose.

CHILDREN: Daily in divided doses, age upto 1 year 100-200 mg, 1-5 years 200-400 mg, 5-10 years 400-600 mg, 10-15 years 600-1000 mg.

Trigeminal neuralgia

The individual dosage requirements of carbamazepine vary considerably. It is recommended that the initial dose should be small but in some patients a high dose early in treatment may be required. In elderly patients an initial dose of 100 mg twice daily is recommended.

The dose may be increased gradually until a satisfactory clinical response is obtained, which in some instances necessitates 1600 mg carbamazepine daily. It has been found that in the majority of patients a dosage of 200 mg three or four times a day is sufficient to maintain a pain-free state. When the pain goes into remission the dose may be gradually reduced and carbamazepine discontinued in the absence of recurrences.

For the prophylaxis of manic-depressive psychosis in patients unresponsive to lithium therapy initial starting dose of 400 mg daily in divided doses, increasing gradually until symptoms are controlled or, a total of 1600 mg given in divided doses is reached. The usual dosage range is 400-600 mg daily, given in divided doses.

CONTRAINDICATIONS

Previous drug sensitivity to carbamazepine or structurally related drugs e.g. tricyclic antidepressants. Because carbamazepine depresses AV conduction, it is inadvisable to administer this drug to patients with atrioventricular conduction abnormalities. Patients with a history of previous bone marrow depression or a history of intermittent porphyria. On theoretical grounds i.e. a structural relationship to tricyclic anti-depressants, the use of carbamazepine is not recommended in combination with monoamine oxidase inhibitors (MAOIs); before administering carbamazepine, MAOIs should be discontinued for a minimum of 2 weeks, or longer if the clinical situation permits.

WARNINGS

Agranulocytosis and aplastic anaemia have been associated with carbamazepine; however, due to the very low incidence of these diseases, meaningful risk estimates for carbamazepine are difficult to obtain. Blood counts should be performed before and periodically during treatment. Clinical monitoring is of primary importance during the whole treatment.

Patients and their relatives should be informed on how to recognise early toxic signs and symptoms indicative of potential haematological problem, or of dermatological or hepatic reactions. If reactions such as fever, sore throat, rash, ulcers in the mouth, easy bruising, petechial, or purpuric haemorrhage appear, the patient should be advised to consult his physician immediately.

Carbamazepine should be discontinued if any evidence of significant bone marrow depression appears.

Liver function tests should also be performed before commencing treatment and periodically thereafter, particularly in patients with a history of liver disease and in elderly patients.

If treatment with carbamazepine has to be withdrawn abruptly, the changeover to another anti-epileptic drug should if necessary be effected under the cover of a suitable drug e.g. i.v. or rectal benzodiazepines, or i.v. phenytoin.

The patient's reactions e.g. as a road user, may be impaired by carbamazepine, especially in the early stages of treatment. Patients should be warned of the possible hazard when driving or operating machinery.

PRECAUTIONS

Carbamazepine should be prescribed only after a critical benefit-risk appraisal and under close monitoring in patients with a history of cardiac, hepatic, or renal damage, adverse haematological reactions to other drugs, or interrupted courses of therapy with carbamazepine.

Baseline and periodic complete urinalysis and BUN determinations are recommended.

Carbamazepine has shown mild anticholinergic activity; patients with glaucoma should therefore be warned and advised regarding possible hazards. The possibility of activation of a latent psychosis, and in elderly patients the possibility of agitation or confusion, especially when high doses of carbamazepine are administered, should be borne in mind.

USE IN PREGNANCY AND LACTATION

If pregnancy occurs in a woman receiving carbamazepine or if the use of carbamazepine is considered necessary during pregnancy the need to control seizures in the mother should be carefully weighed against the possible risk to the foetus. This is particularly important during the first three months of pregnancy. Minimum effective doses should be given and monitoring of plasma levels is recommended.

In women of childbearing age carbamazepine should be administered as monotherapy, whenever possible.

Anti-epileptic drugs may contribute to folic acid deficiency, a possible contributory cause of foetal abnormality. Folic acid supplementation is recommended before and during pregnancy.

Bleeding disorders in the newborn caused by anti-epileptic agents have been reported. As a precaution, vitamin-K1 should be administered as a preventive measure in the last weeks of pregnancy and to the newborn.

Carbamazepine passes into the breast milk in concentrations of about 25-60% of the plasma level. This is not believed to present a significant hazard to the infant, which is likely to receive at most 10% of an appropriate therapeutic dose of carbamazepine for an infant with epilepsy. As with all drugs, the benefits of breast-feeding should be weighed against the remote possibility of an adverse effect occurring in the infant. There is one report of a severe skin (hypersensitivity) reaction in a breast-fed baby.

DRUG INTERACTIONS

Induction of hepatic enzymes in response to carbamazepine may increase the metabolism and reduce the effectiveness of certain other drugs that are metabolised in the liver including : clobazam, clonazepam, ethosuximide, primidone, valproic acid, alprazolam, corticosteroids, hormonal contraceptive agents, cyclosporin, digoxin, doxycycline, felodipine, haloperidol, imipramine, methadone, theophylline, warfarin. The concurrent administration of carbamazepine has been reported to both raise and lower phenytoin levels and in rare instances mephenytoin plasma levels have been reported to increase.

Certain drugs have been shown to increase carbamazepine serum levels: macrolide antibiotics (erythromycin), isoniazid, calcium antagonists (verapamil, diltiazem), dextropropoxyphene, viloxazine, fluoxetine, cimetidine, acetazolamide, danazol, possibly desipramine and nicotinamide (only in adults and at high doses). Since raised carbamazepine levels may produce signs of overdosage (e.g. dizziness, drowsiness, ataxia, diplopia), the dosage of Carbazin[®] should be adjusted accordingly.

Concomitant use of carbamazepine and isoniazid has been reported to increase isoniazid hepatotoxicity.

The combination of lithium and carbamazepine may cause enhanced neurotoxicity in spite of lithium plasma concentrations being within the therapeutic range.

Combined use of carbamazepine with metoclopramide or major tranquillisers, e.g. haloperidol, thioridazine, may also result in an increase in neurological side-effects.

Plasma levels of carbamazepine may be reduced by phenobarbitone, phenytoin, primidone, theophylline, also possibly clonazepam, and valproic acid.

Concomitant medication with carbamazepine and some diuretics (hydrochlorothiazide, frusemide) may lead to symptomatic hyponatraemia.

Carbamazepine may antagonise the effects of non-depolarising muscle relaxants (e.g. pancuronium); their dosage may need to be raised and patients monitored closely for unexpectedly rapid recovery from neuromuscular blockade.

SIDE-EFFECTS

Nausea and vomiting, dizziness, drowsiness, headache, ataxia, confusion and agitation (elderly), visual disturbances (especially double vision and often associated with peak plasma concentrations); constipation or diarrhoea, anorexia; mild transient generalised erythematous rash may occur in a large number of patients (withdraw if worsens or is accompanied by other symptoms); leucopenia and other blood disorders (including thrombocytopenia, agranulocytosis and aplastic anaemia); other side-effects include cholestatic jaundice, hepatitis and acute renal failure, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia, thromboembolism, arthralgia, fever, proteinuria, lymph node enlargement, cardiac conduction disturbances (sometimes arrhythmias), dyskinesias, paraesthesia, depression, impotence (and impaired fertility), gynaecomastia, galactorrhoea, aggression, activation of psychosis; photosensitivity, pulmonary hypersensitivity (with dyspnoea and pneumonitis), hyponatraemia and oedema also reported.

OVERDOSAGE

Signs and symptoms:

The presenting signs and symptoms of overdosage involve the central nervous, cardiovascular, or respiratory systems.

Central nervous system : CNS depression; disorientation, somnolence, agitation, hallucination, coma; blurred vision, slurred speech, dysarthria, nystagmus, ataxia, dyskinesia, initially hyperreflexia, later hyporeflexia; convulsions, psychomotor disturbances, myoclonus, hypothermia.

Respiratory system : Respiratory depression, pulmonary oedema.

Cardiovascular system : Tachycardia, changes in blood pressure (hypotension and at times hypertension), cardiac arrhythmias, conduction disturbance with widening of QRS complex; syncope.

Gastrointestinal system : Vomiting, delayed gastric emptying, reduced bowel motility.

Renal function : Retention of urine, oliguria or anuria; fluid retention, water intoxication due to ADH-like effect of carbamazepine.

Treatment:

There is no specific antidote. Management is according to the patient's clinical condition. Possible admission to hospital. Measurement of the plasma level to confirm carbamazepine poisoning and to ascertain the size of the overdose. Evacuation of the stomach, gastric lavage, and administration of activated charcoal. Supportive medical care in an intensive care unit with cardiac monitoring and careful correction of electrolyte imbalance, if required. Special recommendations :

Hypotension: administer dopamine or dobutamine i.v.

Disturbances of cardiac rhythm: to be managed on an individual basis.

Convulsions: administer a benzodiazepine (e.g. diazepam) or another anticonvulsant, e.g. phenobarbitone (with caution because of increased respiratory depression) or paraldehyde.

Hyponatraemia (water intoxication): Fluid restriction and slow careful NaCl 0.9% infusion i.v. These measures may be useful in preventing brain damage. Charcoal haemoperfusion has been recommended. Forced diuresis, haemodialysis, and peritoneal dialysis have been reported not to be effective. Relapse and aggravation of symptomatology on the 2nd and 3rd day after overdose, due to delayed absorption, should be anticipated.

PHARMACEUTICAL PRECAUTION

Do not store above 30 °C. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Carbazin[®] tablet: Box containing 5 strips of 10 tablets each. Each tablet contains Carbamazepine USP 200 mg.

SK+F

Manufactured by

ESKAYEF PHARMACEUTICALS LTD.

MIRPUR, DHAKA, BANGLADESH

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