xxxxxxxxx-5343

CARBAMAZEPINE

EPAZIN

ANTICONVULSANT

Formulation
Each tablet contains :
Carbamazepine . . . . . .200 mg

Pharmacokinetics
Carbamazepine is a dibenzazepine derivative with antiepileptic and psychotropic properties. It is slowly and irregularly absorbed from the gastro-intestinal tract. It is extensively metabolized in the liver, notably by the cytochrome P450 isoenzymes CYP3A4 and CYP2C8. One of its metabolites, carbamazepine 10-11-epixide is also active. Carbamazepine is excreted in the urine almost entirely in the form of its metabolites; some is 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 its 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 5 to 26 hours; it appears to be considerably shorter in children than in adults. Moreover, the metabolism of carbamazepine is readily induced by drugs which induce hepatic microsomal enzymes.
Carbamazepine crosses the placental barrier and is distributed into breast milk. The pharmacokinetics of carbamazepine are affected by the concomitant administration other antiepileptics.

Interactions
There are complex interactions between antiepileptics and toxicity may be enhanced without a corresponding increase in antiepileptic activity. Such interactions are very variable and unpredictable and plasma monitoring is often advisable with combination therapy.
The metabolism of carbamazepine is reported to be less susceptible to inhibition by other drugs than that of phenytoin but a few drugs are reported to inhibit its metabolism by the cytochrome, P450 isoenzyme CYP3A4, resulting in raised plasma concentrations and associated toxicity. Dugs that induce CYP3A4 may increase the metabolism of Carbamazepine, leading to a reduced plasma concentrations and potentially a decrease in therapeutic effect. Carbamazepine is itself a hepatic enzyme inducer, and induces its own metabolism as well that of a number of other drugs, including some antibacterials (notably, doxycycline), anticoagulants, and sex hormones (notably, oral contraceptives). Carbamazepine and phenytoin may also mutually enhance one anothers metabolism. The metabolism of carbamazepine is similarly enhanced by enzyme inducers such as phenobarbital.

Indication
It is used to control secondarily generalized tonic-clonic seizures and partial seizures and in some primary generalized seizures. Carbamazepine is also used in the treatment of trigeminal neuralgia and has been tried with variable success in glossopharyngeal neuralgia and other severe pain syndromes associated with neurological disorders such as tabes dorsalis and multiple sclerosis. Another use of carbamazepine is in the prophylaxis of bipolar disorder unresponsive to lithium.

Dosage and Administration
Is usually given in divided doses 2 to 4 times daily or as prescribed by the physician.
Epilepsy - Adults: Suggested initial dose is 100 to 200 mg once or twice daily gradually increased by increments of 100 to 200 mg every 2 weeks to a usual maintenance, dose of 800 mg to 1.2 g daily in divided doses; or up to 2.0 g daily may occasionally be necessary or as prescribed by the physician.
Children: Usual dosage in children is 10 to 20 mg/kg daily in divided doses or:
< 1 year old: 100 to 200 mg daily in divided doses
1 to 5 years old: 200 to 400 mg in divided doses
6 to 10 years old: 400 to 600 mg divided doses
11 to 15 years old: 600 mg to 1.0 g daily in divided doses or as prescribed by the physician.
Trigeminal neuralgia - 100 mg once or twice daily (although higher initial doses may be required in some patients) increased gradually by necessary. Usual maintenance dose is 400 to 800mg daily in 2 to 4 divided doses but up to 1.6 g daily or as prescribed by the physician.
Bipolar Disorder - Prophylaxis - Initial dose of 400 mg daily in divided doses, increased gradually as necessary up to a maximum of 1.6 g daily; the usual maintenance dose range is 400 to 600 mg daily or as prescribed by the physician.

Adverse Effects
Fairly common side-effects of carbamazepine, particularly in the initial stages of therapy, include dizziness, drowsiness, and ataxia. These effects may be minimized by starting therapy with a low dose. Drowsiness and disturbances of cerebellar and oculo-motor function (with ataxia, nystagmus, and diplopia) are also symptoms of excessive plasma concentrations of carbamazepine, and may disappear with continued treatment at reduced dosage. Gastro-intestinal symptoms are reported to be less common, and include dry mouth, abdominal pain, nausea and vomiting, anorexia, and diarrhea or constipation. Generalized erythematous rashes may be severe and may necessitate withdrawal of treatment. Photosensitivity reaction, urticaria, exfoliative dermatitis, toxic epidermal necrolysis, erythema multiforme and Steven-Johnson syndrome and systemic lupus erythematosus have also been reported. Occasional reports of blood disorders include agranulocytosis, aplastic anemia, eosinophilia, persistent leucopenia, leucocytosis, thrombocytopenia, and purpura. Lymphadenopathy ,splenomegaly, pneumonitis, abnormalities of liver and kidney function , and cholestatic jaundice have occurred. Some or all of these symptoms as well as fever and rashes may represent a generalized hypersensitivity reaction to carbamazepine.
Other adverse effects reported include paraesthesia, headache, arrhythmias and heart block, heart failure, hyponatraemia and oedema, impotence, male infertility, gynaecomastia, galactorrhoea, and dystonias and dyskinesias with asterixis.

Treatment of Adverse Effects
In the treatment of carbamazepine overdosage repeated doses of activated charcoal may be given by mouth to adults and children who have ingested more than 20mg/kg; the aim not only of preventing absorption but also of aiding elimination. Gastric lavage may be considered if undertaken within 1 hour of ingestion. Supportive and symptomatic therapy alone may then suffice; haemoperfusion has been suggested for severe poisoning.

Overdosage
Gastric lavage may be particularly useful in carbamazepine overdosage as the antimuscarinic effects delay gastric emptying. In patients who are comatose or who have lost the gag reflex gastric lavage may be performed via a large-bore orogastric tube following endotracheal intubation. In alert patients at low risk of loss of consciousness emesis may be induced with ipeccacuanha (although UK authorities consider this to be of very limited value). Supportive measures such as management of airways, ventilation and monitoring of cardiovascular function and electrolyte balance are most important. Administration of activated charcoal, via the patient is free of symptoms. Although charcoal haemoperfusion is also of value, repeated oral doses of activated charcoal seem to be as effective and less invasive. A report of the use of plasmapheresis in the treatment of an acute overdose of carbamazepine concluded that plasmpheresis removed a very small percentage of the total body load of carbamazepine and could not be recommended. Death due to carbamazepine overdosage does occasionally occur and the cause reported in two cases was aspiration of gastric contents; the author considered this to be a major danger of carbamazepine overdosage.

Precautions
Carbamazepine should be avoided in patients with atrioventricular conduction abnormalities. It should not be given to patients with a history of bone marrow depression. Carbamazepine should be given with caution to patients with a history of blood disorders or of cardiac, hepatic, or renal disease. Patients or their carers should be told how to recognize signs of blood, liver, and skin toxicity and they should be advised to seek immediate medical attention if symptoms such as fever, sore throat, rash mouth ulcers, bruising, or bleeding develop. Carbamazepine should be withdrawn, if necessary under cover of a suitable alternative antiepileptic, if leucopenia which is severe, progressive, or associated with clinical symptoms develops. Care is required in identifying patients with mixed seizure disorders that include generalized absence or atypical absence seizures, who may be at risk of an increase in generalized seizures if given carbamazepine. It may also exacerbate absence and myoclonic seizures. Care is required when withdrawing carbamazepine therapy.Since carbamazepine has mild antimuscarinic properties caution should be observed in patients with glaucoma or raised intra-ocular pressure; scattered punctuate lens opacities occur rarely with carbamazepine and it has been suggested that patients should be examined periodically for eye changes.

Caution
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

Storage Condition
Store at temperatures not exceeding 30^{o}C, Protected from moisture.

Availability
CARBAMAZEPINE 200 mg TABLET
In a box of 100's (2 Composite packs of 5 x 10 tablets) -Blister Pack

torrent PHARMA

Manufactured by :
TORRENT PHARMACEUTICALS LTD.
Indrad-382 721, Dist. Mehsana, INDIA

Imported and Distributed by :
TORRENT PHARMA PHILIPPINES INC.
Units 3 & 4, 34th Floor, Zuellig Building
Makati Avenue Corner Paseo de Roxas
Makati City, PHILIPPINES

PRODUCT NAME	:	Epazin	**COUNTRY :** Philippines	**LOCATION :** Chhatral		**Supersedes A/W No.:**		
ITEM / PACK	:	Insert	**NO. OF COLORS:** 1	**REMARK : Folded Size 30 mm**				
DESIGN STYLE	:	-	**PANTONE SHADE NOS.:**	**SUBSTRATE :**				
CODE	:	xxxxxxxxx-5343	Black	**Activities**	**Department**	**Name**	**Signature**	**Date**
DIMENSIONS (MM)	:	150 x 180		Prepared By	**Pkg.Dev**			
ART WORK SIZE	:	S/S		Reviewed By	**Pkg.Dev**			
DATE	:	21-03-2016		Reviewed By	**RA**			
				Approved By	**CQA**			