PRODUCT NAME	:	Carbatol CR	**COUNTRY :** Malaysia	**LOCATION :** Chhatral	**Supersedes A/W No.:**	
ITEM / PACK	:	Insert	**NO. OF COLORS:** 1	**REMARK :**		
DESIGN STYLE	:	Front/Back	**PANTONE SHADE NOS.:**	**SUBSTRATE :**		
CODE	:	xxxxxxxxx-5253	**Activities**	**Dept.**	**Name**	**Signature**	**Date**
DIMENSIONS (MM)	:	180 x 350	Prepared By	**Pkg_Dev**			
ART WORK SIZE	:	S/S	Reviewed By	**Pkg_Dev**			
DATE	:	25-05-2021	Approved By	**Quality**			

This colour proof is not colour binding. Follow Pantone shade reference for actual colour matching.

xxxxxxxxxx-5253

For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory only.

CARBATOL CR

(Carbamazepine Controlled Release Tablets, 200mg & 400 mg)

DESCRIPTION

Carbatol CR (carbamazepine), is an anti-epileptic, neurotropic and psychotropic agent; (ATC Code: N03 AX 1). Dibenzazepine derivative.

COMPOSITION

CARBATOL CR 200: Each film coated controlled release tablet contains Carbamazepine B.P.... 200 mg.

CARBATOL CR 400: Each film coated controlled release tablet contains Carbamazepine B.P.... 400 mg.

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

As an antiepileptic agent spectrum of activity of Carbamazepine embraces: partial seizures (simple and complex) with and without secondary generalisation; generalised tonic-clonic seizures, as well as combinations of these types of seizures.

As a neurotropic agent, Carbamazepine is clinically effective in various neurological disorders like preventing paroxysmal attacks of pain in idiopathic trigeminal neuralgia. It raises the lowered convulsion threshold and helps in decreasing the withdrawal symptoms (eg, hyper-excitability, tremor, impaired gait) in alcohol-withdrawal syndrome and lowers urinary volume and relieves the feeling of thirst in diabetes insipidus.

The mechanism of action of Carbamazepine have been partially evaluated. Carbamazepine reduces synaptic propagation of excitatory impulses by stabilizing hyperexcited nerve membranes and inhibiting repetitive neuronal discharges. The prevention of repetitive firing of sodium-dependent action potentials in depolarized neurons via use and voltage dependent blockade of sodium channels may be the mail mechanism of action. The reduction of glutamate release and stabilization of neuronal membranes may account for antiepileptic effects; whereas the antimanic properties of carbamazepine results from the depressant effect on dopamine and noredrenaline.

PHARMACOKINETICS

Absorption

After oral administration carbamazepine is absorbed completely but relatively slowly from the tablets with the peak plasma levels achieved within 24 hours following oral administration of the controlled release tablets. The rate of absorption of Carbamazepine may vary amongst the various formulations and between patients.

The controlled release formulation shows about 15% lower bioavailability than standard preparations due mainly to the considerable reduction in peak plasma levels occasioned by controlled release of the same dosage of carbamazepine. Plasma concentrations show less fluctuation but auto-induction of carbamazepine occurs as with standard carbamazepine preparations.

The bioavailability of Carbamazepine in various oral formulations has been shown to lie between 85-100%. Ingestion of food has no significant influence on the rate and extent of absorption, regardless of the dosage form of Carbamazepine.

Steady-state plasma concentrations of carbamazepine are attained within about 1-2 weeks, depending individually upon auto-induction by carbamazepine and hetero-induction by other enzyme-inducing drugs, as well as on pre-treatment status, dosage, and duration of treatment.

Various formulations of carbamazepine tend to show different bioavailabilities. Hence to avoid increased risk of breakthrough seizures due to increased availability or reduced therapeutic effect due to lesser availability it is advisable not to change the formulation.

Distribution

Carbamazepine is 70-80% bound to serum proteins. 20-30% of the unchanged drug appears in the cerebrospinal fluid and the saliva, which reflects the unbound fraction of the drug in plasma. The levels in breast milk are about 25-60% of the corresponding plasma levels. The apparent volume of distribution assuming complete absorption is 0.8 - 1.9 L/kg. Carbamazepine crosses the placental barrier.

Elimination

Following single oral dose the elimination half-life of carbamazepine is about 36hours, which after repeated administration reduces to about 16-24 hours due to the auto-induction of the hepatic monooxygenase enzyme system. In patients concomitantly receiving other enzyme inducing drugs [say phenytoin, phenobarbitone] the half-life further reduces to about 9-10 hours.

Carbamazepine is metabolized in liver with the main metabolic pathway being epoxide pathway which yields 10, 11-transdiol derivative and its glucuronide as the major metabolites. Cytochrome P450 3A4 is the main isoform responsible for the formation of epoxide from carbamazepine. The other metabolite formed by this pathway is 9-hydroxy-methyl-10-carbamoyl acridan. The mean elimination half-life of 10, 11 epoxide metabolite of carbamazepine in plasma is 6 hour following single oral dose of epoxide itself. Other metabolic pathways includes formation of monohydroxylated compounds and N-glucuronide of carbamazepine.

About 72% of the single oral dose of 400mg carbamazepine is excreted in urine with about 28% in feces. In urine 2% is recovered as unchanged drug with 1% as pharmacologically active metabolite i.e. 10, 11 epoxide. About 30% of the administered dose appears in urine as end products of epoxide pathway.

Characteristics in patients

The therapeutic range of carbamazepine at steady state is about 4-12mcg/ml [equivalent to 17-50 micromole/litre of Carbamazepine] and vary considerably interindividually. The concentrations for the epoxide metabolite, which is pharmacologically active accounts for 30% of the carbamazepine levels.

Children may require higher doses than adults, to maintain therapeutic levels, due to enhanced elimination in children. The pharmacokinetics of carbamazepine in elderly do not differ significantly to that in young adults.

There is no data available on the kinetics of carbamazepine in patients with impaired renal or hepatic function.

INDICATIONS

Carbatol CR is indicated in the treatment of various epileptic seizures.

- For treatment of partial seizures with simple and complex symptomatology.
- For the treatment of primary or secondarily generalized tonic-clonic seizures as well as mixed forms of these seizures.
- It can be used as monotherapy or in combination with other anticonvulsants.
- Carbatol CR is not usually effective in the absence seizures i.e. petit mal and myoclonic seizures.

Carbatol CR is also indicated in treatment of acute mania and prevention of manicdepressive psychosis (Bipolar Disorders)

It is also useful in alleviating the symptoms of Alcohol-withdrawal syndrome.

Carbatol CR is also used in the treatment of Idiopathic Trigeminal neuralgia and trigeminal neuralgia due to multiple sclerosis and Idiopathic glossopharyngeal neuralgia.

CONTRAINDICATIONS

Carbamazepine should not be used in patients with history of hypersensitivity to carbamazepine or structurally related drugs [e.g. tricyclic antidepressants] or any other components of the formulation. It should not be used in patients with atrioventricular block, history of bone marrow depression or acute intermittent porphyria. Concomitant use of monoamine oxidase (MAO) inhibitors should be avoided as carbamazepine is structurally related to tricyclic antidepressants. If clinical situation permits MAO inhibitors should be discontinued for a minimum of 14 days before Carbamazepine administration.

WARNING AND PRECAUTIONS

Potential for an increase of suicidal thoughts or behaviours.

Carbamazepine should be given under medical supervision only. In patients with a history of cardiac, hepatic or renal damage and in patients with adverse hematological reactions to other drugs or interrupted courses of carbamazepine therapy; carbamazepine should be used only after critical risk-benefit appraisal and under close medical surveillance. In patients receiving carbamazepine therapy full blood count, hepatic function, complete urinalysis and BUN determinations at baseline and periodically thereafter are recommended.

Due to its mild anticholinergic activity, carbamazepine should be used with caution in patients with increased intraocular pressure and patients should be warned regarding the possible hazards.

Carbamazepine may also cause activation of latent psychosis and, in elderly patients, of confusion or agitation.

Carbamazepines have been associated with decreased platelet or white blood cell counts occuring occasionally to frequently and rarely with agranulocytosis. The patients and their relatives should be informed about the early signs and symptoms indicative of potential hematological problem and symptoms of dermatological or hepatic reactions. The physician should be consulted immediately on occurrence of events like fever, sore throat, rash, mouth ulcers, easy bruising, petechial or purpuric hemorrhage.

The patient showing a definite low or decreased platelet count during treatment should be closely monitored and treatment with carbamazepine should be discontinued if any evidence of significant bone marrow depression appears and in case of leucopenia which is severe, progressive or accompanied by fever or sore throat.

Carbamazepine should be used with caution in patients with history of liver disease and in elderly patients and liver function tests should be performed before starting the carbamazepine therapy. Therapy should be discontinued immediately in case of acute liver disease or aggravated liver dysfunction. However, it should not be withdrawn in cases of abnormal liver function tests resulting from the hepatic enzyme inhibition property of carbamazepine.

Mild skin reactions [e.g. macular or maculopapular exanthemata] are transient and non-hazardous, disappearing within few days or weeks during the course of treatment or with slight decrease in the dosage. Severe dermatologic reactions including Stevens- Johnson syndrome and toxic epidermal necrolysis (Lyell's Syndrome) have been reported with carbamazepine. Patients treated with carbamazepine should closely be monitored for sign of hypersensitivity reactions, particularly during the first month of therapy. Immediate discontinuation of therapy should be made when cutaneous reactions occur.

Carbamazepine treatment may exacerbate seizures in patients with mixed seizures which include absence seizures either typical or atypical. Hence carbamazepine should be used with caution in such patients and therapy discontinued following exacerbation of the seizures.

Abrupt withdrawal of carbamazepine precipitates seizures:

If abrupt withdrawal of carbamazepine therapy is essential the changeover to other suitable antiepileptic should be made under cover of a suitable drug like diazepam (I.V., rectal) or phenytoin (I.V.). About 25-30% patients have reported crosshypersensitivity between carbamazepine and oxcarbamazepine. Crosshyersensitivity can also occur between carbamazepine and phenytoin.

Carbamazepine and oestrogen and/or progesterone preparations:

Carbamazepine may cause failure of therapeutic effect of oestrogen and/or progesterone containing preparations due to its hepatic enzyme inducing properties; thus resulting in failure of contraception, recurrence of symptoms of breakthrough bleeding or spotting.

Monitoring of Carbamazepine plasma levels may of useful in cases of dramatic increase in seizure frequency or verification of patient compliance, during pregnancy, while treating children or adolescents, in suspected absorption disorders or suspected toxicity when two or more drugs are used together.

Few incidences of neonatal seizures and respiratory depression associated with maternal carbamazepine and other anti-epileptic drug use have been reported.

There are few cases of neonatal withdrawal syndrome associated with maternal carbamazepine, which includes neonatal vomiting, diarrhea and/or decreased feeding.

Effects on the ability to drive or operate machinery:

Carbamazepine may impair the concentration and ability to react by causing drowsiness and dizziness. This mainly occurs at the start of the therapy or during dose adjustments. Therefore patients should be advised to exercise caution while driving a vehicle, operating machinery or performing other tasks requiring alertness.

USE IN PREGNANCY, LACTATION AND CHILDREN

Usage in Pregnancy - Carbamazepine belongs to category D for pregnancy, i.e. there is a definite evidence of risk to human fetus; however this may be outweighed by the therapeutic benefit to the mother. Special care is recommended while prescribing carbamazepine in pregnant women with epilepsy.

Carbamazepine should be prescribed as a monotherapy, whenever possible, due to increased incidences of congenital abnormalities in offsprings of women treated with combination of antiepileptic drugs.

If women receiving carbamazepine becomes pregnant or if the need arises to initiate treatment of pregnant women with carbamazepine the potential benefit with the treatment must be weighed against the possible risk involved especially in the first trimester of pregnancy. Also the lowest effective dose should be given with close monitoring of plasma levels.

The offsprings of epileptic mothers with untreated epilepsy are known to be more prone to developmental disorders and malformations. Although there are reports on developmental disorders and malformations including congenital abnormalities like craniofacial defects, cardiovascular malformations and various anomalies involving other body systems, there is no conclusive evidence of the increased risk with carbamazepine monotherapy. Hence, patients should be informed regarding the possibility of increased risk of malformations and antenatal screening may be carried out.

Anti-epileptic drugs have shown to aggravate folic acid deficiency, which generally occurs during pregnancy. The folic acid deficiency may contribute to the higher incidence of malformations in children of women taking anti-epileptic drugs.

Hence folic acid supplements should be given before and during pregnancy. It is recommended to give vitamin K1 to mother during the last weeks of pregnancy and to newborn with a view to prevent bleeding disorders.

Usage in Lactation - Concentration of carbamazepine in breast milk is approximately 25-60% of the maternal plasma concentration. Because of the potential for adverse reactions in the infants, decide whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. Infants of the mothers taking carbamazepine should be monitored for symptoms of possible adverse reactions e.g. excessive somnolence, allergic skin reactions.

Children - Safety and efficacy for use in children below the age of 6 years have not been established.

ADVERSE REACTIONS

CNS adverse reactions [e.g. dizziness, headache, ataxia, drowsiness, fatigue, diplopia], gastrointestinal disturbances [e.g. nausea, vomiting] and allergic skin reactions are very commonly seen, especially at the start of treatment or if the initial dose is too high or in elderly patients.

The dose related adverse effects usually disappear in few days either spontaneously or after a transient reduction in the dosage. The plasma levels should be monitored and the daily dosage should be divided in smaller fractions as the occurrence of the CNS events occurs due to manifestation of the relative overdosage or fluctuations in the plasma levels.

Central Nervous System:

Neurological: The commonly seen neurological side effects are: Dizziness, ataxia, drowsiness, fatigue, headache, diplopia, accommodation disorders (e.g. blurred vision). Also observed rarely are abnormal involuntary movements (e.g. tremor, asterixis, dystonia, tics); nystagmus, Orofacial dyskinesia, oculomotor disturbances, speech disorders (e.g. dysarthria or slurred speech), choreoathetotic disorders, peripheral neuritis, paraesthesia, muscle weakness, and paretic symptoms.

Although isolated cases of neuroleptic malignant syndrome have been reported the causative role of carbamazepine in inducing or contributing to the development of a neuromalignant syndrome, especially in conjunction with neuroleptics, is unclear.

Psychiatric: Hallucinations (visual or acoustic), depression, loss of appetite, restlessness, aggressive behaviour, agitation, confusion, activation of psychosis.

Skin and appendages: Allergic skin reactions, urticaria, which may be severe. Also reported are Exfoliative dermatitis and erythroderma, Lupus erythematosus-like syndrome, pruritus, Stevens Johnson syndrome, toxic epidermal necrolysis, photosensitivity, erythema multiforme and nodosum, alterations in skin pigmentation, purpura, acne, sweating, hair loss.

Blood: Leucopenia, Thrombocytopenia, eosinophilia, leucocytosis, lymphadenopathy, folic acid deficiency, agranulocytosis, aplastic anaemia, pure red cell aplasia, megaloblastic anaemia, acute intermittent porphyria, reticulocytosis, and possibly haemolytic anaemia.

Liver: Elevated gamma-GT (due to hepatic enzyme induction: usually not clinically relevant), Elevated alkaline phosphatase, Elevated transaminases, hepatitis of cholestatic, parenchymal (hepatocellular) or mixed type, jaundice, granulomatous hepatitis or hepatic failure.

Gastro-intestinal tract: Nausea, vomiting, dryness of the mouth, with suppositories rectal irritation may occur. Diarrhoea or constipation, abdominal pain, glossitis, stomatitis and pancreatitis are also reported in rare cases.

Hypersensitivity reactions: A delayed multi-organ hypersensitivity disorder with fever, skin rashes, vasculitis, lymphadenopathy, disorders mimicking lymphoma, arthralgia, leucopenia, eosinophilia, hepato-splenomegaly and abnormal liver function tests, occurring in various combinations. Other organs like liver, lungs, kidneys, pancreas, myocardium, colon may also be affected. Also reported are aseptic meningitis, with myoclonus and peripheral eosinophilia; anaphylactic reaction, angioedema.

Treatment with carbamazepine must be stopped immediately if such hypersensitive reactions occur.

Cardiovascular system: The adverse reactions are rare including disturbances of cardiac conduction, hypertension or hypotension, bradycardia, arrhythmias, AV-block with syncope, collapse, congestive heart failure, aggravation of coronary artery disease, thrombophlebitis, thromboembolism.

Endocrine system and metabolism: The commonly reported adverse events include oedema, fluid retention, weight increase, hyponatraemia and reduced plasma osmolality due to an antidiuretic hormone (ADH)-like effect, leading in rare cases to water intoxication accompanied by lethargy, vomiting, headache, mental confusion, neurological abnormalities.

Some other reactions which are rarely observed are increase in prolactin with or without clinical symptoms such as galactorrhoea, gynaecomastia, abnormal thyroid function tests; decreased 1-thyroxin (FT4, T4, T3) and increased TSH, usually without clinical manifestations, disturbances of bone metabolism (decrease in plasma calcium and 25-OH-cholecalciferol) leading to osteomalacia, elevated levels of cholesterol, including HDL cholesterol and triglycerides.

Urogenital system: Interstitial nephritis, renal failure, renal dysfunction (e.g. albuminuria, haematuria, oliguria and elevated BUN/ azotaemia), urinary frequency, urinary retention, sexual disturbances/impotence.

Sense organs: Taste disturbances; lens opacities, conjunctivitis, hearing disorders, e.g. tinnitus, hyperacusis, hypoacusis, change in pitch perception.

Musculoskeletal system: Arthralgia, muscle pain or cramp.

Respiratory tract: Pulmonary hypersensitivity characterized by fever, dyspnoea, pneumonitis or pneumonia.

DRUG INTERACTIONS:

Formation of carbamazepine 10, 11- epoxide is catalysed by cytochrome P450 3A4 [CYP 3A4].

Drugs inhibiting the CYP 3A4 may result in increased plasma concentrations of carbamazepine, which may induce adverse reactions and hence plasma levels of carbamazepine should be monitored and dosage of carbamazepine should be adjusted accordingly. These include agents like Isoniazid, verapamil, diltiazem, ritonavir, dextropropoxyphene, viloxazine, fluoxetine, fluvoxamine, possibly cimetidine, acetazolamide, danazol, nicotinamide (in adults, only in high dosage), nefazodone, macrolide antibiotics (e.g. erythromycin, clarithromycin), azoles (e.g. itraconazole, ketoconazole, fluconazole), terfenadine, loratadine, grapefruit juice, protease inhibitors for HIV treatment (e.g. ritonavir).

On the other hand drugs inducing the enzyme system increases the rate of carbamazepine metabolism thus reducing the serum levels and hence decreasing therapeutic effect. Phenobarbitone, phenytoin, primidone, or theophylline, rifampicin, cisplatin or doxorubicin and, although the data are partly contradictory, possibly also clonazepam or valproic acid, oxcarbazepine.

Mefloquine may antagonise the anti-epileptic effect of Carbamazepine. On the other hand, valproic acid and primidone have been reported to raise the plasma level of the pharmacologically active carbamazepine 10, 11-epoxide metabolite. The dose of carbamazepine may consequently need to be adjusted.

Also, discontinuation of CYP3A4 inducer may decrease metabolism rate of carbamazepine thereby increasing carbamazepine plasma levels.

Bioavailability and/or clearance of carbamazepine and carbamazepine-10, 11-epoxide may be affected by Isotretinoin; hence carbamazepine plasma concentrations should be monitored.

Concomitant use of the herbal remedy St John's wort (Hypericum perforatum) can reduce the serum levels of carbamazepine.

Effect of Carbamazepine on plasma levels of concomitant agents:

Carbamazepine may lower the plasma level, diminish or even abolish the activity of certain drugs. The dosage of the such drugs may have to be adjusted to clinical requirement: viz. levothyroxine, clobazam, clonazepam, ethosuximide, primidone, valproic acid, alprazolam, corticosteroids, (e.g. prednisolone, dexamethasone); cyclosporin, digoxin, doxycycline; dihydropyridine derivatives, e.g. felodipine and isradipine; indinavir, saquinavir, ritonavir, haloperidol, imipramine, methadone, tramadol, products containing oestrogens and/or progestogens (alternative contraceptive methods should be considered), gestrinone, tibolone, toremifene, theophylline, oral anticoagulants (warfarin), lamotrigine, tiagabine, topiramate, tricyclic antidepressants (e.g. imipramine, amitriptyline, nortriptyline, clomipramine), clozapine, oxcarbazepine, olanzapine, itraconazole and risperidone.

There are reports of increase as well as decrease in the plasma phenytoin levels when used concomitantly with carbamazepine, and plasma mephenytoin levels have been reported in rare instances to increase.

Combinations to be taken into consideration:

Simultaneous administration of carbamazepine and paracetamol may reduce the bioavailability of paracetamol/acetaminophen.

Carbamazepines when given with isoniazid have reported to increase the isoniazidinduced hepatotoxicity.

The co-administration of lithium and carbamazepine may cause enhanced neurotoxicity eventhough the lithium plasma concentrations being within the therapeutic range. Increase in neurological side effects may be caused with combined use of carbamazepine with metoclopramide or major tranquillisers, e.g. haloperidol, thioridazine.

Carbamazepine being structurally related to tricyclic anti-depressants should not be used in combination with monoamine oxidase inhibitors (MAOIs); MAOIs should be discontinued for a minimum of 14 days before Carbamazepine administration.

Co-administration of some diuretics [hydrochlorothiazide, durosemide] causes symptomatic hyponatraemia.

Carbamazepine may antagonise the effects of non-depolarising muscle relaxants (e.g. pancuronium); therefore their dosage should be increased accordingly and patients closely monitored for a more rapid recovery from neuromuscular blockade than expected.

Patients should be advised to abstain from alcohol since carbamazepine may reduce alcohol tolerance.

DOSAGE AND ADMINISTRATION

Carbatol CR is given orally, generally in the same total daily dose as conventional Carbamazepine dosage forms but usually in two divided doses. In a few patients when changing from other oral dosage forms of Carbamazepine to Carbatol CR the total daily dose may need to be increased, particularly when it is used in polytherapy.

Carbatol CR (either the whole or half divisible tablet as prescribed), should not be chewed but should be swallowed with a little liquid, before, during or between meals. The divisible tablet presentation enables flexibility of dosing to be achieved.

Epilepsy:

Carbatol CR should be prescribed as monotherapy wherever possible. It is advised that with all formulations of Carbamazpine, a gradually increasing dosage scheme is used and this should be adjusted to suit the needs of the individual patient. It may be helpful to monitor the plasma concentration of carbamazepine to establish the optimum dose. The dose can be reduced to the lowest effective level once adequate seizure control is achieved.

When added to existing anti-epileptic therapy, do so gradually while maintaining or if necessary adapting the dosage of other anti-epileptics.

Adults and children over 15years of age: When starting treatment with Carbatol CR in monotherapy, 100-200mg once or twice daily is recommended. This may be followed by a slow increase in dosage until the best response is obtained, often 800-1200mg daily. In some instances,1600mg or even 2000mg daily may be necessary.

Children aged 6-15 years of age:

A low initial daily dosage is recommended with carbamazepine, which should be increased gradually to suit the needs of the patient. The plasma levels of carbamazepine should be monitored to optimize the effective dose. The usual dose in children is 10-20mg/kg bodyweight daily in several divided doses.

Children with 6-10 years of age: 400-600mg daily

Children with 11-15 years of age: 600-1000mg

Elderly:

Due to the potential for drug interactions, the dosage of Carbatol CR should be selected with caution in elderly patients.

Trigeminal Neuralgia:

The usual recommended initial dose is 200-400mg daily, which should be increased gradually until freedom from pain is achieved (normally at 200mg 3-4 times daily). In the majority of patients a dosage of 200mg 3 or 4 times a day is sufficient to maintain a pain free state. Once the pain is in remission, the dosage should be gradually reduced to the lowest possible maintenance level.

Elderly: The recommended initial dose for elderly population is 100mg twice daily.

Alcohol withdrawal Syndrome:

The usual mean dosages for treating the symptoms of alcohol withdrawal symptoms is 200mg 3-4 times daily. This may be further increased in severe cases to about 400mg thrice daily. During the initial treatment for severe cases Carbatol CR should be combined with other sedative/hypnotic drugs (e.g. Clomethiazole, chlordiazepoxide). Once the acute phase is over, Carbatol CR may be continued as a monotherapy.

Mania and Prevention of manic-Depressive psychosis:

Initial starting dose is 400mg daily, in divided doses, which can be increased gradually until symptoms are controlled or a total of 1600mg given in divided doses is reached. The usual dosage range is 400-600mg daily, given in divided doses. The dosage range should be increased rapidly in acute mania, whereas the smaller dose increases are recommended for the prevention of bipolar disorder in order to ensure optimum tolerability.

OVERDOSAGE

Signs and symptoms:

The symptoms of Carbamazepine overdosage mainly involve the central nervous system, cardiovascular system and respiratory systems.

Central Nervous System: CNS depression, disorientation, somnolence, agitation, hallucination, coma, blurred vision, slurred speech, dysarthia, nystagmus, ataxia, dyskinesia, initially hyperreflexia, later hyporeflexia, convulsions, psychomotor disturbances, myoclonus, hypothermia, mydriasis.

Respiratory System: respiratory depression, pulmonary oedema Cardiovascular System: Tachycardia, hypotension and at times hypertension, widening of QRS complex, syncope in association with cardiac arrest Other symptoms include Vomiting, delayed gastric emptying, reduced bowel motility, retention of urine, oliguria or anuria; fluid retention, water intoxication due to ADH-like effect of carbamazepine, Hyponatraemia, possibly metabolic acidosis, possibly hyperglycaemia, increased muscle creatinine phosphokinase.

Treatment:

As there is no specific antidote to the carbamazepine overdose, management of the overdose should depend on the patient's clinical condition and admission to hospital.Plasma levels should be monitored to assess the levels of carbamazepine poisoning and extend of overdose.

Activated charcoal should be administered and gastric levage performed to evacuate to stomach; to prevent the absorption of the drug. Delay in evacuating the stomach may result in delayed absorption, which may lead to relapse during recovery from intoxication. One should provide supportive treatment under medical supervision with cardiac monitoring and careful correction of electrolyte imbalance. Charcoal hemoperfusion is recommended since forced diuresis, hemodialysis and peritoneal dialysis are not useful. In treatment of the overdosage relapse and aggravation of the symptoms on the second or third day due to delayed absorption should be anticipated.

The following steps should be taken in case of specific symptoms:

Hypotension- Dopamine or dobutamine I.V. should be administered.

Convulsions A benzodiazepine[e.g. diazepam] or other anticonvulsants e.g. phenobarbitone (which should be used with caution due to increased respiratory depression) or paraldehyde.

Water intoxication or hyponatraemia: Fluid restriction and slow and careful NaCl infusion I.V.[0.9%] should be given, which may help in preventing brain damage.

EXPIRY DATE

Do not use later than date of expiry

STORAGE

Store below 30°C, protected from moisture.

Keep out of reach and sight of children.

PRESENTATION

Carbatol CR tablets are packed in blister strips of printed aluminium foil sealed with clear PVC film. Each blister strip contains 10 tablets. 1, 3 and 10 such blister strips and a patient information leaflet are packed in printed cartons.

Both Carbatol CR-200 and Carbatol CR-400 mg are light brown coloured, biconvex film coated tablets with bisecting line on one side of tablet and other side plain.

Date of Revision

25-05-2021

torrent PHARMA

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