

CARBAMAZEPINE (Systemic)

Category

Anticonvulsant; antineuralgic (specific pain syndromes); antimanic; antidiuretic; antipsychotic.

Indications

Note: Bracketed information in the Indications section refers to uses that are not included in U.S. product labeling.

Accepted

Epilepsy (treatment)³ Carbamazepine is indicated for the treatment of partial seizures with simple or complex symptomatology (psychomotor, temporal lobe) 59, 61, 62, 63, 64, 65, 66, 67, 69 ; generalized tonic-clonic seizures (grand mal) 59, 61, 62, 63, 67, 69 ; mixed seizure patterns that include the above 59, 61, 62, 63, 64, 65, 66 ; or other partial or generalized seizures 61, 62, 63.

Carbamazepine is a first-choice anticonvulsant 67, 80 because of its relatively low behavioral and psychological toxicity and the rarity of serious adverse effects. 1, 2

Neuralgia, trigeminal (treatment) 59, 61, 62, 63, 64, 65, 66, 69³ Carbamazepine is indicated for relief of pain due to true trigeminal neuralgia 59, 61, 62, 63, 64, 65, 66 (tic douloureux) and glossopharyngeal neuralgia 61, 62, 63, 64, 65, 66.

[Bipolar disorder (prophylaxis and 50, 69 treatment)]³ Carbamazepine is used alone or in combination with lithium and/or antidepressants or antipsychotic agents 35 to treat patients with manic-depressive illness who are unresponsive to, or cannot tolerate, lithium or neuroleptics alone.

[Pain, neurogenic, other (treatment)] ³ Carbamazepine may also be used in some patients to relieve the lightning pains of tabes dorsalis; neuralgic pain associated with multiple sclerosis, acute idiopathic neuritis (Guillain-Barre syndrome), peripheral diabetic neuropathy, phantom limb, restless leg syndrome (Ekbom's syndrome) 12, 13 , and hemifacial spasm 4, 5, 6 ; post-traumatic neuropathy or neuralgia; and postherpetic neuralgia.

[Diabetes insipidus, central partial (treatment)] ³ Carbamazepine is used alone 90 or with other agents such as clofibrate or chlorpropamide in the treatment of partial central diabetes insipidus.

[Alcohol withdrawal (treatment)] ³ Carbamazepine is used for the detoxification of alcoholics. It has been found to be effective in rapidly relieving anxiety and distress of acute alcohol withdrawal and for such symptoms as seizures, hyperexcitability, and sleep disturbances. 3, 4

[Psychotic disorders (treatment)] ³ Carbamazepine has been shown to be effective in certain psychiatric disorders including schizoaffective illness, resistant schizophrenia, and dyscontrol syndrome associated with limbic system dysfunction. 5

Unaccepted

Carbamazepine is not a simple analgesic and should not be used to relieve general aches or pains. 59, parameters of carbamazepine disposition are similar in children and adults, there is a poor correlation between plasma concentrations and carbamazepine dose in children. Carbamazepine is more rapidly metabolized to the active 10,11-epoxide metabolite in younger age groups than in adults. In children younger than 15 years of age, there is an inverse relationship between the carbamazepine-10,11-epoxide to carbamazepine ratio (CBZ-E/CBZ) and increasing age. 116, 121

Precautions to Consider

Cross-sensitivity and/or related problems

Patients who are sensitive to tricyclic antidepressants may be sensitive to carbamazepine also. Carbamazepine should be given with caution, if at all, to such patients.

Carcinogenicity/Tumorigenicity

Carbamazepine is considered carcinogenic in Sprague-Dawley rats because doses of 25, 75, and 250 mg per kg per day for 2 years caused a dose-related increase in the incidence of hepatocellular tumors in females and of benign interstitial cell adenomas in the testes of males. 59, 61, 62, 63, 64 The significance of these findings for use of carbamazepine in humans is not known. 59, 61, 62, 63, 64

Pregnancy/Reproduction

Pregnancy% Carbamazepine crosses the placenta. 61, 62, 63 Although adequate and well-controlled studies in humans have not been done, there have been reports of babies prenatally exposed to carbamazepine having small head circumferences 82, 83, low birth weights 15, 83, craniofacial defects 71, fingernail hypoplasia 71, developmental delays 71, 72, and spina bifida 81, 93.

When it is essential to continue carbamazepine therapy during pregnancy, serum carbamazepine concentrations must be monitored closely, since adverse effects in the fetus have been associated with high blood concentrations. 52

Studies in animals have shown that carbamazepine caused kinked ribs in 1.5% of the offspring of rats receiving 250 mg per kg. 59, 61, 62, 63, 64 Also, carbamazepine caused cleft palate, deformities of the foot, or anophthalmos in about 3% of the offspring of rats receiving 650 mg per kg. 59, 61, 62, 63, 64 These doses are 10 to 25 times the human daily dose.

FDA Pregnancy Category C 61, 62, 63.

Also, it must be kept in mind that other anticonvulsants used during pregnancy have been implicated in birth defects in infants born to epileptic mothers. In addition, retrospective studies have suggested that there may be a higher incidence of teratogenic effects with the use of combinations of anticonvulsants than with monotherapy. 81, 93

Delivery% To prevent neonatal bleeding disorders, administration of vitamin K to the mother during the last weeks of pregnancy has been recommended. 119

Breast-feeding

Carbamazepine is distributed into breast milk. 61, 62, 63 Concentrations in breast milk 61, 62, 63 and in the plasma of nursing infants 35, 96 have been reported to reach 60% of the maternal plasma concentration. Therefore, the possibility exists that carbamazepine may cause adverse effects in the nursing infant. 61, 62 In animal studies, nursing rats showed a lack of weight gain and an unkempt appearance with maternal doses of 200 mg per kg. 59, 61, 62, 63, 64

Pediatrics

Appropriate studies have not been performed in children up to 6 years of age 46, 61, 62, 63.

However, behavioral changes are more likely to occur in children. 34

Geriatrics

Geriatric patients may be more susceptible to carbamazepine-induced confusion or agitation, atrioventricular (AV) heart block, syndrome of inappropriate antidiuretic hormone (SIADH) 49 , and bradycardia than younger patients.

Dental

The leukopenic and thrombocytopenic effects of carbamazepine may result in an increased incidence of microbial infection, delayed healing, and gingival bleeding. If leukopenia or thrombocytopenia occurs, dental work should be deferred until blood counts have returned to normal. Patient instruction in proper oral hygiene should include caution in use of regular toothbrushes, dental floss, and toothpicks.

Surgical

Carbamazepine antagonizes the effects of nondepolarizing muscle relaxants, such as pancuronium. Patients should be monitored closely for more rapid recovery from neuromuscular blockade than expected. 117, 119