Carbamazepine (CBZ)

Anticonvulsant-class drugs.

Indications

Generalized tonic-clonic seizure, mixed Sz, ✖ not for absence.

Partial seizures with or without secondary generalization. Trigeminal neuralgia. An IV form for use in e.g. status epilepticus is in development.

Carbamazepine (Tegretol®) may be useful for paroxysmal, lancinating pain..

Dose

℞ oral route. Adult range: 600–2000 mg/d. Peds: 20–30 mg/kg/d. MDF = BID.

Before starting, check: CBC & platelet count (consider reticulocyte count) & serum Fe. Package insert says “recheck at frequent intervals, perhaps q week × 3 mos, then q month × 3 yrs.”

Do not start CBZ (or discontinue it if patient already on CBZ) if: WBC < 4K, RBC < 3 × 106, Hct < 32%, platelets < 100K, reticulocytes < 0.3%, Fe > 150 mcg%.

Start low and increment slowly: 200 mg PO q d × 1 wk, BID × 1 wk, TID × 1 wk. As an inpatient, dosage changes may be made every 3 days, monitoring for signs of side effects. As an outpatient, changes should be made only ≈ weekly, with levels after each change. Carbatrol® (extended-release CBZ) is usually dosed BID.

Supplied: oral form. Scored tabs 200 mg. Chewable scored tabs 100 mg. Suspension 100 mg/5- ml. IV form: not available in the U.S. at the time of this writing. Carbatrol® (extended-release CBZ): 200 & 300 mg tablets. Caveats with oral forms: oral absorption is erratic, and smaller, more frequent doses are preously with other liquid medicinal agents, as it may result in the precipitation of a rubbery, orange ferred.

mass. ✖ May aggravate hyponatremia by SIADH-like effect.

Pharmacokinetics

Oral suspension is absorbed more readily, and also ✖ should not be administered simultaneous- t1/2 (half-life) tPEAK (peak tSS tD/C Therapeutic levels) (steady state) (discontinue) level (mcg/ml)a single dose: 20–55 hrs after 4–24 hrs up to 10 daysb 4 wks 6–12 chronic therapy: 10–30 hrs (adults), 8–20 hrs (peds) amay be misleading since the active metabolite carbamazepine-10,11-epoxide may cause toxicity and must be assayed separately btSS may subsequently fall due to autoinduction, which plateaus at 4–6 wks CBZ induces hepatic enzymes that result in increased m

Carbamazepine (CBZ) and oxcarbazepine (OXC) are first-choice medical treatments. Although other drugs may be effective, these are indicated when the patient cannot reach the therapeutic dosage of CBZ/OXC because of adverse events. Patients unresponsive to CBZ/OXC should be made aware of the available surgical interventions. Surgical procedures (including percutaneous lesions to the ganglion/root, microvascular decompression (MVD) in the posterior fossa, and gamma knife radiosurgery) are extremely efficacious with relatively few complications: each procedure has some advantage and disadvantage with respect to the other. Only MVD is a non-destructive procedure [1)]

Carbamazepine-associated withdrawal reaction (CAWR) is dependent on the pre-operative dosage and the changing rate of pre-and post-operative CBZ blood concentrations [2)].

Female patients with epilepsy and older age, AED polytherapy, and carbamazepine treatment had a higher risk of low fT4. Thyroid function in these patients should be monitored closely. [3)].

Folate antagonists (e.g. carbamazepine) double the incidence of MM

The goal of a study was to determine if the incorporation of carbamazepine, into a biodegradable microparticle for local sustained perineural release would be an efficacious analgesic following a peripheral injury.

Following induction of the chronic constriction injury model in Sprague-Dawley rats, mechanical allodynia testing was performed using von Frey filaments and thermal allodynia was evaluated using the Hargreaves method. Histology and blood work were performed to evaluate toxicity as well to monitor drug and metabolite presence over time.

A 2-fold increase in hindpaw withdrawal thresholds in animals receiving carbamazepine loaded microparticles relative to controls was observed for up to 14 days after treatment. Drug and metabolite had a peak blood concentration of 54.7ng/mL and dropped off exponentially to less than 5ng/mL over a few days.

This formulation reduced systemic exposure to carbamazepine over 1,000-fold relative to traditional analgesic dosing regimens. This two-component drug-delivery system has been specifically engineered to release a controlled amount of carbamazepine over a 14 day period providing significant pain relief with no toxicological or observable adverse events via behavioral or histochemical analysis [4)].

Drug that release ADH or potentiate it

Side effects

✖ Drug-drug interaction: caution, cimetidine, erythromycin, and isoniazid may cause a dramatic elevation of CBZ levels due to inhibition of hepatic cytochrome oxidase that degrades CBZ.

1. drowsiness and GI upset: minimized by slow dose escalation

2. relative leukopenia in many: usually does not require discontinuing drug

3. transient diplopia

Side effects include:

4. ataxia

5. less effect on cognitive function than PHT

6. hematological toxicity: rare. It Maybe serious → agranulocytosis & aplastic anemia

7. Stevens-Johnson syndrome

8. SIADH

9. hepatitis (occasionally fatal) reported

Case reports

Fohlen M, Taussig D, Bulteau C, Audren F. Reversible downbeat nystagmus induced by carbamazepine in a three-year-old child. Epileptic Disord. 2021 Dec 17. doi: 10.1684/epd.2021.1400. Epub ahead of print. PMID: 34933835 [5)].

1)
Cruccu G, Bonamico LH, Zakrzewska JM. Cranial neuralgias. Handb Clin Neurol. 2010;97:663-78. doi: 10.1016/S0072-9752(10)97056-5. PubMed PMID: 20816462.
2)
Chen MJ, Zhang WJ, Guo ZL, Zhang WH, Chai Y, Li YW. Withdrawal reaction of carbamazepine after neurovascular decompression for trigeminal neuralgia: A preliminary study. J Neurol Sci. 2013 Dec 11. pii: S0022-510X(13)03084-0. doi: 10.1016/j.jns.2013.12.013. [Epub ahead of print] PubMed PMID: 24387898.
3)
Shih FY, Chuang YC, Chuang MJ, Lu YT, Tsai WC, Fu TY, Tsai MH. Effects of antiepileptic drugs on thyroid hormone function in epilepsy patients. Seizure. 2017 Mar 19;48:7-10. doi: 10.1016/j.seizure.2017.03.011. [Epub ahead of print] PubMed PMID: 28364656.
4)
Dai H, Tilley DM, Mercedes G, Doherty C, Gulati A, Mehta N, Khalil A, Holzhaus K, Reynolds FM. Opiate-free pain therapy using carbamazepine-loaded microparticles provides up to two weeks of pain relief in a neuropathic pain model. Pain Pract. 2018 May 3. doi: 10.1111/papr.12705. [Epub ahead of print] PubMed PMID: 29723917.
5)
Fohlen M, Taussig D, Bulteau C, Audren F. Reversible downbeat nystagmus induced by carbamazepine in a three-year-old child. Epileptic Disord. 2021 Dec 17. doi: 10.1684/epd.2021.1400.

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