



# Clinical Pharmacology & Toxicology Pearl of the Week

## ~ Carbamazepine ~

- ✓ Carbamazepine (CBZ) is an antiepileptic drug commonly prescribed for seizure disorders, trigeminal neuralgia, neuropathic pain, schizophrenia & bipolar disorder
- ✓ It is structurally related to the Tricyclic Antidepressants (amitriptyline, imipramine, nortriptyline)
- ✓ Its mechanism of action involves:
  - Antagonism of inactivated voltage-dependent Na<sup>+</sup> channels
  - Antagonism of L-type voltage-gated Ca<sup>2+</sup> channels
  - Adenosine receptor agonism (at therapeutic doses) & antagonism (at toxic doses)
  - Anticholinergic properties (antimuscarinic)
  - Serotonin reuptake inhibition
  - Inhibition of glutamate neurotransmission
- ✓ At therapeutic doses CBZ is well absorbed, highly protein bound and has a V<sub>d</sub> of 0.8-2.0 L/kg
- ✓ CBZ is largely metabolized by CYP3A4, has a number of active metabolites that are excreted mostly via the kidneys and should be avoided in CrCl < 60
- ✓ CBZ is a **strong** CYP & P-glycoprotein inducer and has [MANY drug interactions](#); it should NOT be taken with grapefruit juice
- ✓ HLA-B\*1502 testing should be considered prior to starting CBZ, especially in patients with ancestry from China, India and South East Asia, as these patients are at a significantly increased risk of SJS/TEN
- ✓ Carbamazepine undergoes enterohepatic recirculation, and as such is amenable to multi-dose activated charcoal therapy after overdose
- ✓ Carbamazepine is moderately dialyzable. Dialysis may be considered for severe poisonings, particularly those with recurrent seizures or dysrhythmias

**Table 1. Complications of Carbamazepine at Therapeutic Doses and in Toxic Ingestions**

Adverse Effects of Carbamazepine Therapy		Acute Carbamazepine Toxicity	
		System/Toxidrome	Signs/Symptoms
Common	Dizziness	Neurologic	Confusion
	Drowsiness		Drowsiness
Ataxia	Ataxia		
Nausea	Dysmetria		
Vomiting	Nystagmus		
Constipation	Myoclonus, Dyskinesia		
Rash &/or photosensitivity	Seizure		
SIADH	Coma		
Less common/ Severe	Vitamin D deficiency	Cardiovascular	Tachycardia
	Osteomalacia		Hypotension
	SJS/TEN	wide QRS	
	DRESS, AGEP	Anticholinergic toxidrome	
Myelosuppression (can be severe)	Serotonin Syndrome		
Elevated liver enzymes & hepatitis			



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



The Poison and Drug Information Service ([PADIS](#)) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

References →

