

	Drug	Pharmacokinetics	Mechanism of action	Therapeutic uses	Side effects	Notes
1 st generation	1-Carbamazepine	<ul style="list-style-type: none"> Available only orally Potent enzyme inducer including its own metabolism 	<ul style="list-style-type: none"> Blockade of Na⁺ channels which reduces cell excitability. Reduces propagation of abnormal impulses in brain Suppresses repetitive neuronal firing Attenuates action & release of glutamate 	<ul style="list-style-type: none"> Drug of choice in partial & 2ry generalized tonic-clonic seizures. Trigeminal neuralgia Bipolar depression (mood stabilizer) <p>Not used in : Myoclonic or absence seizures</p>	<ul style="list-style-type: none"> GIT upset. Skin rashes CNS toxicity (confusion , ataxia, double vision) Leucopenia (decrease in WBCs) , aplastic anemia & agranulocytosis Hyponatremia & water intoxication Teratogenicity . Induction of hepatic P₄₅₀ (drug interactions) 	
	2-Phenytoin	<ul style="list-style-type: none"> Given orally fosphenytoin IVI & IMI Enzyme inducer 	<ul style="list-style-type: none"> Blockade of Na⁺ channels. Interferes with the release of excitatory transmitters Potentiates the action of GABA 	<ul style="list-style-type: none"> Partial and generalized tonic-clonic seizures Not in absence seizure (Because the rate of sodium channel opening and closing too slow in absence seizure, phenytoin works mainly on highly active sodium channels). <p>In status epilepticus, IV .</p> <ul style="list-style-type: none"> Cardiac arrhythmias (especially that induced by digoxin) <p>N.B : Drug of choice for generalized tonic-clonic seizures , while carbamazepine for drug of choice in partial seizures</p>	<p>Acute:</p> <ul style="list-style-type: none"> C.N.S. toxicity (diplopia, vertigo,) Cardiac arrhythmias Nausea, vomiting <p>Chronic:</p> <ul style="list-style-type: none"> connective tissue effects (gum hyperplasia, coarsening of facial features, hirsutism , acne) . Better to be avoided in young women or adolescents . Folic acid deficiency (megaloblastic anemia) Vitamin D deficiency (osteomalacia) Teratogenic effects Induction of P450 enzymes 	<p>Fosphenytoin :</p> <p>*A Prodrug. Given I.V. or I.M and rapidly converted to phenytoin in the body.</p> <p>* Avoids local complications associated with phenytoin: vein irritation, tissue damage, pain and burning at site, muscle necrosis with i.m. injection, need for large fluid volumes.</p> <p>* Otherwise similar toxicities to phenytoin.</p>
	3-Sodium Valproate	<ul style="list-style-type: none"> Available as capsules, Syrup , I.V Enzyme inhibitor 	<p>Broad spectrum antiepileptic</p> <ul style="list-style-type: none"> Blocks activated Na⁺ channels. Enhances GABA synthesis & reduces degradation Suppress glutamate action. Blocks T-type Ca²⁺ channels 	<p>[I] Epilepsy:</p> <p>It is effective for all forms of epilepsy e.g.</p> <ul style="list-style-type: none"> Generalized tonic-clonic seizures (1ry or 2ry). Absence seizures (not responding to ethosuximide) Complex partial seizures Myoclonic Atonic photosensitive epilepsy 	<ul style="list-style-type: none"> Weight gain (↑appetite). Transient hair loss, with re-growth of curly hair Thrombocytopenia Severe hepatotoxicity Teratogenicity (spina bifida) Enzyme inhibitor of P -450 	

				<ul style="list-style-type: none"> • drug of choice in combination seizures <p>[II] Other uses:</p> <ul style="list-style-type: none"> • Bipolar disorder and mania • Prophylaxis of migraine • <u>Lennox-Gastaut syndrome</u> 		
	Ethosuximide		Inhibits T- type Ca^{2+} channels in thalamo- cortical neurons.	Absence seizures (Absence seizure not controlled with ethosuximide, valproic acid and lamotrigen, alternative is clonazepam)	Gastric distress : pain , nausea and vomiting	
2nd generation	Lamotrigine		<ul style="list-style-type: none"> • Blockade of Na^{+} channels • Interferes with synthesis of glutamate & aspartate • Reduces glutamate release 	<ul style="list-style-type: none"> • <u>Add-on</u> therapy for partial & generalized seizures • <u>Monotherapy</u> in partial seizures • <u>Lennox-Gastaut syndrome</u> 	<ul style="list-style-type: none"> • Influenza-like symptoms. • Skin rashes (may progress to Steven –Johnson syndrome) • Somnolence • Blurred vision • Diplopia • Ataxia 	
	Topiramate		<ul style="list-style-type: none"> • Blockade of Na^{+} channels • Enhancing the action of GABA 	<u>Add-on</u> therapy for : <ul style="list-style-type: none"> • refractory partial seizures • Secondary generalized seizures 	<ul style="list-style-type: none"> • Ataxia • Dizziness • Somnolence • Weight loss • Renal stones • Decreases the ethinyl estradiol concentration of oral contraceptive preparations 	

General rules for treatment of epilepsy :

- Antiepileptic drugs suppress but not cure seizures.
- Antiepileptic drugs are indicated when there is two or more seizures occurred in short interval (6m-1y).
- An initial therapeutic aim is to use only one drug (monotherapy).
- Drugs are usually administered orally (in severe case or during attack I.V/IM).
- Monitoring plasma drug level is useful.
- Triggering factors (listed above) can affect seizure control by drugs.
- Sudden withdrawal of drugs should be avoided - Withdrawal should be slow.
- Withdrawal of drugs should be after 2-3 years up to 5 years of seizure-free period.
- To check if the patient is seizure-free you must perform EEG on the patient

Targets for Anti-Epileptic Drugs:

These drugs inhibit depolarization of neurons by the following mechanisms:

- Inhibition of excitatory neurotransmission :Glutamate
- Enhancement of inhibitory neurotransmission : GABA
- Blockage of voltage-gated positive current : Na⁺ - Ca²⁺
- Increase outward positive current : K⁺

** Many anti-seizure drugs act via multiple mechanisms.

Drugs used for treatment of Status Epilepticus :

Most seizures stop within 5 minutes. When seizures follow one another without recovery of consciousness, it is called “status epilepticus”. It has a high mortality rate . Death is from cardiorespiratory failure.

Antiepileptic drugs used in status epilepticus :

- Lorazepam /diazepam I.V
- Phenytoin / fosphenytoin (I.V)
- Phenobarbital

Pregnancy & antiepileptic medications

- NO antiepileptic drug is safe in pregnancy.
- Patient has to continue therapy.
- Using the less risky drug follow up pregnancy .