Hashemite University
H · U · M
Medical School Committee

Scientific Team
الفريق العلمي

PHARMACOLOGY

DONE BY : Volunteer

	MOA	INDICATION	PHARMACOKINATIC	ADVERSE EFFECT
Phenytoin	Blocks voltage-gated Na+channels by binding to inactive state so slow recovery	**•Focal seizures •Tonic-clonic •NOTgood for absence seizures •Status epilepticus (after BZD) •Antiarrhythmic/digoxin toxicity**	**•InducesCYP2C, CYP3A, UGT •"saturable enzyme metabolism" •Non-linear kinetics •Toxicity**	**•Nystagmus, ataxia •Diplopia, sedation •Gingival hyperplasia •Peripheral neuropathy/osteoporosis •Teratogenic •Blood: ↓ folate → Megaloblastic anemia •Drug-drug interactions: e.g., warfarin**
Carbamazepine	**Blocks Na+ channels**	**•Focal seizures •Tonic-clonic •NOTgood for absence seizures •Trigeminal neuralgia •Bipolar disorder**	**•Absorbed slowly •Long half-life (~ 30 hours) •InducesCYP2C, CYP3A, UGT**	**•Hyponatremia •Aplastic anemia •Teratogenic: Spina Bifida •Drowsiness; headache; dizziness; nausea**
Valproic acid	**•Blocks Na+ channels •Blocks GABA transaminase (GABA-T) •Blocks T-type Calcium channels**	**•Focal seizures •Generalized seizures •Absence seizures •Bipolar disorder**	**InhibitsCYP2C9, UGT, epoxide hydroxylase**	**•Hepatotoxicity •Teratogenicity •CNS-related**
Lamotrigine	**•Blocks Na+ channels •Blocks voltage-gated Ca++channels**	**•Focal seizures •Generalized seizures •Absence •Lennox-Gastautsyndrome •Bipolar disorder**	**Metabolized by UGT**	**•CNS-related side effects •Severe skin reaction (life-threatening)**
Topiramate	**•Blocks Na+ channels •Blocks L-type Calcium channels •Carbonic anhydrase inhibitor •NMDA blocker**	**•Focal seizures •Generalized seizures •Migraine prevention**	**InhibitsCYP2C9**	**•Somnolence •Weight loss •Paresthesia •Renal stones •Oligohidrosis •hyperthermia**

Zonisamide	**•Blocks Na+ channels •Blocks T-type Calcium channels •Limited carbonic anhydrase inhibitor**	**Focal seizures**	**********	**•CNS adverse effects •Nephrolithiasis •Oligohidrosis •Contraindicated in patients with sulfonamide hypersenesitivity**
Ethosuximide	**Blocks T-type Calcium channels**	**Absence seizure only (Drug of choice)**	**Half life: 30 60 hrs**	**********
Benzodiazepines Phenobarbital	**Bind to GABAA receptors and enhance GABA binding facilitates Cl-entry inhibitory**	**•*Clonazepam*adjunctive antiseizure therapy •*Diazepam*status epilepticus (drug of choice)**	**********	**********
Gabapentin Pregabalin	**•Analog of GABA •It does NOTact at GABA receptor •MOA is unknown**	**•Adjunct therapy for focal seizures •Neuropathic pain, e.g., postherpetic neuralgia, diabetic neuropathy**	**•Secreted unchanged •Few drug interactions •Suitable for elderly**	**•Sedation •Euphoria**
Felbamate	**•Blocks voltage-gated Na+channels •Blocks NMDA receptors •Blocks Ca++channels •Potentiates GABA**	**•Reserved for refractory epilepsy •Lennox-Gastautsyndrome**	**•InhibitsCYP2C19 •InducesCYP3A4**	**•Aplastic anemia •Hepatic failure •Dangerous drug**
Ezogabine	**Open voltage gated M type potassium channels stabilizing resting membrane potential**	**********	**No drug interactions at low doses**	**•Urinary retention •QT interval prolongation •Blue skin discoloration •Retinal abnormalities**

Levetiracetam	unknown	•Focal (simple and complex) seizures •Adjunct therapy for generalized seizures	**********	•Dizziness •somnolence

Mechanism of action

1-Na+-channels inhibitors •Phenytoin •Carbamazepine •Oxcarbazepine •Valproic acid •Lamotrigine •Topiramate

2-Ca++-channels inhibitors •Ethosuximide •Lamotrigine •Valproic acid

3-↑ GABAergic transmission •Benzodiazepines •Phenobarbital •Valproicacid •Gabapentin?, Pregabalin? •Felbamate

4-NMDAreceptorblockers: Felbamate,topiramate

5-AMPAreceptorblockers: Perampanel

6-H-currentmodulators: Gabapentin,lamotrigine

7-Carbonicanhydraseinhibitors: Topiramate,zonisamide

8-Neuronalpotassiumchannel(KCNQ[Kv7]) opener Ezogabine

Teratogenic : 1- Phenytoin 2- Carbamazepine 3- Valproic acid

Focal seizures : 1- Phenytoin 2- Carbamazepine 3- Valproic acid 4- Lamotrigine 5-Topiramate 6- Zonisamide 7-Levetiracetam

Tonic-clonic :1- Phenytoin 2- Carbamazepine

Status epilepticus :1- Phenytoin

Lennox-Gastautsyndrome : 1-Lamotrigine 2- Felbamate

absence seizures :1- Valproic acid 2- Lamotrigine 3- Ethosuximide 4- Gabapentin+Pregabalin(adjusant)

Generalized seizures :1- Valproic acid 2- Lamotrigine 3- Topiramate 4- Levetiracetam

Trigeminal neuralgia : 1- Carbamazepine

Bipolar disorder : 1-Carbamazepine 2- Valproic acid 3- Valproic acid

Migraine prevention : 1- Topiramate

Induce hepatic metabolism :1- Phenytoin 2- Carbamazepine

Inhibit hepatic metabolism : 1-Valproic acid 2- Topiramate 3- Felbamate

Aplastic anemia : 1- Carbamazepine 2- Felbamate

Hyponatremia : 1- Carbamazepine

Hepatotoxicity : 1- Valproic acid 2- Felbamate

Severe skin reaction (life-threatening) :1- Lamotrigine

Somnolence : 1-Topiramate 2- Levetiracetam

Weight loss : 1- Topiramate

Paresthesia :1- Topiramate

Renal stones: 1- Topiramate 2- Zonisamide

Oligohidrosis: 1- Topiramate 2- Zonisamide

Hyperthermia: 1- Topiramate

•Urinary retention 1-Ezogabine

•QT interval prolongation 1-Ezogabine

•Blue skin discoloration 1-Ezogabine

•Retinal abnormalities 1- Ezogabine

EXTRA NOTE

- **Fosphenytoin Is prodrug of Phenytoin**
- **Oxcarbazepine Prodrug to Carbamazepine with Less side effects**
- **Other preparation of Valproic acid 1-Sodium valproate 2-Divalproex sodium**
- **Zonisamide has sulfonamide hypersenesitivity**
- **Gabapentin + Pregabalin use for neuropathic pain**