

Anti-Epileptic Agents ⚡

1. Carboxamide derivatives	2. Benzodiazepines	3. Barbiturates	4. Hydantoin derivative	5. Fatty acid derivative
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Cabamazepine	Clonazepam	Phenobarbital	Phenytoin	Valproate
	Diazepam			
	Lorazepam			
	Midazolam			

1. Cabamazepine

Trade names: Tegretol, Degranol and Sandoz-Carbamazepine

Oral dosage form tablet: sustained release tablet and suspension

Primary drug for partial and generalized tonic clonic seizures

Not effective in absence seizure

Mechanism of action ⚡

- In seizure dysfunctional sodium channels allow for too much influx of Sodium ion which prolongs neuronal excitability (depolarization)
- Carbamazepine limits repetitive firing of action potential (limits too much influx of sodium ion)
- This is due to prolonging the Sodium channel inactivation

Side effects and Toxicity

Cardiac arrhythmias with or without hypertension

Behavioral change

Gastrointestinal symptoms

Hirudism

Megaloblastic anemia

Pharmacokinetics ⚡

- Phenytoin distributes into the body tissues, including the brain, within **30 to 60 minutes after reaching the systemic circulation**
- **Effective for up to 24 hours**
- Metabolized by hepatic cytochrome P450

Drug interactions:

Reduces the effect of **oral contraceptives** Reduces the effect of **warfarin**

Could result in unplanned pregnancy Could result in deep vein thrombosis

Cytochrome P450 inducer

5. Valproate

Trade Names: Epilium liquid, Epilium CR, Epilium IV, Epilium crushable, Convulox, Navalpro, Eprolep

Oral and paranal dosage form: Tablet, capsule, suspension, IV

Effective against absence, myoclonic partial and tonic clonic seizures, suitable for **HIV positive children with epilepsy**

Mechanism of action ⚡

- Mechanism of action is not fully understood
- It is believed that valproic acid leads to increased production of GABA
- In addition to this, valproate is also thought to enhance the effect of GABA that already exists in the area on the receptors.
- Valproate mimics the action of GABA

Pharmacokinetics

- Absorbed rapidly and completely after oral administration with 81-89% bioavailability. Active for around 9-16 hours
- Metabolized by hepatic cytochrome P450

Side Effects and Toxicity ⚡

Anorexia

Vomiting

Nausea

Sedation ataxia

Tremor

Rash

Alopecia

Increased appetite

Drug interactions

All benzodiazepines cause excessive sedation when combined with other medications that slow the brain's processes. (i.e, alcohol, barbiturates narcotics, and tranquilizers)

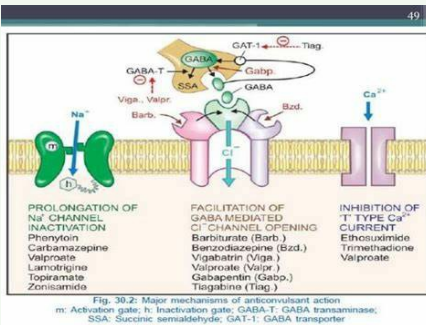
For Benzodiazepines

2. BENZODIAZEPINES ⚡

Drug type:	Trade names:	Indication:
Clonazepam	Rivotril, Clonam	Drops, tablet, IV
Diazepam	Pax, Valium, A-Lenon, Transjet, Betapam, Doval	Tablet, IV
Lorazepam	Ativan, Tranqipam	Tablet, IV
Midazolam	Accord, Sabax, Midaium, Dormicum, Midazoject	IV, tablet, INF



Mechanism of action ⚡



Indication of Benzodiazepines

- Prolonged seizure activity, less than **5 minutes between seizures**
- Can last up to **20 minutes or more**
- EML recommends which drug to stop status epilepticus

In Status Epilepticus

Mechanism of action ⚡

- Benzodiazepines cause activation of the GABA_A receptor and opening of the Chlorine channels associated with the receptor
- The neuronal membrane is hyperpolarized and is less likely to fire
- Also inhibit excitatory glutamate receptors

Benzodiazepines

Clonazepam	Diazepam	Lorazepam	Midazolam
Used for broad spectrum of seizures	First line treatment in Status Epilepticus	First line treatment in Status Epilepticus	First line treatment in Status Epilepticus

Benzodiazepines (cont)

Effective in Status Epilepticus	Rarely used for long term	Rarely used for long term	Rarely used for long term	Not for long term use - develops tolerance Completely metabolized in liver and excreted in urine
Absence seizure	Good oral absorption	Better than Diazepam	Effective in Status Epilepticus that has not improved following other treatments or when intravenous access can not be obtained	Side Effects and Toxicity ⚡ Drowsiness and confusion Blurred vision Slurred speech Lack of coordination and weakness Difficulty breathing Coma
For Benzodiazepines				

3. Phenobarbital

Given in combination	Completely metabolized in liver and excreted in urine	Good oral absorption	Good oral absorption	Phenobarbital, Propain Forte, Donatal Elixir, Lethyl Sedabarb Tablet, syrup Low toxicity, inexpensive, widely used for young children
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Good oral absorption

Completely metabolized in liver and excreted in urine

3. Phenobarbital (cont)

Non-selective to the type of seizure. **Mainly used for generalized tonic clonic and partial seizures and status epilepticus 20mg/kg, crushed and given by nasogastric tube** (if one dose of midazolam or two doses of diazepam fail to show response)

Mechanism of action ⚡

- ❑ Through its action on GABA receptors, phenobarbital increases flux of chlorine ions into the neuron which decreases excitability.
- ❑ Direct blockade of excitatory glutamate signaling is also believed to contribute to the hypnotic/anticonvulsant effect

Pharmacokinetics

- Oral absorption is complete but slow
- Peak concentration in plasma is seen after several hours (8-12 hours) after oral administration
- Remains in the body for a long time (2-7 days)
- Metabolized by liver (cytochrome p450)

Side effects and Toxicity

Sedation (tolerance develops after continues use)

Driving and use of heavy machinery must be avoided

Irritability and hyperactivity in children

Agitation and confusion in the elderly

Some skin allergies in rare cases

Drug interactions:

Reduces the effect of oral contraceptives	Reduces the effect of warfarin
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Drug interactions: (cont)

Could result in unplanned pregnancy	Could result in deep vein thrombosis
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Cytochrome P450 inducer

4. Phenytoin

Trade Names:	Epanutin Forte suspension, Epanutin Infatabs, Epanutin Ready Mixed Parantal
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Oral and parantal dosage form: Tablet, capsule, suspension, IV

Active against **all types of partial and tonic clonic seizures but not absence seizures**

Causes **antiseizure activity without causing general CNS depression**

Mechanism of action ⚡

- In seizure dysfunctional sodium channels allow for too much influx of Sodium ion which prolongs neuronal excitability (depolarization)
- Phenytoin Limits repetitive firing of action potential (too much influx of sodium ion)
- This is due to slowing the rate of recovery of Sodium channels from inactivation.

Pharmacokinetics ⚡

- Phenytoin distributes into the body tissues, including the brain, within **30 to 60 minutes after reaching the systemic circulation**
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Side effects and Toxicity

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