



ANTI-SEIZURE MEDICATIONS

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Epilepsy Treatments

- **Pharmacologic Therapy**
 - Antiepileptic drugs (AEDs)
- Non-pharmacologic Therapy
 - Ketogenic diet
- Surgical Therapy
 - Epilepsy surgery
- Non-Drug Therapies



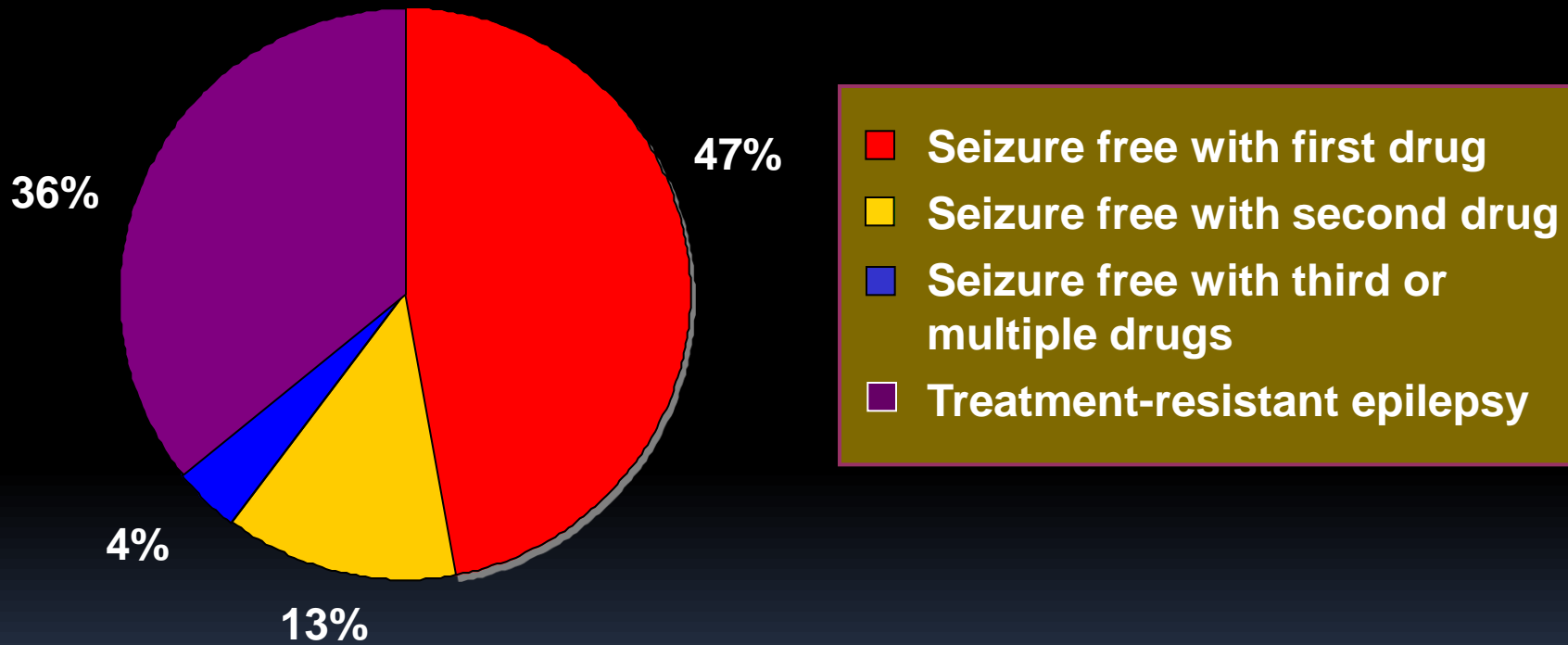
Epilepsy Treatment

- Step 1
 - See a doctor, preferably an epilepsy specialist
 - Clinical history
 - Diagnostic testing
 - Establish the diagnosis
 - Characterize and Classify the events
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What Is Treatment-resistant Epilepsy?

- Seizures that continue even on AEDs
 - Frequency
 - Severity
 - Duration
 - Adverse effects
- Persistence of seizures despite at least 2 anti-seizure drugs that work by different mechanisms and have achieved therapeutic levels
- Applies to ~1/3 of all newly treated patients
- Very negative impact on quality of life

Intractable Epilepsy



Goals of Epilepsy Therapy

- Long-term seizure control
- Long-term quality-of-life benefits
- Safety
- Assured compliance
- No interactions with other medications
- No side-effects or complications
- *There is no single treatment modality that guarantees all of these goals*

Pharmacologic Treatment

- Wide range of anti-seizure drugs to choose from
- Can change medications fairly easily
- Adjunctive (polypharmacy) often used
- Current AEDs have been thoroughly researched
- Prescribed for neonates, children, adults, & elderly

Pharmacologic Treatment

- Factors in choosing Treatment
 - Diagnosis
 - Syndrome v.s. Localization
 - Cost
 - Patient Profile
 - Wishes, co-morbidity, profession, resources
 - Drug Profile
 - Mechanism of action, side effects, quantitation
 - FDA Approval

Pharmacologic Treatment

New AED's

- Fewer serious adverse effects
 - i.e. many are better tolerated
- Class C
 - Fetal abnormalities in animals*
- Rash +/- SJS
- HA
- Sedation
- Visual blurring
- Irritability
- Cognitive Disturbance
- glaucoma
- Kidney stones
- SIADH
- Hematologic d/o
- Hepatotoxicity, Anemia, MOF

Old AED's

- Sedation
- Hair Loss
- Weight gain
- Tremor
- Gingival hyperplasia, hirsutism
- Hepatic Necrosis +/- MOF
- Hematologic d/o
- Rash +/- SJS, TEN
- SIADH
- Osteoporosis
- Known teratogenicity
- Cortical & Cerebellar Atrophy
- Cognitive Dysfunction
- Ataxia

Pharmacologic Treatment

	Enzyme Inducer	Enzyme Inhibitor	Other AEDs	Warfarin	Digoxin
Keppra®	0	0	0	0	0
Carbamazepine	✓	0	✓	✓	0
Phenytoin	✓	0	✓	✓	✓
Valproic acid	0	✓	✓	✓	0
Gabapentin	0	0	0	0	0
Lamotrigine	✓	0	0	0	0
Oxcarbazepine	✓	✓	✓	0	0
Pregabalin	0	0	0	0	0
Tiagabine	0	0	✓	0	0
Topiramate	✓	✓	✓	0	✓
Zonisamide	0	0	✓	0	0

Antiepileptic Drugs: Mechanism of Action

	Generic Name	<i>Mechanism of Action</i>				
		Sodium Channel Inhibitor	Ca ²⁺ Channel Modifier	GABA Augmenting	Glutamate Reducing	SV2A
Older AEDs	Carbamazepine	X				
	Valproate			?		
	Phenytoin	X				
	Phenobarbital			X		
Newer AEDs	Gabapentin		X			
	Lamotrigine	X			?	
	Oxcarbazepine	X				
	Tiagabine			X		
	Topiramate				X	
	Levetiracetam					X
	Zonisamide	?	?			
	Pregabalin		X			

Carbamazepine (Carbatrol/Tegreto1)

Indications

- Monotherapy for Partial seizures with complex symptomatology (psychomotor, temporal lobe); generalized tonic-clonic seizures (grand mal); mixed seizure patterns that include the above, or other partial or generalized seizures.

Forms

- Immediate and Extended/Controlled release
- Tablets (200 mg IR; 100xr/200xr/cr/300cr/400xr mg), Chewable Tablets (100 mg), Suspension (100 mg/5 ml)

How to take

- As directed; not with grapefruit juice;

Specific Cautions

- Rash (Stevens Johnson Syndrome); Blood disorders; liver disease; bone health

Clonazepam (Klonipin)

Indications

- absence and myoclonic seizures (e.g. LGS), seizure clusters

Forms

- 0.5, 1.0, 2.0 mg tablets (not chewable)

How to take

- Begin with low dose, at night, increasing slowly as tolerated

Specific Cautions

- Benzodiazepine (sedative-hypnotic class of drug)
- Sedation, rash, behavioral/mood/memory disturbance, blood/liver disorder, tolerance

Ethosuximide (Zarontin)

Indications

- Absence (Petit mal) Epilepsy

Forms

- 250 mg tablets (not chewable); suspension – 250 mg/5 mL

How to take

- The optimal dose for most pediatric patients is 20mg/kg/day

Specific Cautions

- Nausea, anorexia, abdominal pain, vomiting, gum overgrowth, blood disorders, behavioral changes, rash, SJS, SLE, visual disturbance

Felbamate (Felbatol)

Indications

- monotherapy and adjunctive therapy for partial-onset seizures and tonic-clonic seizures in adults 14 years of age and older; adjunctive therapy for partial and generalized seizures, including the atonic seizures associated with LGS, in children aged 2 to 14 years;

Forms

- 400, 600 mg tablets; 600 mg/5 mL suspension

How to take

- 200-300 mg twice a day and increase as tolerated; children is 15 mg per kilogram; frequent and regular blood work

Specific Cautions

- Felbatol is recommended only for those patients whose epilepsy is so severe that a substantial risk of aplastic anemia or liver failure is considered acceptable in light of the potential benefits of its use; if these criteria are met, and the patient has been fully advised of the risk, Felbatol can be considered for use either alone or in combination with other seizure medicines.

Gabapentin (Neurontin)

Indications

- Add-on therapy for partial seizures with or without secondary generalization in patients 12 years of age and older.
- It does not prevent primary generalized seizures such as absence, myoclonic, or primary generalized tonic-clonic seizures.

Forms

- 100, 200, 400 mg capsules/tablets

How to take

- Usually begin at 100-300 mg 2-3 times a day; may increase up to 1200 mg 3 times a day

Specific Cautions

- unsteadiness, weight gain, fatigue, dizziness



Lacosamide (Vimpat)

Indications

- Add-on therapy for adults with partial-onset seizures


Forms

- 50, 100, 150, 200 mg pill sizes; suspension;

How to take

- Swallowed whole;
- Begin with 50 mg twice a day and increase weekly or bi-weekly.

Specific Cautions

- dizziness, headache, nausea or vomiting, double vision, sleepiness and fatigue, unsteadiness and shakiness; EKG abnormalities
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Lamotrigine (Lamictal)

Indications

- A broad-spectrum alternative to Depakote with a better side effect profile; it may not be as effective for myoclonic seizures;
- Add-on therapy for 2 yrs and up: simple and complex partial seizures; generalized seizures of Lennox-Gastaut syndrome (LGS); primary generalized tonic-clonic seizures and monotherapy for adults (after conversion from older generation aed)

Forms

- Immediate & Extended Release
- IR – 2,5,25 (chewable); 25,50,100,150,200; ER – 50, 100, 200

How to take

- As directed

Specific Cautions

- Dizziness, fatigue, insomnia; rarely Stevens Johnson Syndrome

Levetiracetam (Keppra)

Indications

- Add-on therapy – for partial-onset seizures in patients aged 4 years or older with epilepsy, for myoclonic seizures in patients aged 12 years or older with JME (juvenile myoclonic epilepsy), and for primary generalized tonic-clonic seizures in patients 6 years of age and older with idiopathic generalized epilepsy

Forms

- Capsule: 250, 500, 750, 1000; Suspension (100 mg/5 ml); Injectable 100 mg/1 ml);

How to take

- As directed; usually begin with 250-500 mg twice a day

Specific Cautions

- Irritability, hostility, depression in up to 1/3 of patients; rash

Oxcarbazepine (Trileptal)

Indications

- Same as Carbamazepine (4 years and up); not effective against absence or myoclonic seizures

Forms

- 150, 300, 600 mg tablets; 300 mg/5 mL suspension

How to take

- As directed
- Usually start with 75-300 mg twice a day

Specific Cautions

- Anaphylaxis, angioedema, hyponatremia, SJS

Phenobarbital (Luminal)

Indications

- add-on therapy for partial and tonic-clonic seizures; also used for treatment of status epilepticus; in use for nearly a century

Forms

- 15, 30, 60, 100 mg pills; 20mg/5 ml suspension

How to take

- As Directed; usually once a day at bed time;

Specific Cautions

- Overdose, sedation, respiratory suppression, rash, SJS, liver/blood disorder, dependence, withdrawal, bone health, fetal health

Phenytoin (Dilantin/Phenytek)

Indications

- Monotherapy (all ages) for partial seizures & primary GTC (grand mal)
- Phenytoin is best partial-onset seizures; generally is not effective against generalized-onset absence seizures or infantile spasms; limited value in clonic, myoclonic, and atonic seizures and in the Lennox-Gastaut syndrome. It may control the tonic-clonic component of the syndrome.

Forms

- 100 mg capsules (IR/ER); 125 mg/5 mL suspension

How to take

- As directed; usual daily dose is 300 mg once daily

Specific Cautions

- unsteadiness and moderate cognitive problems;
- potential cosmetic (body/face hair growth, skin problems); difficult to control levels; bone health; fetal health; rash; SJS

Pregabalin (Lyrica)

Indications

- add-on treatment for partial and secondarily generalized; it does not prevent primary generalized seizures such as absence, myoclonic, or primary generalized tonic-clonic seizures

Forms

- 25, 50, 75, 100, 150, 200, 225, 300 mg capsules

How to take

- Typical adult dose is 150 - 600 mg bid; begin with 50 mg 1-2 times daily, increasing weekly

Specific Cautions

- Pregabalin has no drug interactions, no liver metabolism, no protein binding, and similar side effects to gabapentin;

Primidone (Mysoline)

Indications

- Add-on for grand mal, psychomotor, and focal epileptic seizures in adults and children years 4 of age and older. It may control grand mal seizures and myoclonic seizures (e.g JME) refractory to other anticonvulsant therapy.

Forms

- 50, 250 mg tablets

How to take

- As directed; usually begin with 50-100 mg 1-2 times daily and increased as tolerated

Specific Cautions

- Sedation, blurred vision, allergic/anaphylaxis, fetal health, blood disorders

Rufinamide (Banzel)

Indications

- Add-on (adjunctive) seizure medicine in children 4 years and older and adults with the Lennox-Gastaut (LGS) syndrome.

Forms

- Banzel is marketed in the United States by Eisai, Inc.
- Tablets : 200 mg and 400 mg salmon colored tablets
- There is presently no injectable form of rufinamide.

How to take Banzel:

For adults, a starting dose of 200 mg twice a day is recommended;

- Dosing can be increased by adding an extra 200 (or 400) mg twice a day every two days, to a maximum of 1600 mg twice a day (3200 mg per day total).
- For children, a starting dose of 10 mg/kg/day in 2 equal doses, increased by the same amount every two days, up to 45 mg/kg/day or 3200 mg/day.

Specific Cautions

- Short QT Syndrome

Topiramate (Topamax)

Indications

- monotherapy and adjunctive therapy for: partial-onset seizures in adults and children ages 2-16 years, primary, generalized tonic-clonic seizures in adults and children ages 2-16 years, seizures associated with LGS two years of age and older
- Topamax is FDA-approved as initial monotherapy for patients 10 years of age and older with partial-onset or primary generalized tonic-clonic seizures.

Forms

- Tablets (25, 50, 100, 200 mg) and Sprinkle Capsules (15, 25 mg)

How to take

- As directed; Typical adult dose is 150-200 mg twice a day, beginning with 25 mg twice a day, increasing by same amount weekly.

Specific Cautions

- Cognitive problems in about 1/3rd, renal stones in 1-2%, rare cases of glaucoma, weight loss, metabolic acidosis, behavioral issues including depression, agitation, hostility, psychosis; sulfa allergy

Valproic Acid (Depakote)

Indications

- All ages - monotherapy or adjunctive therapy for simple or complex absence seizures, either alone or with other seizure types (such as for juvenile myoclonic epilepsy); also effective for partial seizures.

Forms

- Pill (immed/extended release) -250/500 mg , suspension (depakene) – 250 mg/5 mL; injectable (depacon)

How to take

- Typical adult dose is 250 mg - 500 mg three times a day, but can be higher

Specific Cautions

- weight gain, tremor, hair loss, GI upset, blood disorders, hepatic or pancreatic injury, bone health(osteoporosis), fetal health

Vigabatrin (Sabril)

Indications

- partial seizures, with or without secondary generalization; infantile spasms

Forms

How to take

- A typical regimen begins with 500 mg twice a day, increased bi-weekly or longer as tolerated to 1500 mg twice a day.

Specific Cautions

- Blindness/retinal toxicity

Zonisamide (Zonegran)

Indications

- Add-on therapy for partial seizures in adults with epilepsy; may be effective for other types of epilepsy and epilepsy syndromes, including: LGS, infantile spasms (West syndrome), progressive myoclonic epilepsy (PME)

Forms

- capsule

How to take

- As directed; 200-400 mg once daily is typical adult dose, beginning with 50-100 mg once daily;

Specific Cautions

- Similar to Topiramate, but less evidence of glaucoma and cognitive side effects
- Sulfa allergy

Acetazolamide (Diamox)

Indications

- Absence seizures, unlocalized seizures, catamenial seizures

Forms

- 125, 250 mg tablets

How to take

- As directed
- total daily dose is 8 - 30 mg per kg in twice a day; optimum range is 375 - 1000 mg daily, though some patients do better on lower dose

Specific Cautions

- Tinnitus, numbness, tingling, nausea, vomiting, loss of appetite, rash (sulfa allergy), SJS, blood disorders, acidosis

Investigational AEDs

- Brivaracetam (UCB: UCB100406: Rikelta)
 - 2-pyrrolide derivative - (2S)-2-[(4R)-2-oxo-4-propylpyrrolidin-1-yl] butanamide - modulates SV₂A activity and inhibits Na⁺ channels;
 - structurally related to Levetiracetam – 10-100x greater affinity for SV₂A
 - Targeted for adjunctive treatment of partial onset sz, myoclonic sz
 - Reductions in sz frequency >50% with 50 mg/day

Investigational AEDs

- Carisbamate (OMN: YKP-509, RWJ-333369, JNJ-10234094)
 - [(2*R*)-2-(2-Chlorophenyl)-2-hydroxy-ethyl] carbamate
 - Structurally related to Felbamate
 - Unique MOA – SV₂A + augments GABAergic transmission
 - No cognitive, behavioral, psychiatric side effects;
 - Weight neutral

Investigational AEDs

- Eslicarbazepine (Bial: BIA 2-093)
- [(S)-(--)-10-acetoxy-10,11-dihydro-5H-dibenz[b,f]azepine-5-carboxamide]
- voltage-gated Na⁺ channel (VGSC) blocker
- shares with carbamazepine and oxcarbazepine the dibenzazepine nucleus bearing the 5-carboxamide substitute, but is structurally different at the 10,11-position - preventing the formation of toxic epoxide metabolites such as carbamazepine-10,11 epoxide.
- rapidly and extensively metabolized to eslicarbazepine (S-licarbazepine), which is responsible for pharmacological activity

Investigational AEDs

- Retigabine (Valeant Pharmaceuticals)
- N - [2 - amino - 4 (4 - fluorobenzylamino) - phenyl] carbamic acid ethyl ester
- Neuronal K⁺ channel ligand (KCN Q₂/Q₃)
- Enhances GABA-ergic transmission
- Blocks 4-AP induced synthesis of EAA
- Phase 2 studies revealed a reduction in monthly seizure rates of 23 to 35 percent as adjunctive therapy in patients with partial seizures (300-1200 mg/day).
- Phase 3 studies currently ongoing (adjunctive treatment for partial-onset seizures in adult patients with refractory epilepsy).

Generic and Name Brand

- People who switch from brand-name to generic drug possibly risk having more seizures or side effects during the changeover, because the body does not absorb the different types in the same way.
- Switching from one company's generic to another company's generic may have similar risks and so can switching from generic to brand-name;
- All these risks are not fully known;
- For some people the effects of changing from one type to another are very small.
- Some patients use generic drug successfully by always using the same company's product - then the dosage can be adjusted to achieve the best results.

Epilepsy Treatment

- Multiple Treatment Options
 - Drugs, diets, invasive/non-invasive surgery, alternative therapies
- Step 1
 - See a doctor, preferably an epilepsy specialist
 - Sometimes repeat testing is necessary (to clearly define the diagnosis, to make sure the medications are working, to adjust the medications, if spells change or worsen)
- Step 2
 - Take treatments as recommended
 - Establish care plans in the office
- Step 3
 - Follow-up with your Doctor – don't disappear
 - Report side effects, positive benefit, no benefit, etc
 - Ask for help