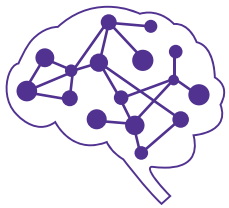

AMERICAN EPILEPSY SOCIETY

CURRENT REVIEW IN CLINICAL SCIENCE

Summary of **Antiepileptic Drugs** Available in the United States of America

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AMERICAN EPILEPSY SOCIETY

WORKING TOWARD A WORLD WITHOUT EPILEPSY

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The current review summarizes the main antiepileptic drugs available for prescription in the United States as of July 2018. One condensed, and one expanded, table of the major properties of 28 AEDs are presented both to assist clinicians in providing care to persons with epilepsy and to facilitate the training of those in health care educational programs.

This table is not intended to constitute recommendations, only to provide an easy reference listing of products on the market.

Two and one-half decades ago, the choice of antiepileptic drugs (AEDs) was relatively limited. Beginning in August 1993 in the United States, the first new AED in approximately 15 years was approved by the U.S. Food and Drug Administration (FDA). Since then a panoply of AEDs have been approved. The vast majority of these are in new drug classes, and many have novel mechanisms of action. Furthermore, most have pharmacokinetic properties which are different from older AEDs.

Now that approximately 28 AEDs are available in the U.S. it can be challenging for epileptologists, neurologists, pharmacists, nurses, trainees, and other healthcare professionals to quickly access and cross-reference information needed in clinical practice to optimally select and use these medications. The Treatments Committee of the American Epilepsy Society created this document as a tool to help meet this need. Data for these summaries were obtained in July 2018 from the most recent FDA-approved prescribing information (PI) for each AED available on the www.FDA.gov website (1). It was noted that PIs for all AEDs approved since 1993, carbamazepine, divalproex and phenytoin were substantially more detailed than were PIs for other older drugs. Phenobarbital is no longer listed on the FDA website, but an older PI was used to obtain FDA-approved information (2). In instances where PIs lacked important data to permit comparison of one AED to another, AED pharmacology texts were used to supplement the tables (3,4). Serum level ranges are based on the clinical experience of the Treatments Committee members. The FDA-approved PI was the primary source of information to compile these tables. It is important to emphasize that the actual practice of providers may differ substantially from official approved indications, doses, dose frequency and other parameters.

Table 1 is a condensed summary of data on all AEDs currently available in the United States as of July 5, 2018. Table 2 is an expanded summary of these AEDs, adding additional data on pharmacokinetics, adverse effects, and drug-drug interactions. These tables will also be made available as PDF documents on the website of the American Epilepsy Society, and will be updated periodically. The hope is that providers will find these to be beneficial in the advanced care of persons with epilepsy.

References:
1. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm Accessed July 2018
2. Eli Lilly and Company. Phenobarbital. In: Physicians' Desk Reference. 1997;1523-5. Medical Economics Company, Montvale, New Jersey USA
3. White HS and Rho JM. Mechanisms of Action of Antiepileptic Drugs. 2010 Professional Communications, Inc., West Islip, New York, USA
4. Levy RH, Mattson RH, Meldrum BS, Perucca E. Antiepileptic Drugs, 5th Edition. 2002 Lippincott Williams Wilkins, Philadelphia, Pennsylvania, USA

TABLE 1. CONDENSED LIST OF AEDS

DRUG AND FORMULATIONS	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (METABOLISM AND T½)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
Adrenocortico-tropic hormone (ACTH) I.M. injection (80 IU/mL)	epileptic spasms, mono, <2	Stimulates adrenal secretion of cortisol, corticosterone, aldosterone and other steroids	Not adequately characterized. T ½ = 0.25 (i.v.)	--	Multiple regimens. Manufacturer: 75 IU/m² IM BID for 2 weeks, then taper over 2 weeks	N.A.	Infections, adrenal insufficiency, HTN, Cushing syndrome, salt/water retention, ↓ K^+ alkalosis, gastric ulcers, bleeding, weight gain, bowel perforation, behavior or mood disturbances.	Contra-indicated to give i.v., with congenital or other infections, recent surgery, uncontrolled hypertension, sensitivity to porcine proteins, or with live or live-attenuated vaccines.	DDI not studied. Consider BP and glucose monitoring, and GI prophylaxis with an H2 blocker.
brivaracetam (BRV) Tablet; oral solution; i.v. solution	Focal, mono, 4+ (i.v. formulation not approved below age 16 years)	Inhibits synaptic vesicle SV2A protein	Metabolism: 1° hydrolysis, 2° CYP2C19 hydroxylation, CYP2C9 hydrolysis then renal excretion. T ½ = 9 hrs.	50 mg BID	25-100 mg BID	Not determined	Sedation, N/V, dizzy, suicidal thoughts, anger, psychosis	Bronchospasm, angioedema	Rifampin ↓ BRV 45%; EIAEDs ↓ BRV 19-26%; BRV ↑ PHT 20% and CBZ-epoxide 100%
cannabidiol (CBD) Oral solution (100 mg/mL) C - to be determined	Seizures associated with LGS or Dravet 2+	Unclear. Does not interact at CB1 or CB2 receptors. Potential targets include blockade of orphan G protein-coupled receptor 55 (GPR55); agonist at transient receptor potential vanilloid receptor (TRPV1); modulation of adenosine-	Extensively metabolized, principally via CYP3A4, 2C19. 7-OH-CBD metabolite appears to be active Elimination T1/2 ~ 60 hrs; Effective T ½ ~17 hrs	2.5 mg/kg given BID x 1 week	10-20 mg/kg/d, divided BID Reduce dose in moderate to severe hepatic impairment. May take with or without food, but pt. must be consistent	Not established	Somnolence/ sedation, that may be increased by CLB. Elevated transaminases.....(as is through)....VPA. Decreased appetite/weight loss, diarrhea, fatigue, malaise, rash, insomnia, sleep disorder, infections, irritability	LFT and bilirubin monitoring before, and at 1, 3 and 6 months of, treatment, especially with concomitant VPA. Artisanal formulations of CBD are not biopharmaceu-tically equivalent and should not be substituted	Other drugs which inhibit or induce CYP3A4 or 2C19 may alter CBD kinetics. CBD inhibits CYP2C19 thereby ↑ 3x the plasma concentration of N-desmethyl CLB. CBD may also inhibit CYP2C9, 2C8 and 1A2, and UGT1A9 and UGT2B7 substrates

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…*Continued* **cannabidiol (CBD)**		mediated signaling						May cause fetal harm, hypersensitivity reactions.	
carbamazepine (CBZ) IR/ER tablet, ER capsule, chewable tablet, suspension 20 mg/mL	Focal, mono; GTCS; mixed types	Enhances Na^+ channel rapid inactivation; block L-type Ca^{2+} channel	CYP3A4 to CBZ 10-11 epoxide; metabolites found in urine > feces. T ½ = 25-65 hrs initially, then T ½ = 12-17 hrs 3-5 wks later (autoinduction).	2-3 mg/ kg/day divided BID or TID	Increase q 2-3 weeks, up to 2400 mg/day (divided TID or 4/day for IR; BID for ER).	4-12	Sedation, diplopia, ataxia, dizziness, blurred vision, hyponatremia, N/V; low WBC counts; decreased T3, T4; increased LFTs; worsens GTCS in pts with absence seizures	SJS & TEN (↑ risk with HLA-B*1502), aplastic anemia, agranulocyto-sis, DRESS, rash. Avoid in porphyria. Contraindica-tions: bone marrow suppression, hypersensitivity to TCAs, or with nefazadone, boceprevir, delavirdine, and MAOIs	Induces CYP1A2, 2B6, 2C9/19, & 3A4 so OCs, warfarin, and others are affected. CBZ is inhibited by macrolides. In hepatic impairment, monitor CBZ concentration.
clobazam (CLB) tablet, oral suspension (2.5 mg/mL). C-IV	LGS, adj, 2+	$GABA_A$ receptor agonist	CYP3A4 > 2C19 & 2B6, to N-desmethyl-CLB, then metabolized by CYP2C19. T ½ = 36-42 hrs; 71-82 hrs. for metabolite	If ≤30 kg = 5 mg/d; If >30 kg = 5 mg BID	If ≤30 kg = up to 10 mg BID; If >30 kg = up to 20 mg BID	0.25-0.75	Sedation, fever, UTI, URI, drooling, constipation, insomnia, vomiting, irritability, ataxia, depression, dependence, withdrawal	Rash, rarely SJS and TEN. Use with opioids can cause profound sedation, respiratory depression, coma & death	Weak CYP3A4 inducer, so may affect OCs. CLB inhibits CYP2D6. Cannabadiol, ethanol and CYP2C19 inhibitors inhibit CLB metabolism.
clonazepam (CZP) Tablet, ODT tablet. C-IV	LGS. Myoclonic and absence Sz, mono- or adj, no age specified	$GABA_A$ receptor agonist	Reduced by CYP3A4; the derivative is further metabolized. T ½ = 30-40	If ≤30 kg = 0.01-0.03 mg/kg/ day divided BID or TID	1-20 mg/day divided TID If ≤30 kg = 0.1-0.2 mg/kg/day	0.04-0.07	Sedation, dizziness, ataxia, drooling, resp. depression, impaired cognition or motor skills, agitation, anger, anxiety, nightmares, hallucination, psychoses, depression,	With opioids can cause respiratory depression, coma & death. Contraindica-tions: acute narrow angle glaucoma, significant liver	Worsened or new TCS. VPA + CZP may cause absence SE. Withdraw gradually to avoid SE. Periodic CBC and liver tests recommended. CBZ, LTG, PB and PHT ↓ CZP levels ~38%. Oral antifungal agents (e.g.,

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…*Continued* **clonazepam (CZP)**							dependence, tolerance.	disease, sensitivity to BDZs	fluconazole) may inhibit CZP metabolism.
diazepam (DZP) Tablet; rectal gel (5 mg/mL); i.v. solution. C-IV	Acute repetitive (rectal gel, adj., age 2+)	$GABA_A$ receptor agonist	CYP2C19 & 3A4 to desmethyl-diazepam. Clearance is highly variable likely due to CYP2C19 slow metabolism in 3-5% of Caucasians. T ½ for i.v: infant = 40-95, child = 15-20, adult = 15, elderly = up to 95 hrs. T ½ for p.r. = 46 hrs.	Oral and i.v. = 0.15 - 0.2 mg/ kg/dose, max 10 mg/dose P.R. = age 2-5 = 0.5 mg/kg; age 6-11 = 0.3 mg/kg; age 12+ = 0.2 mg/kg	Oral and i.v. = N.A. P.R. = weight-based, repeat once prn 4-12 hrs. after first dose, give no more than every 5 days or 5 times/month	N.A.	Sedation, dizziness, depression, fatigue, motor and cognitive impairment, dependence. Not recommended for chronic, daily use (tolerance). Tonic SE has occurred with i.v. DZP use for absence SE. Withdrawal effects after chronic use.	Use with opioids can cause respiratory depression, coma & death. Contraindica-tion: narrow angle glaucoma.	Absence SE. ↓ clearance in alcoholic cirrhosis. CNS-depression ↑ by VPA, PB, narcotics, phenothiazines, other antidepressants. Inhibitors of CYP2C19 (cimetidine) and CYP3A4 (azoles) may ↓ DZP clearance. Inducers of 2C19 (rifampin) and 3A4 (CBZ, PB, PHT, dexamethasone) may ↑ elimination.
eslicarbazepine (ESL) acetate Tablet	Focal, mono, 4+	Enhances Na^+ channel rapid inactivation; blocks HCav3.2 Ca^{2+} channel; enhances K+ conductance	ESL acetate hydrolyzed to ESL; renal excretion as ESL and ESL glucuronide. Linear. T ½ = 13-20 hrs.	11 - 21 kg = 200 mg/day; 22 - 38 kg = 300 mg/day; 39+ kg = 400 mg/day.	11 – 21 kg = 400-600 mg/day; 22 - 31 kg = 500 - 800 mg/day; 31 - 38 kg = 600-900 mg/day; 39+ kg = 800 – 1600 mg/day.	possibly 10-35 (as OXC MHD)	1-1.5% hyponatremia (<125); dizziness, sedation; diplopia, HA, N/V ataxia, tremor	SJS & TEN (↑ with HLA-B*1502), angioedema, DRESS, anaphylaxis	EIAEDs induce ESL metabolism. ESL induces OCs, statins and S-warfarin. ESL inhibits CYP2C19: ↑ PHT level
ethosuximide (ESM) Capsule (gel); oral solution	absence	Affects low-threshold, slow, T- Ca^{2+} thalamic currents	Metabolism: CYP3A4 & CYP2E1 Clearance may be nonlinear at higher doses (saturable) T ½ ~ 30 hrs. (children),~ 60 hrs. (adults).	Children age 3-6: 250 mg/d. Age 6+: 250 mg BID.	Children: optimal is 20 mg/kg/day. Adults: 1500 mg divided BID - TID	40-100	N/V, abd. pain, anorexia, weight loss, diarrhea, sedation, dizziness, ataxia, ↓WBC, depression, hyperactivity, irritability, psychosis, sleep disturbance, gum hypertrophy, tongue swelling	SJS, rash, DRESS, pancytopenia, eosinophilia, lupus. Use cautiously with renal or hepatic disease.	TDM: CBC & CMP. May increase TCS.

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everolimus Tablets for suspension	Adj for TSC focal, 2+	mTOR inhibitor	CYP3A4 substrate; T ½= 30 hr	5 mg/m^2 once daily	New dose = current dose x (target concentration divided by current concentration)	Target 5-15 ng/mL	Stomatitis, noninfectious preamonitis GI, infection, thrombocytopenia, neutropenia, ↑ cholesterol, ↑ LFTs ↑ glucose	Impaired wound healing, hypersensitivity reaction, renal failure, angioedema with ACE-inhibitor, myelo-suppression, avoid vaccines, embryo-fetal toxicity	10% ↑ CBZ, CLB, OXC. Adjust dose with strong 3A4 and P-glycoprotein inhibitors or inducers and with hepatic impairment. Avoid grapefruit juice.
felbamate (FBM) Tablet; Suspension	Refractory focal, mono, 4+; LGS, adj	Enhances Na^+ channel rapid inactivation; blocks Ca^{2+} channel, inhibits NMDA receptor, potentiates $GABA_A$ conductance	40-50% excreted in urine unchanged; remainder metabolized to multiple metabolites and conjugates. Linear. T ½ = 22 hrs.	Children: 15 mg/kg/d divided TID or 4X/day. Adults: 1200 mg divided TID or 4X/day.	800-1200 mg TID	60 - 100	HA, insomnia, N/V, abd pain, anorexia, weight loss, facial edema, anxiety, acne, rash, constipation, diarrhea, ↑ SGPT, hypophosphatemia, rhinitis, infection, somnolence, ataxia, dizziness, tremor	Aplastic anemia, hepatic failure. Contraindicat-ed with history of blood dyscrasia or hepatic dysfunction.	TDM: full hematologic and liver tests before, frequently during and after treatment. DDI: FBM ↑ CBZ-epoxide, PB, PHT and VPA levels. EIAEDs ↓ FBM level. FBM ↓ progestin in OCs. Renal impairment ↓ clearance and ↑ $T_{1/2}$.
gabapentin (GBP) Capsule; tablet; refrigerated oral solution	Focal, adj, 3+	Binds pre-synaptic α_2-δ subunit of Ca^{2+} channel to modulate Ca^{2+} current	Renal excretion. Non-linear. T ½ = 6 hrs.	Age 3-11 = 10-15 mg/kg/day divided TID. Age 12+ = 300 mg TID	Age 3-4 = 40 mg/kg/day divided TID. Age 5-11 = 25 - 35 mg/kg/day divided TID. Age 12+ = 600 TID.	4 - 8.5	Sedation, ataxia, dizziness, diplopia, nystagmus, peripheral edema, fever, viral infection, N/V, tremor	DRESS, anaphylaxis, angioedema. Neuropsychi-atric changes (emotional, aggression, cognitive, hyperkinesia) in children 3-12 years.	Renal insufficiency requires lower dose. GBP concentration ↑ by morphine. GBP ↓ hydrocodone exposure.
lacosamide (LCM) Tablet, oral solution, i.v. C-V	Focal, mono, 4+ (injection = 17+)	Enhances Na^+ channel slow inactivation	Demethylated by CYP3A4, 2C9 and 2C19; 95% renally excreted – 40% as	11-49 kg = 1 mg/kg BID. 50+ kg = 50 mg BID. Age 17+ mono = 100 BID	11-29 kg = 3-6 mg/kg BID. 30-49 kg = 2-4 mg/kg BID. 50 + kg = 100-200 mg BID (adj),	4 - 12	Dizziness, ataxia, diplopia, HA, nausea, prolonged PR interval, atrial arrhythmias. Ventricular arrhythimias in	Syncope (esp with diabetes). In 2nd or 3rd degree block obtain pretreatment EKG. Use	May "load" with 200 mg oral or i.v. Consider baseline EKG or if exceeding maximum approved dose.

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…*Continued* **lacosamide (LCM)**			LCM/60% as metabolites. Linear. T ½ = 15 hrs.		150-200 mg BID (mono)		proarrhythmic conditions (rare).	caution with drugs known to prolong PR interval (including sodium channel blocking AEDs) and with antiarrythimic drugs.	
lamotrigine (LTG) Tablet (standard, chewable-dis-persable, orally-disintegrating, ER)	Focal, mono, 16+; or focal, LGS, primary TCS adj. 2+	Enhances Na^+ channel rapid inactivation; Inhibits Ca^{2+} channels	Mostly glucuronidated then renally excreted. Linear. T ½ = 25 hrs.; 13 hrs. with EIAEDs; 70 hrs. with VPA	25 mg q 2nd day (with VPA only), 25 mg/day; 50 mg/ day (with EIAEDs only)	50-100 mg BID with VPA alone; 75-200 mg BID without VPA or EIAEDs; 150-250 mg BID with EIAEDs. For children: see PI.	4-20	Dizziness, HA, diplopia, ataxia, nausea, vomiting, somnolence, insomnia in high doses, aseptic meningitis.	Rash, SJS & TEN, and since 1994 eight cases of hemophago-cytic lymphohistio-cytosis (HLH).	EIAEDs (CBZ, PB, PHT, PRM), rifampin, and OCs ↓ LTG level 40+%; pregnancy ↓ LTG level ~50-67% VPA inhibits LTG >2-fold.
levetiracetam (LEV) IR/ER tablet; oral solution; i.v. solution	Focal, adj, 1 month+; myoclonic in JME, adj, 12+; primary TCS, adj 6+	Inhibits synaptic vesicle SV2A protein; partially inhibits N-type Ca^{2+} currents.	Enzymatic hydrolysis (non-CYP) to inactive metabolite. ~66% renally eliminated unchanged. T ½ = 7 hrs.	1 - 5 mo: 7mg/kg BID; Age 6 mo - <4: 10 mg/kg BID; Age 4 - <16: 10 mg/kg BID; Age 16 +: 500 BID	1 - <6 mo: 42 mg/kg BID; 6 mo - <4 yr: 25 mg/kg BID; Age 4 - <16: 30 mg/kg BID; Age 16 +: 1500 BID	20-50	Somnolence, fatigue, asthenia, dizziness, infection, irritability, depresssion, psychotic symptoms (esp children), ataxia, anemia, ↓ WBC, ↓ platelets; increased diastolic BP age <4 yr.	Suicidal ideation and behavior; SJS & TEN; pancytopenia; rhabdomyoly-sis; angioedema; anaphylaxis.	In renal insufficiency, reduce dose proportionate to CrCl. Hemodialysis eliminates 50% in 4 hrs.
methsuximide (MSM) Capsule	Absence	Affects low-threshold, slow, T- Ca^{2+} thalamic currents	Extensively metabolized to n-desmethyl-methsuximide (active) T ½ = 34-80 hrs (adults); T ½ = 16-45 hrs (children)	300 mg BID	600 mg BID	10-40	N/V, abd. pain, anorexia, diarrhea, sedation, dizziness, ataxia, ↓ WBC, behavior changes, sleep disturbance, hyperactivity, irritability, psychosis, depression.	SJS, rash, DRESS, pancytopenia, lupus. Use cautiously with renal or hepatic disease.	Monitor CBC & CMP. May increase TCS. May ↑ serum levels of PHT and PB.
oxcarbazepine (OXC) Tablet (IR and ER); oral suspension	Focal, mono 4+, adj. 2+	Enhances Na^+ channel rapid inactivation; blocks HCav3.2 (?M &	Hepatic reduction 80% to S- and 20% to R-licarbaze-pine (the	Age 2-16 = 8-10 mg/kg/ day not to exceed 300	Age 2-16: <20 kg = 16-60 mg/kg/day; 20-29 kg = 900 mg/day; 30-39	10-35 (as MHD)	Dizziness, nausea, headache, diarrhea, vomiting, URI, constipation, dyspepsia, ataxia,	SJS & TEN (risk ↑ w/ HLA-B*1502, 10 X ↑ with Asian ancestry)	Induces CYP3A4: at 1200 mg/day, it ↓ OC estrogen level. Inhibits CYP2C19: at 2400 mg/day PHT level ↑

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…*Continued* **oxcarbazepine (OXC)**		P/Q fast) Ca^{2+} channel; enhances K+ conductance	MHDs). MHD is glucuronidated, then renally excreted. Unlike CBZ, no autoinduction or formation of 10-11 epoxide. Linear. T ½ = 9 (MHD), 2 (OXC) hrs	BID. Age 17+ = 300 mg BID (wk 1) then add no more than 300 BID weekly	kg = 1200 mg/day; 40+ kg = 1800 mg/day divided BID-TID. Age 17+ = 1200 -2400 mg divided BID - TID		nervousness; hyponatremia (<125 mMol/L = 2.5%, but the % increases with age)		40%. CBZ, PB and PHT and rifampin ↓ OXC levels 29-40%. Mild-mod hepatic failure: no adjustment. Renal failure: adjust dose
perampanel (PER) Tablet, oral solution. C-III	Focal, mono, 12+; primary TCS, adj, 12+	Selective, noncompetitive antagonist of AMPA glutamate receptor	Metabolism via CYP3A4 and 3A5 to multiple inactive metabolites. Linear. T ½ = 105 hours (~ 24 hrs with EIAEDs)	2 mg qHS (4 mg w/ EIAEDs)	Increase by no more than 2 mg weekly (long T-1/2 suggests slower). Min = 4 mg. Max = 8-12 mg qHS	?	Dizziness, somnolence, irritability, hostility, aggression, ataxia, anxiety, paranoia, HA, euphoria, agitation, falls, nausea, ataxia, mental status changes	Homicidal ideation (6 in 4,368 subject in pre-clinical trials)	CBZ, OXC, PHT (not PB) ↑ PER metabolism 2-3 fold. PER ↑ OC metabolism.
phenobarbital (PB) Tablet, elixir (4 mg/mL), IV solution C-IV.	Focal-onset and generalized -onset	Binds synaptic and extrasynaptic $GABA_A$ receptors	Hepatically para-hydroxylated and glucuronidated. 25-50% of unchanged PB, and its metabolites, are renally excreted. T ½ = 79 hrs. (110 hr in children and newborns)	Age < 6 = 3-5 mg/kg /day; Age 6-12 = 2-3 mg/kg/day; Age 13+ = 60 mg/day or 1 – 4 mg/kg/ day	Infant = 5-6 mg/kg/day; Age 1-5 = 8 mg/kg/day; Age 6-12 = 4-6 mg/kg/day; Age 13+ = 1-4 mg/kg/day. Adult max. = 240 mg qDay	15-45	Sedation, cognitive slowing, HA, N/V, depression, tolerance, dependence, ↓ REM sleep, hepatic dysfunction, osteoporosis. With pain: agitation or delirium. Children: irritability, hyperactivity, reduced IQ. Megaloblastic anemia	SJS, TEN, DRESS, rash, angioedema, respiratory depression, synergistic effects with EtOH or sedatives. Do not use in hepatic encephalopa-thy. Taper very slowly after chronic use.	Elimination is ↑ by diuretics, alkaline urine and activated charcoal, but is ↓ by VPA. PB is a strong CYP3A4 inducer: it ↑ the metabolism of PHT, LTG, OCs, warfarin and many drugs. Monitor CBC & CMP.
phenytoin (PHT) fosphenytoin (FOS) PHT: Delayed-release capsule – has 8% less PHT than prompt tablet and	Focal-onset; Generalized -onset TCS	Enhances rapid inactivation of Na^+ channels	Metabolized by CYP2C9 & 2C19, then renal tubular secretion. Nonlinear (zero order) kinetics	Children: 5 mg/kg/day. Adult: 300 mg/day divided BID or TID. i.v. load: 15-20	Adults: 100 mg BID – 200 mg TID	10 – 20+ (~10% as free PHT)	Nystagmus, ataxia, dysarthria, cognitive slowing, gingival hyperplasia, rash, hypertrichosis, lymphadenopathy, pseudolymphoma, hepatotoxicity, ↓	SJS and TEN, esp. in patients with Chinese ancestry with HLA-B*1502. DRESS	Never give PHT i.m.. Never give i.v. in diluents other than normal saline or > 50 mg/min (hypotension, bradyarrhythmia). FOS may be given I.M. and i.v. up to 150 mg PE/min.

DRUG AND FORMULATIONS	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (METABOLISM AND T½)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
suspension (25 mg/mL). PHT and FOS: IV(FOS is prodrug of PHT and has higher molecular weight)			(saturable at higher doses). T ½ = Adult: 22 (7-40) hrs.; (longer at higher doses and older age)	mg/kg (PHT) or 15-20 mg/kg PE (FOS)			platelets, ↓ WBC, pancytopenia, osteoporosis, ↓ vitamin D, porphyrgenic. i.v. PHT = thrombophlebitis		ESL, ESM, FBM, OXC, MSM, and TPM ↑ PHT levels. CBZ, DZP, VGB ↓ PHT levels. PB and VPA have variable effects on PHT and vice versa. PHT induces metabolism of CBZ, FBM, LTG, OXC, TPM & many drugs.
pregabalin (PGB) Capsule, oral solution. (CR not approved for epilepsy). C-V	Focal, adj, adult	Binds α_2-δ subunit of Ca^{2+} channel	Negligible metabolism, renal excretion. T ½ = 6 hrs.	≤150 mg/day, divided BID or TID	200-600 mg, divided BID or TID. Reduce for ↓CLcr	3-10	Dizziness, edema, somnolence, dry mouth, blurred vision, weight gain, ataxia, abnormal thinking, ↑CK, slight ↓ platelets, ↑ PR interval	Angioedema (face, mouth, throat, larynx), hives, dyspnea, wheezing	No DDI with AEDs. Additive cognitive and gross motor effects with opiates, benzodiazepines and EtOH
primidone (PRM) Tablet C-IV	Focal and TCS, mono	Binds synaptic and extrasynaptic $GABA_A$ receptors	PRM and its metabolites (PB and PEMA) are active. T ½ = 12 (derived PB is 79) hrs	Children < 8: 50 mg qhs. Age 8+: 100-125 mg qhs.	Age <8 = 375-750 mg/day (10-25 mg/kg/day), age 8+ = 750 - 2000 mg/day divided TID or 4/day	6-12 (plus derived PB)	Diplopia, vertigo, N/V, nystagmus, drowsiness, ataxia, fatigue, irritability, emotional disturbance	Rash, red blood cell hypoplasia and aplasia, agranulocyto-sis, megaloblastic anemia	Contraindications: porphyria, PB allergy. DDI similar to PB.
rufinamide (RUF) Tablet, oral suspension	LGS, adj, 1+	Enhances Na^+ channel rapid inactivation	Extensively metabolized by hydrolysis, then renal excretion. T ½ = 6-10 hrs.	Children: 10 mg/kg/d, 400 mg/d. Adult: 400 - 800 mg/d divided BID	Child max = 45 mg/kg/d or 3200 mg/d divided BID. Adult max = 3200 mg/day divided BID.	5-48	Leukopenia, shortening of QT interval, HA, N/V, dizziness, fatigue, ataxia, somnolence	Rash, DRESS, status epilepticus. Contraindi-cations: familial short QT syndrome.	Induces CYP3A4: ↓ estradiol, CBZ, LTG. RUF levels. ↑PB and PHT levels. VPA ↑RUF level. CBZ, PHT, PB and PRM ↓ RUF level. Dialyzable. Not recommended in severe liver failure.
tiagabine (TGB) Tablet	Focal, adj, 12+	Selective GABA reuptake inhibitor (SGRI)	Metabolized by CYP3A4 and glucuro-nidation. Metabolites excreted in urine and feces. T ½ = 8 (2-5 with EIAEDs) hrs.	4 mg once daily	32-56 mg/day divided BID (56 mg is with concomitant EIAEDs)	5-70	Dizziness, N/V, sedation, tremor, cognitive slowing, anxiety, diarrhea, abdomen pain, worsened pre-existing spike-and-wave discharges	↑ generalized sz and SE in epilepsy patients. Sz and SE in patients without epilepsy	PHT, CBZ, PB and PRM ↓ TGB levels. VPA ↑free TGB level 40%. Hepatic failure ↑ free TGB level.

DRUG AND FORMULATIONS	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (METABOLISM AND T½)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
topiramate (TPM) Tablet, capsule (IR and ER), sprinkle	Focal and primary GTCS, mono, 2+; LGS, adj, 2+	Inhibits Na^+ channels, kainate receptors and carbonic anhydrase. Enhances $GABA_A$	Not extensively metabolized. Urinary excretion 70% as unchanged drug. T ½ = 21 hr.	Age 2-9 = 25 mg qPM; Age 10+ = 25 mg BID	≤ 11 kg = 75-125 mg BID; 12-22 kg = 100-150 mg BID; 23-31 kg = 100-175 mg BID; 32-38 kg = 125-175 mg BID; >38 kg = 125-200 mg BID	7-30	Paresthesia, anorexia, weight loss, speech and cognitive disturbance, sedation, dizziness, anxiety, abnormal vision, fever, diarrhea, nausea, abdominal pain, URI	Acute myopia, glaucoma, visual field defects, ↓ sweating and hyperthermia, hyperchlor-emic, MA, Hyperamm-onemia +/- encephalo-pathy, kidney stones, hypothermia +/- ↑ NH_3 with VPA.	↓ OC efficacy (TPM >200 mg/d). Renal failure: use ½ dose and supplement after hemodialysis. PHT and CBZ ↓ TPM level. Other carbonic anhydrase inhibitors (AZM, ZNS) increase risk of MA and kidney stones.
valproic acid/ divalproex (VPA) Tablet (IR and ER), capsule, sprinkle, i.v. solution	Focal and absence, mono, 10+ yr. Mixed sz types (including absence), adj.	Inhibits voltage-dependent Na^+ and T-type Ca^{2+} channels, enhances GABA transmission	ER: F = 85% of IR. Metabolism: >40% mitochondrial β-oxidation, 30-50% glucuronic-dation, <15-20% via other oxidation. Nonlinear: total level increases with dose, free VPA level linear. Elimination: children age 3 mo – 10 yr have 50% faster clearance, age 68+ 40% lower clearance. T ½ = 9-16 hrs.	15 mg/kg/ day; increase by 5 -10 mg/kg/ day at weekly intervals	60 mg/kg/day divided BID – TID (IR), or qDay (ER)	50-100+	Hyperammonemia +/- encephalopathy, thrombocytope-nia, coagulopathy, hypothermia. Abd. pain, alopecia, anxiety, ataxia, asthenia, constipation, depression, diarrhea, diplopia, dizziness, dyspnea, emotional lability, fever, infection, HA, insomnia, N/V, nystagmus, edema, pharyngitis, rash, sedation, thinking abnormal, tinnitus, tremor, weight gain or loss	Hepatotoxicity (esp. with age <2 yr on multiple AEDs, metabolic disorders, or mental retardation or organic brain disease, and also with mitochondrial disorders), DRESS, pancreatitis. Fetal exposure: major congenital malformations (esp. neural tube defects), mental retardation, autism. Contraindica-tions: hepatic disease, POLG mutation, urea cycle disorders, pregnant	TDM: platelets, INR, PTT, CBC, NH_3, liver enzymes. CBZ, PHT, PB, PRM and rifampin ↓ VPA level. FBM ↑ VPA level. Monitor VPA levels with aspirin and estrogen-OC use. VPA may inhibit metabolism or affect PB of CZP, DZP, ESM, LTG, PHT. With RUF, start VPA at low dose. TPM + VPA ↑ risk of ↑ NH_3 and encephalopathy.

DRUG AND FORMULATIONS	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (METABOLISM AND T½)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
…*Continued* **valproic acid/ divalproex (VPA)**								patient for migraine prophylaxis.	
vigabatrin (VGB) Tablet; powder for oral solution.	Refractory FIAS, adj, >10; epileptic spasms	Inhibits GABA-transaminase	No significant hepatic metabolism. Renal excretion. Linear. T ½ = 10 (age 10+), 5.7 (infants) hrs.	ES: 25 mg/kg BID FIAS: Age 10-16 = 250 mg BID, Age 17+ = 500 mg BID.	ES: 75 mg/kg BID FIAS: Age 10-16 = 1000 mg BID, Age 17+ = 1500 mg BID.	Not established	Sedation, tremor, nystagmus, blurred vision, ↓ memory, weight ↑, ataxia, arthralgia, tremor, diplopia, aggression, URI, withdrawal sz with rapid stop, anemia, neuropathy, edema.	Permanent bilateral visual field constriction. Central retinal damage with ↓ visual acuity. Abnormal MRI signal changes in infants. ↓ALT and AST levels.	Adjust dose in renal impairment. Induces CYP2C9: ↓ PHT level 18%. Increases CZP level 30%. Stop if no substantial ↓ in FIAS in 3 months.
zonisamide (ZNS) Capsule	Focal, adj, 16+	Enhances rapid inactivation of Na^+ channels; ↓ low-threshold T-type Ca^{2+} current; binds $GABA_A$ ionophore; carbonic anhydrase inhibition	Partial hepatic metabolism. Renal excretion. Linear up to 800 mg/day, but nonlinear above that. T ½ = 69, 27-38 (w/ EIAED), 46 (w/ VPA) hrs..	100 mg/d, increase by 100 mg every 2 weeks	400 – 600 mg/d, given daily or BID	10-40	Kidney stones, rash, sedation, anorexia, weight loss, dizziness, ataxia, agitation, psychosis, irritability, speech or language disturbance, depression	SJS, TEN, DRESS, ↓ WBC, anemia, oligohydrosis and hyperthermia in children, hyperchloremic MA.	T ½ significantly ↓ with CBZ, PB, PHT, and moderately ↓ with VPA. ↑ severity of MA and risk of kidney stones when used with other carbonic anhydrase inhibitors (AZM, TPM).

TABLE 2. EXPANDED LIST OF AEDS

DRUG – GENERIC NAME, FORMULATION, DEA SCHEDULING	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (ADME)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
Adrenocortico-tropic hormone (ACTH) I.M. injection (80 IU/mL)	Epileptic spasms, mono, <2	Stimulates adrenal gland to secrete cortisol, corticosterone, aldosterone and several weakly androgenic steroids	Not adequately characterized. T ½ = 0.25 (i.v.)	--	Multiple regimens. Manufacturer: 75 IU/m² IM BID for 2 weeks, then taper over 2 weeks	N.A.	New, or worsening of latent, infections; adrenal insufficiency, Cushing syndrome, decreased growth with prolonged therapy, salt and water retention, HTN, hypokalemic alkalosis, gastric ulcers, bleeding, weight gain, bowel perforation, behavior or mood disturbances. Long-term use: worsened diabetes or myasthenia gravis, cataracts, glaucoma, loss of endogenous ACTH, osteoporosis.	Contraindicat-ed to give i.v., with congenital or other infections, recent surgery, uncontrolled hypertension, or sensitivity to porcine proteins. Do not administer with live or live-attenuated vaccines.	DDI not studied. Consider weekly – twice weekly BP and glucose monitoring, and treatment with an H2 blocker
brivaracetam (BRV) Tablet; oral solution; i.v. solution	Focal, mono, 4+ (i.v. formulation not approved below age 16 years)	Inhibits synaptic vesicle SV2A protein	F~100%; lipophilic. Metabolism: 1° hydrolysis, 2° CYP2C19 hydroxylation, CYP2C9 hydrolysis then renal excretion. T ½ = 9 hrs.	50 mg BID	25-100 mg BID	Not determined	Sedation, N/V, dizzy, suicidal thoughts, anger, psychosis	Bronchospasm, angioedema	Rifampin ↓ BRV 45%; EIAEDs ↓ BRV 19-26%; BRV ↑ PHT 20% and CBZ-epoxide 100%
cannabidiol (CBD) Oral solution (100 mg/mL) C - to be determined	Seizures associated with LGS or Dravet 2+	Unclear. Does not interact at CB1 or CB2 receptors. Potential targets include blockade of orphan G protein-coupled receptor 55 (GPR55);	Extensively metabolized, principally via CYP3A4, 2C19. 7-OH-CBD metabolite appears to be active Protein binding > 90%	2.5 mg/kg given BID x 1 week	10-20 mg/kg/d, divided BID Reduce dose in moderate to severe hepatic impairment. May take with or without food, but pt. must be consistent	Not established	Somnolence/ sedation, that may be increased by CLB. Elevated transaminases.....(as is through)....VPA. Decreased appetite/weight loss, diarrhea, fatigue, malaise, rash, insomnia, sleep	LFT and bilirubin monitoring before, and at 1, 3 and 6 months of, treatment, especially with concomitant VPA.	Other drugs which inhibit or induce CYP3A4 or 2C19 may alter CBD kinetics. CBD inhibits CYP2C19 thereby ↑ 3x the plasma concentration of N-desmethyl CLB. CBD may also inhibit CYP2C9, 2C8 and 1A2, and UGT1A9 and UGT2B7 substrates

DRUG – GENERIC NAME, FORMULATION, DEA SCHEDULING	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (ADME)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
…*Continued* **cannabidiol (CBD)**		agonist at transient receptor potential vanilloid receptor (TRPV1); modulation of adenosine-mediated signaling	Tmax 4-5 hrs. Food, especially high fat will increase extent of absorption > 4 fold. Elimination T1/2 ~ 60 hrs; Effective T ½ ~17 hrs CBD can inhibit CYP2C19, and can significantly increase plasma concentrations of active metabolite of clobazam, N-desmethyl clobazam				disorder, infections, irritability	Artisanal formulations of CBD are not biopharma-ceutically equivalent and should not be substituted. May cause fetal harm, hypersensi-tivity reactions.	
carbamazepine (CBZ) IR/ER tablet, ER capsule, chewable tablet, suspension 20 mg/mL	Focal, mono; GTCS; mixed types	Enhance rapid inactivation of Na^+ channels; block L-type Ca^{2+} channel	F = 70%, PB = 76%. Metabolism: CYP3A4 to CBZ 10-11 epoxide; hydroxylated and conjugated metabolites found in urine > feces. Time dependent clearance (autoinduction) T½ = 25-65 hrs. initially, then T½ = 12-17 after autoinduction is	2-3 mg/ kg/day divided BID or TID	Increase q 2-3 weeks up to 2400 mg/day (divided TID or 4/day for IR; BID for ER).	4-12	Sedation, diplopia, ataxia, dizziness, blurred vision, hyponatremia, N/V; low WBC counts; decreased T3, T4; increased LFTs; worsens GTCS in pts with absence seizures	SJS & TEN (↑ risk w/ HLA-B*1502, 10 X increase with Asian ancestry), aplastic anemia, agranulo-cytosis, DRESS, rash (SJS, TEN, rash & DRESS mod. association with HLA-A*3101). Avoid with porphyria. Contraindi-cated in bone marrow suppression,	Induces CYP1A2, 2B6, 2C9/19, & 3A4 so OCs, warfarin, & many drugs are affected. CBZ is inhibited by macrolides and propoxyphene. In hepatic impairment, monitor CBZ concentration.

DRUG – GENERIC NAME, FORMULATION, DEA SCHEDULING	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (ADME)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
…*Continued* **carbamazepine (CBZ)**			completed 3-5 wks later.					with use of nefazadone, boceprevir or delavirdine, in hypersensitivity to TCAs, and with MAOIs (serotonin syndrome).	
clobazam (CLB) tablet, oral suspension (2.5 mg/mL)C-IV	LGS, adj, 2+	$GABA_A$ receptor agonist, binds between α and γ subunits	F = 100%. PB = 85%. Tmax 0.5 – 4h. Lipophilic; Metabolism: N-demethyl-ated by CYP3A4 > 2C19 & 2B6, to N-desmeth-yl clobazam, which is metabolized by CYP2C19. T ½ = 36-42 hrs; 71-82 hrs. for metabolite	If ≤30 kg = 5 mg/day; If >30 kg = 5 mg BID	If ≤30 kg = up to 10 mg BID; If >30 kg = up to 20 mg BID; use lower dose in elderly, known CYP2C19 poor metabolizers, and mild or moderate liver failure	0.25-0.75	Sedation, fever, URI, drooling, constipation, UTI, insomnia, irritability, depression. Dependence, withdrawal effects, vomiting, ataxia, bronchitis, pneumonia	Rash, rarely SJS and TEN. Use with opioids can cause profound sedation, respiratory depression, coma & death	Weak CYP3A4 inducer, so may affect OCs. CLB inhibits CYP2D6 (dextromethorphan). Cannabadiol, ethanol and CYP2C19 inhibitors (fluconazole, fluvoxamine, omeprazole) inhibit CLB metabolism. CLB is a 1,5 BDZ (all other BDZs are 1,4)
clonazepam (CZP) Tablet, ODT tablet. C-IV	LGS. Myoclonic and absence Sz, mono- or adj, no age specified	$GABA_A$ receptor agonist, binds between α and γ subunits	F = 90%; PB = 85%. CYP3A4 reduces the 7-nitro group; 4-amino derivative is acetylated, hydroxylated and glucuronidated; effects of renal or hepatic disease unknown. T ½ = 30-40	If ≤30 kg = 0.01-0.03 mg/kg/ day divided BID or TID	If ≤30 kg = 0.1-0.2 mg/kg/day. 1-20 mg/day divided TID	0.04-0.07	Sedation, dizziness, ataxia, hypersaliva-tion, respiratory depression, porphyrogenic. Impaired judgment, cognition or motor skills. Paradoxical agitation, irritability, anger, anxiety, nightmares, hallucination, psychoses, depression. Dependence, tolerance.	With opioids can cause respiratory depression, coma & death. Contraindica-tions: acute narrow angle glaucoma, significant liver disease, sensitivity to BDZs	Worsened or new TCS. VPA + CZP may cause absence SE. Withdraw all BDZs gradually to help avoid SE. Periodic CBC and liver tests recommended. CBZ, LTG, PB and PHT ↓ CZP levels ~38%. Oral antifungal agents (e.g., fluconazole) may inhibit CZP metabolism.

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diazepam (DZP) Tablet; rectal gel (5 mg/mL); i.v. solution C-IV	Acute repetitive (rectal gel, adj., age 2+)	$GABA_A$ receptor agonist, binds between α and γ subunits	i.v.: F = 100%; Rectal gel: F = 90%, Tmax = 1.5 hr. PB = 95+%. Metabolism (CYP2C19 & 3A4) to desmethyl-diazepam (active). Clearance is highly variable likely due to CYP2C19 slow metabolism in 3-5% of Caucasians. T ½ for i.v: infant = 40-95, child = 15-20, adult = 15, elderly = up to 95 hrs. T ½ for p.r. = 46 hrs.	Oral and i.v. = 0.15 - 0.2 mg/ kg/dose, max 10 mg/dose P.R. = age 2-5 = 0.5 mg/kg; age 6-11 = 0.3 mg/kg; age 12+ = 0.2 mg/kg	Oral and i.v. =N.A. P.R. = weight-based, repeat once prn 4-12 hrs. after first dose, give no more than every 5 days or 5 times/month.	N.A.	Sedation, dizziness, depression, fatigue, motor and cognitive impairment, dependence. Not recommended for chronic, daily use due to tolerance. Tonic SE has occurred with i.v. DZP use for absence SE. Withdrawal effects after chronic use.	Use with opioids can cause respiratory depression, coma & death. Contraindicat-ed in narrow angle glaucoma.	May cause absence status epilepticus. Clearance is slowed 2 to 5-fold in alcoholic cirrhosis. CNS-depressant effects potentiated by VPA, PB, narcotics, phenothiazines, MAO inhibitors, other antidepressants. Inhibitors of CYP2C19 (cimetidine) and CYP3A4 (azoles) may ↓ DZP clearance. Inducers of 2C19 (rifampin) and 3A4 (CBZ, PB, PHT, dexamethasone) may ↑ elimination.
eslicarbazepine (ESL) acetate Tablet	Focal, mono, 4+	Enhances Na^+ channel rapid inactivation; blocks HCav3.2 Ca^{2+} channel; enhances K+ conductance	F = >90%, PB = 40%. ESL acetate hydrolyzed to ESL; renal excretion as ESL and ESL glucuronide. Linear. T ½ = 13-20 hrs.	11 - 21 kg = 200 mg/day; 22 - 38 kg = 300 mg/day; 39+ kg = 400 mg/day.	11 – 21 kg = 400-600 mg/day; 22 - 31 kg = 500 - 800 mg/day; 31 - 38 kg = 600-900 mg/day; 39+ kg = 800 – 1600 mg/day.	Possibly 10-35 (as OXC MHD)	1-1.5% hyponatremia (<125); dizziness, sedation; diplopia, HA, N/V ataxia, tremor	SJS & TEN (↑. with HLA-B*1502), angioedema, DRESS, anaphylaxis	EIAEDs induce ESL metabolism. ESL induces OCs, statins and S-warfarin. ESL inhibits CYP2C19, so PHT level rises.
ethosuximide (ESM) Capsule (gel); oral solution	Absence	Affects low-threshold, slow, T- Ca^{2+} thalamic currents	F ~ 93% Metabolism: CYP3A4 & CYP2E1 Clearance may be non-linear at higher doses (saturable)	Children age 3-6 yr: 250 mg/day. Age 6+ yr: 250 mg BID.	Children: optimal is 20 mg/kg/day. Adults: 1500 mg divided BID - TID	40-100	N/V, abd. pain, anorexia, weight loss, diarrhea, sedation, dizziness, ataxia, ↓ WBC, behavior changes, sleep disturbance, depression, hyperactivity, irritability, psychosis,	SJS, rash, DRESS, pancytopenia, eosinophilia, lupus. Use cautiously with renal or hepatic disease.	Monitor CBC & CMP. May increase TCS.

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…*Continued* **ethosuximide (ESM)**			T ½ ~ 30 hrs. (children),~ 60 hrs. (adults).				hallucinations, gingival hypertrophy, tongue swelling		
everolimus Tablets for suspension	Adj for TSC focal, 2+	mTOR inhibitor	CYP3A4 substrate; T ½= 30 hr	5 mg/m^2 once daily	New dose = current dose x (target concentration divided by current conc.)	Target 5-15 ng/mL	Stomatitis, noninfectious preamonitis GI, infection, thrombocytopenia, neutropenia, ↑cholesterol, ↑LFTs ↑ glucose	Impaired wound healing, hypersensitivity reaction, renal failure, angioedema with ACE-inhibitor, myelo-suppression, avoid vaccines, embryo-fetal toxicity	10% ↑ CBZ, CLB, OXC. Adjust dose with strong 3A4 and P-glycoprotein inhibitors or inducers and with hepatic impairment. Avoid grapefruit juice.
felbamate (FBM) Tablet; suspension	Refractory focal, mono, 4+; LGS, adj	Enhance Na^+ channel rapid inactivation; blocks Ca^{2+} channel, inhibits NMDA receptor, potentiates $GABA_A$ conductance	F = 90%, PB = 23%. 40-50% excreted in urine unchanged; remainder hepatically metabolized to multiple metabolites and conjugates. Linear. T ½ = 22 hrs.	Children: 15 mg/kg/d divided TID or 4X/day. Adults: 1200 mg divided TID or 4X/day.	800-1200 mg TID	60 - 100	HA, insomnia, N/V, abd. pain, anorexia, weight loss, facial edema, anxiety, acne, rash, constipation, diarrhea, SGPT, hypophosphatemia, rhinitis, infection, somnolence, ataxia, dizziness, tremor	Aplastic anemia, hepatic failure. Contraindica-tions: history of blood dyscrasia or hepatic dysfunction.	Hepatic enzyme inhibitor: ↑ CBZ-epoxide, PB, PHT and VPA levels. EIAEDs ↓ FBM level. FBM ↓ the progestin, but not the estradiol, in OCs. ↓ clearance and ↑ $T_{1/2}$ in renal impairment. Monitor full hematologic and liver tests before, frequently during and after treatment.
gabapentin (GBP) Capsule; tablet; refrigerated oral solution	Focal, adj, 3+	Binds pre-synaptic α_2-δ subunit of Ca^{2+} channel to modulate Ca^{2+} current, resulting in ↓ glutamate, NE, and substance P release	PB = 3%. Renal excretion. Non-linear (absorption from gut via L-amino acid transferase is saturable – F = 34% at 2400 mg/day). T ½ = 6 hrs.	Age 3-11 = 10-15 mg/kg/ day divided TID. Age 12+ = 300 mg TID	Age 3-4 = 40 mg/kg/day divided TID. Age 5-11 = 25 - 35 mg/kg/ day divided TID. Age 12+ = 600 TID.	4 - 8.5	Drowsiness, sedation, fatigue, ataxia, dizziness, nystagmus, diplopia, peripheral edema, fever, viral infection, N/V, tremor	DRESS, anaphylaxis, angioedema. Neuropsychia-tric changes (emotional, aggression, cognitive, hyperkinesia) in children 3-12 years.	Renal insufficiency requires lower dose. GBP concentration ↑ by morphine. GBP ↓ hydrocodone exposure. Magnesium / aluminum antacids ↓ GBP level 20%

DRUG – GENERIC NAME, FORMULATION, DEA SCHEDULING	FDA APPROVED SEIZURE TYPE OR SYNDROME, AGE (YR.)	PROPOSED MECHANISM OF ACTION(S)	PHARMACO-KINETICS (ADME)	SUGGESTED INITIAL DOSE (AGE, IN YEARS)	COMMON MAINTENANCE DOSE RANGE (OR MAX.) (AGE IN YEARS)	SERUM LEVEL RANGE (MCG/ ML)	SELECTED ADVERSE EFFECTS	CONTRA-INDICATIONS, WARNINGS AND PRECAUTIONS	DRUG-DRUG INTERACTIONS (DDI), AND OTHER CONSIDERATIONS
lacosamide (LCM) Tablet, oral solution, i.v. C-V	Focal, mono, 4+ (injection = 17+)	Enhances Na^+ channel slow inactivation	F = 100%; linear, Demethylated by CYP3A4, 2C9 and 2C19; 95% renally excreted – 40% as LCM/60% as metabolites. T ½ = 15 hrs.	11-49 kg = 1 mg/kg BID. 50+ kg = 50 mg BID. Age 17+ mono = 100 BID	11-29 kg = 3-6 mg/kg BID. 30-49 kg = 2-4 mg/kg BID. 50 + kg = 100-200 mg BID (adj), 150-200 mg BID (mono)	4-12	Dizziness, ataxia, diplopia, HA, nausea, prolonged PR interval, atrial arrhythmias. Ventricular tachyarrhythmias (rare) in proarrhythmic conditions.	Syncope (esp with diabetes). In 2nd or 3rd degree block obtain pretreatment EKG. Use with caution in patients with drugs known to prolong PR interval (including Na+ channel blocking AED's) and in pts taking antiarrhythmic drugs.	May "load" with 200 mg oral or i.v.
lamotrigine (LTG) Tablet (standard, chewable-dispersable, orally-disintegrating, ER)	Focal, mono, 16+; or focal, LGS, primary TCS adj. 2+	Enhances Na^+ channel rapid inactivation; Inhibits Ca^{2+} channels; Activates postsynaptic HCN channels.	F = 98%. PB = 55%. Linear; Vd = 0.9-1.3 L/kg; mostly glucuronidated then renally excreted. T ½ = 25 hrs.; 13 hrs. with EIAEDs; 70 hrs. with VPA	25 mg every 2nd day (with VPA only), 25 mg/day; 50 mg/day (with EIAEDs only)	50-100 mg BID with VPA alone; 75-200 mg BID without VPA or EIAEDs; 150-250 mg BID with EIAEDs. For children w/ and w/o VPA see PI.	4-20	Dizziness, HA, diplopia, ataxia, nausea, vomiting, somnolence, insomnia in high doses, aseptic meningitis.	Rash, SJS & TEN, and since 1994 eight cases of hemophago-cytic lymphohistio-cytosis (HLH).	EIAEDs (CBZ, PB, PHT, PRM), rifampin, and OCs ↓LTG level 40+%; pregnancy ↓LTG level ~50-67% VPA inhibits LTG >2-fold; LTG inhibits dihydrofolate reductase.
levetiracetam (LEV) IR/ER tablet; oral solution; i.v. solution	Focal, adj, 1 month+; myoclonic in JME, adj, 12+; primary TCS, adj 6+	Inhibits synaptic vesicle SV2A protein; partially inhibits N-type Ca^{2+} currents.	F = 100%; linear; PB <10%. Enzymatic hydrolysis (non-CYP) to inactive metabolite. ~66% renally eliminated unchanged. T ½ = 7 hrs.	1 - 5 mo: 7mg/kg BID; 6 mo - <4 yr: 10 mg/kg BID; 4 - <16 yr: 10 mg/kg BID; 16 + yr: 500 BID	1 - <6 mo: 42 mg/kg BID; 6 mo - <4 yr: 25 mg/kg BID; Age 4 - <16: 30 mg/kg BID; Age 16 +: 1500 BID	20-50	Somnolence, fatigue, asthenia, dizziness, infection, irritability, depression, psychotic symptoms (esp children), ataxia, anemia, leukopenia, thrombocytopenia; increased diastolic BP age <4 yr.	Suicidal ideation and behavior; SJS & TEN; pancytopenia; rhabdomyoly-sis; angioedema; anaphylaxis.	In renal insufficiency, dose must be reduced proportionate to CrCl. Hemodialysis eliminates 50% in 4 hrs.

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methsuximide (MSM) Capsule	Absence	Affects low-threshold, slow, T- Ca^{2+} thalamic currents	F : not established. PB = 45-60% (n-desmethyl-methsuximide). Extensively metabolized to n-desmethyl-methsuximide (active) T ½ = 34-80 hrs (adults); T ½ = 16-45 hrs (children)	300 mg BID	600 mg BID	10-40	N/V, abd. pain, anorexia, weight loss, diarrhea, sedation, dizziness, ataxia, ↑ WBC, behavior changes, sleep disturbance, hyperactivity, irritability, paranoid psychosis, hallucinations, depression, gingival hypertrophy, periorbital edema.	SJS, rash, DRESS, pancytopenia, lupus. Use cautiously with renal or hepatic disease.	Monitor CBC & CMP. May increase TCS. May ↑ serum levels of PHT and PB.
oxcarbazepine (OXC) Tablet (IR and ER); oral suspension	Focal, mono 4+, adj. 2+	Enhances Na^{+} channel rapid inactivation; blocks HCav3.2 (?M & P/Q fast) Ca^{2+} channel; enhances K+ conductance	F = 100%. PB = 40%. Linear. OXC is a prodrug: reduced 80% to S- and 20% to R-licarba-zepine (the MHDs), by hepatic cytosolic enzymes. MHD is glucuronic-dated, then renally excreted. Unlike CBZ, there is no autoinduction or formation of a 10-11 epoxide. T ½ = 9 (MHD), 2 (OXC) hrs.	Age 2-16 = 8-10 mg/kg/day not to exceed 300 BID. Age 17+ = 300 mg BID (wk 1) then add no more than 300 BID each week.	Age 2-16: <20 kg = 16-60 mg/kg/day; 20-29 kg = 900 mg/day; 30-39 kg = 1200 mg/day; 40+ kg = 1800 mg/day divided BID-TID. Age 17+ = 1200 -2400 mg divided BID (TID may improve tolerability)	10-35 (as MHD)	Dizziness, nausea, headache, diarrhea, vomiting, URI, constipation, dyspepsia, ataxia, nervousness; hyponatremia (<125 mMol/L = 2.5%, but the % increases with age)	SJS & TEN (risk ↑ w/ HLA-B*1502, 10 X ↑ with Asian ancestry)	Induces CYP3A4: at 1200 mg/day, it ↓ OC estrogen level. Inhibits CYP2C19: at 2400 mg/day PHT level ↑ 40%. CBZ, PB and PHT and rifampin ↓ OXC levels 29-40%. Mild-mod hepatic failure: no adjustment. Renal failure: adjust dose, MHD is not (metabolites may be) dialyzable
perampanel (PER) Tablet, oral solution. C-III	Focal, mono, 12+; primary TCS, adj, 12+	Selective, noncompeti-tive antagon-ist of AMPA glutamate receptor,	F = 100%, but food delays by 2 hrs. PB= 96%. Metabolized by CYP3A4	2 mg qHS (4 mg w/ EIAEDs)	Increase by no more than 2 mg weekly (long T-1/2 suggests slower). Min = 4 mg. Max = 8-12	?	Dizziness, somnolence, fatigue, irritability, hostility, aggression, anger, headache, ataxia, anxiety, paranoia, euphoric	Homicidal ideation (6 in 4,368 subject in pre-clinical trials)	CBZ, OXC, PHT (not PB) ↑ PER metabolism 2-3X). PER ↑ OC metabolism.

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…*Continued* **perampanel (PER)**		inhibiting synaptic-driven influx of Na^+	and 3A5 to multiple inactive metabolites. Linear. T ½ = 105 hours (~ 24 hrs with EIAEDs)		mg qHS (may need lower if not on EIAEDs)		mood, agitation, falls, nausea, ataxia, and mental status changes		
phenobarbital (PB) Tablets, elixir (4 mg/mL), IV solution C-IV.	Focal-onset and generalized-onset	Nonspecific $GABA_A$ receptor binding: affects both synaptic (phasic) and extrasynaptic (tonic) $GABA_A$ receptors	F ~95%. PB = 45%. Hepatically parahydroxy-lated and glucuroni-dated. 25-50% of unchanged PB, and its metabolites, are renally excreted. T ½ = 79 hrs. (110 hr in children and newborns)	Age < 6 = 3-5 mg/kg /day; Age 6-12 = 2-3 mg/kg/day; Age 13+ = 60 mg/day or 1 – 4 mg/kg/day	Infant = 5-6 mg/kg/day; Age 1-5 = 8 mg/kg/day; Age 6-12 = 4-6 mg/kg/day; Age 13+ = 1-4 mg/kg/day. Adult max. = 240 mg qDay	15-45	Sedation, cognitive slowing, HA, depression, N/V, tolerance, depen-dence, confusion, ↓ REM sleep, hepatic dysfunction, osteoporosis. With pain: agitation or delirium. Children: irritability, hyperactivity, reduced IQ. Megaloblastic anemia w/ chronic use.	SJS, TEN, DRESS, rash, angioedema, respiratory depression, synergistic effects with EtOH or sedatives. Do not use in hepatic encephalopa-thy. Taper very slowly after chronic use.	Elimination is ↑ by diuretics, alkaline urine and activated charcoal, but is ↓ by VPA. PB is a strong CYP3A4 inducer: it ↑ the metabolism of PHT, LTG, OCs, warfarin and many drugs. Monitor CBC & CMP.
phenytoin (PHT) and fosphenytoin (FOS) PHT: Delayed-release (sodium salt) capsule – has 8% less PHT than prompt (acid) tablet and suspension (25 mg/mL). PHT and FOS: IV(FOS is prodrug of PHT and has higher molecular weight due to PO4 molecule)	Focal-onset; Generalized-onset TCS	Enhances rapid inactivation of Na^+ channels	F ~100% varies by formulation; PB = 90-95%. Metabolized by CYP2C9 & 2C19. Excreted in bile as inactive metabolites, reabsorbed in intestines, then renal tubular secretion. Nonlinear (zero order) kinetics (saturable at higher doses). T ½ = Adult: 22 (7-40) hrs.; (longer at	Children: 5 mg/kg /day. Adult: 300 mg/day divided BID or TID. i.v. load: 15-20 mg/kg (PHT) or 15-20 mg/kg PE (phenytoin equivalent) (FOS)	Adults: 100 mg BID – 200 mg TID	10 – 20+ (~10% as free PHT)	Nystagmus, ataxia, dysarthria, cognitive slowing, gingival hyperplasia, rash, hypertrichosis, lymphadenopathy, pseudolymphoma, hepatotoxicity, thrombocytopenia, leukopenia, pancytopenia, osteoporosis, ↓ vitamin D, porphyrgenic. i.v. PHT = thrombophlebitis	SJS and TEN, esp. in patients with Chinese ancestry with HLA-B*1502. DRESS	PHT must never be given I.M., or i.v. in diluents other than normal saline or > 50 mg/min (hypotension, bradyarrhythmia). FOS may be given I.M. and i.v. up to 150 mg PE/min. ESL, FBM, OXC, MSM, TPM and many drugs ↑ PHT levels. CBZ, DZP, VGB and many drugs ↓ PHT levels. PB and VPA have variable effects on PHT and vice versa. PHT induces metabolism of CBZ, FBM, LTG, OXC, TPM & many other drugs.

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			higher doses and older age)						
pregabalin (PGB) Capsule, oral solution. (CR form not FDA approved for epilepsy). C-V	Focal, adj, adult	Binds pre-synaptic α_2-δ subunit of Ca^{2+} channel to modulate Ca^{2+} current, resulting in ↓ glutamate, NE, and substance P release	F =≥90%; low protein binding. Negligible metabolism, renal excretion. T ½ = 6 hrs.	≤150 mg/day, divided BID or TID	200-600 mg, given BID or TID. Maximum: 300 mg/d for CLcr 30-60, 150 mg/d for Clcr 15-30, and 75 mg/d for CLcr <15 mL/min	3-10	Dizziness, somnolence, dry mouth, edema, blurred vision, weight gain, ataxia, abnormal thinking, ↑CK, slight ↓ in platelets, ↑ in PR interval	Angioedema (face, mouth, throat, larynx), hives, dyspnea, wheezing	Taken with thiazolidinedione antidiabetes drugs weight gain occurs. No DDI with AEDs. Additive cognitive and gross motor effects with opiates, benzodiazepines and EtOH
primidone (PRM) Tablet C-IV	Focal and TCS, mono	Nonspecific $GABA_A$ receptor binding: affects both synaptic (phasic) and extrasynaptic (tonic) $GABA_A$ receptors	<5% PB; PRM and its metabolites (PB and PEMA) are active. T ½ = 12 (derived PB is 79) hrs	Children < 8: 50 mg qhs. Age 8+: 100-125 mg qhs.	Age <8 = 375-750 mg/day (10-25 mg/kg/day), age 8+ = 750 - 2000 mg/day divided TID or 4/day	6-12 (plus derived PB)	Diplopia, nystagmus, drowsiness, ataxia, vertigo, N/V, fatigue, irritability, emotional disturbance, impotence	Rash, red blood cell hypoplasia and aplasia, agranulocyto-sis, megaloblastic anemia (folate responsive)	Contraindications: porphyria, PB allergy. DDI similar to PB.
rufinamide (RUF) Tablet, oral suspension	LGS, adj, 1+	Enhances Na^+ channel rapid inactivation	PB=34% Absorption is slow (T_m = 4-6 hr) and nonlinear – due to low solubility at higher doses, but is helped by food. Extensively metabolized by hydrolysis, then renal excretion. T ½ = 6-10 hrs.	Children: 10 mg/kg/d (400 mg/d); Adult: 400-800 mg/d divided BID. Lower dose w/ VPA	Child max = 45 mg/kg/d or 3200 mg/d divided BID. Adult max = 3200 mg/day divided BID.	5-48	Leukopenia, shortening of QT interval, HA, N/V, dizziness, fatigue, ataxia, somnolence	Rash, DRESS, status epilepticus	Induces CYP3A4: ↓ estradiol 22% at ≥800 mg BID, mildly ↓ CBZ, LTG. RUF mildly inc PB and PHT. VPA ↑RUF level 16-70%. CBZ, PHT, PB and PRM ↓ RUF level 19-46%. Hemodialysis ↓ level ~30%. Not recommended in severe liver failure. Contraindication: familial short QT syndrome
tiagabine (TGB) Tablet	Focal, adj, 12+	selective GABA reuptake inhibitor	F = 90 %; PB = 96 %; Linear;	4 mg once daily	32-56 mg/day divided BID (56 mg is with	5-70	Dizziness, N/V, somnolence, fatigue, tremor, cognitive slowing, anxiety,	Worsened generalized sz and SE in epilepsy	EIAED's (PHT, CBZ, PB and PRM) ↓ TGB levels. VPA ↑ free TGB level 40% due to high protein

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…*Continued* **tiagabine (TGB)**		(SGRI): inhibits GABA reuptake from synapse into neurons and glia	Metabolized by CYP3A4 and glucuroni-dation. Metabolites excreted in urine and feces. T ½ = 8 (2-5 with EIAEDs) hrs.		concomitant EIAEDs)		diarrhea, abdomen pain, worsened pre-existing spike-and-wave discharges	patients. Sz and SE in patients without epilepsy	binding. Hepatic failure ↑ free TGB level.
topiramate (TPM) Tablet, capsule (IR and ER), sprinkle	Focal and primary GTCS, mono, 2+; LGS, adj, 2+	Inhibits voltage-dependent Na^+ channels, kainate glutamate receptors and carbonic anhydrase. Enhances $GABA_A$ currents.	F = 80%. PB = 15-41% and ↓ at higher concentrations. Not extensively metabolized. Urinary excretion 70% as unchanged drug. T ½ = 21 hr.	Age 2-9 = 25 mg qPM; Age 10+ = 25 mg BID	≤ 11 kg = 75-125 mg BID; 12-22 kg = 100-150 mg BID; 23-31 kg = 100-175 mg BID; 32-38 kg = 125-175 mg BID; >38 kg = 125-200 mg BID	7-30	Paresthesia, anorexia, weight loss, speech and cognitive disturbances, fatigue, somnolence, dizziness, anxiety, abnormal vision, fever, taste perversion, diarrhea, hypesthesia, nausea, abdominal pain, URI	Acute myopia w/ secondary angle closure glaucoma and vision loss. Visual field defects. Oligohydrosis and hyperthermia esp. in children. Hyperchlor-emic- MA, hyperammon-emia +/- encephalopa-thy, kidney stones, hypothermia +/- hyperammone-mia with VPA. Chronic untreated MA may lead to ↓growth in children, increased alkaline phosphatase, hypophosphate mia, and osteomalacia.	↓ OC efficacy (TPM >200 mg/d). Monitor Li^{2+} level with higher dose TPM. In renal impairment, use ½ dose, and supplement after hemodialysis. PHT and CBZ lower TPM concentration. Other carbonic anhydrase inhibitors (AZM, ZNS) increase risk of MA and kidney stones. Other DDI exist.

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valproic acid/ divalproex (VPA) Tablet (IR and ER), capsule, sprinkle, I.V. solution	Focal and absence, mono, 10+ yr. Mixed sz types (including absence), adj.	Inhibits voltage-dependent Na^+ and T-type Ca^{2+} channels, enhances biosynthesis and inhibits degradation of GABA	F = 90% at 40 mcg/mL, 81.5% at 135 mcg/mL, so free VPA level is dose-dependent. ER F = 85% of IR. Metabolism: >40% mitochondrial β-oxidation, 30-50% glucuronidation, <15-20% other oxidation. Nonlinear: total level increases with dose to a lesser extent due to saturable PB, Free VPA level increases linearly. Elimination: children age 3 mo – 10 yr have 50% faster clearance, and age 68+ years have 40% lower clearance. T ½ = 9-16 hrs.	15 mg/kg/ day; increase by 5 -10 mg/kg/ day at weekly intervals	60 mg/kg/day divided BID – TID (IR), or qDay (ER)	50-100+	Hyperammonemia +/- encephalopathy, thrombocytopenia, coagulopathy, hypothermia, somnolence in elderly. Abdomen pain, alopecia, blurred vision, anorexia, ataxia, amnesia, asthenia, back pain, constipation, depression, diarrhea, diplopia, dizziness, dyspepsia, dyspnea, emotional lability, fever, infection, HA, increased appetite, insomnia, N/V, nervousness, nystagmus, peripheral edema, pharyngitis, rash, rhinitis, thinking abnormal, tinnitus, tremor, weight gain or loss	Hepatotoxicity (esp. with age <2 yr on multiple AEDs, metabolic disorders, or mental retardation or organic brain disease, and also with mitochondrial disorders), DRESS, pancreatitis. With gestational exposure: major congenital malformations (esp. neural tube defects), mental retardation, autism. Contraindications: hepatic disease or significant dysfunction; mitochondrial disorders with POLG mutation, urea cycle disorders), pregnant patient for migraine prophylaxis.	TDM: platelets, INR, PTT, CBC, NH_3, liver enzymes. DDI: CBZ, PHT, PB, PRM and rifampin ↓ VPA level. FBM ↑ VPA level. Monitor VPA levels with aspirin, carbapenem, and estrogen-OCs. VPA may inhibit metabolism or affect binding of CZP, DZP, ESM, LTG, PHT. With RUF, start VPA at low dose and increase to clinical effect. TPM with VPA ↑ risk of ↑ NH_3 and encephalopathy. Other DDIs: TCAs, propofol, warfarin, zidovudine.
vigabatrin (VGB) Tablet; powder for oral solution.	Refractory FIAS, adj, >10; epileptic spasms	Inhibits GABA-transaminase irreversibly resulting in	F = 100%, PB = 40 %. Extensive binding to RBCs. No significant	ES: 25 mg/kg BID FIAS: Age 10-16 = 250 mg BID, Age	ES: 75 mg/kg BID FIAS: Age 10-16 = 1000 mg BID, Age 17+ = 1500 mg BID.	Not established	Somnolence, nystagmus, tremor, blurred vision, memory impairment, weight gain, arthralgia, ataxia,	Permanent bilateral visual field constriction. Central retinal damage with	Adjust dose in renal impairment. Induces CYP2C9: ↓ PHT level 18%. Increases CZP level 30%. Stop if no

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…*Continued* **vigabatrin (VGB)**		↑ GABA level in central nervous system	hepatic metabolism. Renal excretion. Linear. T ½ = 10 (age 10+), 5.7 (infants) hrs.	17+ = 500 mg BID.			tremor, URI, aggression, diplopia, withdrawal sz with rapid discontinuation, anemia, neuropathy, edema.	↓ visual acuity. Abnormal MRI signal changes in infants. ↓ALT and AST levels.	substantial ↓ in FIAS in 3 months.
zonisamide (ZNS) Capsule	Focal, adj, 16+	Enhances rapid inactivation of Na^+ channels; ↓ low-threshold T-type Ca^{2+} currents; binds $GABA_A$ BDZ ionophore; mild carbonic anhydrase inhibiting effects, and facilitates DA & 5HT transmission.	PB = 40% Linear up to 800 mg/day, but increases dispro-portionally above that dose due to an 8-fold binding to RBCs. Partial hepatic metabolism. Renal excretion. T ½ = 69, 27-38 (w/ EIAED), 46 (w/ VPA) hrs.	100 mg/d, increase by 100 mg every 2 weeks	400 – 600 mg/d, given daily or BID	10-40	Somnolence, fatigue, anorexia, weight loss, dizziness, ataxia, agitation, irritability, depression, psychosis, speech or language disturbance, kidney stones, rash	SJS, TEN, DRESS, ↓ WBC, anemia, oligohydrosis and hyperthermia in children, hyperchlore-mic MA. Chronic untreated MA may lead to decreased growth rate in children, ↑ risk of kidney stones, ↑ alkaline phosphatase, hypophos-phatemia, osteomalacia.	Adjust dose in renal impairment. ZNS T ½ significantly ↓ with CBZ, PB, PHT, and moderately ↓ with VPA. ↑ severity of MA and risk of kidney stones when used with other carbonic anhydrase inhibitors (AZM, TPM).

Notes: All AEDs confer an elevated risk of suicidal ideation and behavior, as well as increased risk of teratogenesis. All women becoming pregnant while taking AEDs are encouraged to enroll themselves with the North American AED Pregnancy Registry by calling 1-888-233-2334 or at www.aedpregnancyregistry.org. In the USA, report AED adverse effects to www.fda.gov/medwatch.

Key: 5HT = serotonin; adj = adjunctive treatment; AMPA = aminohydroxy methylisoxazole propionic acid; BDZ = benzodiazepine; BP = blood pressure; CBC = complete blood count; CMP = complete metabolic profile; CYP=cytochrome P450; DA = dopamine; DDI = drug-drug interaction; DRESS = drug reaction with eosinophilia and systemic symptoms (formerly, multiorgan hypersensitivity); EIAED = enzyme-inducing anti-epileptic drug e.g., CBZ, PHT, PB, PRM; EtOH = ethanol; F = bioavailability; FIAS = focal impaired awareness seizure; focal = focal-onset seizures with or without progression to bilateral tonic-clonic seizures; GABA = gamma aminobutyric acid; GTCS = generalized-onset tonic-clonic seizures; HA = headache; HTN = hypertension; LGS = Lennox-Gastaut syndrome; MA = metabolic acidosis; MAOI = monoamine oxidase inhibitor; MHD = monohydroxy derivative of OXC (R- and S-licarbazepine); mono = monotherapy; N/V = nausea and vomiting; OC = oral contraceptive; PB = protein binding; PI = prescribing information; POLG = mitochondrial DNA polymerase γ; RBC = red blood cell; SE = status epilepticus; SJS = Stevens Johnson syndrome; sz = seizure; TCA gamma = tricyclic antidepressant; TEN = toxic epidermal necrolysis; TCS = tonic-clonic seizure; TDM= therapeutic drug monitoring; TSC = tuberous sclerosis complex; URI = upper respiratory infection; WBC = white blood cells.

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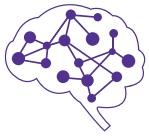
WORKING TOWARD A WORLD WITHOUT EPILEPSY



AMERICAN EPILEPSY SOCIETY

CURRENT REVIEW IN CLINICAL SCIENCE

Summary of **Antiepileptic Drugs**

Available in the United States of America