

ANTIEPILEPTICS (Antiseizure)

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Generic/ TRADE / form	SIDE EFFECTS	MONITOR Annually/iff indicated	USES √ COMMENTS/ DRUG LEVEL	DRUG INTERACTIONS	INITIAL & MAX DOSE	USUAL SEIZURE DOSE RANGE	\$  /100day
Carbamazepine TEGRETOL/generic CBZ (100 ^s ;200 ^{sx} ▼mg chew tab; 200 ^s mg tab) (200 ^s ;400 ^s mg CR tab  ▼) (20mg/ml susp)	Common: gastric distress (N/V), drowsy, dizzy, unsteady , pruritic rash<10% , ↓WBC (dose related) CR tab has fewer side effects . Rare: aplastic anemia, ↑ liver enzymes (GGT/ALK some ↑ normally), cardiac abnormalities; ↓ serum sodium (mild & asymptomatic often, but <125 important); SLE, exfoliative dermatitis, alopecia, ocular effects, ↓ WBC (persistent ~2%), ↓ T3/T4, osteomalacia & neural tube defects (<1%). WEIGHT GAIN = minimal	CBC, Platelets, TSH, LFT, Lytes, Level ? ECG for pts >45yrs  Pregnancy	√ Generalized tonic-clonic Sz , Partial (1-18yr) -not myoclonic Sz, may worsen absence Sz. √ BPAD -acute mania, rapid cycle, mixed & prophylaxis √ trigeminal neuralgia Option: for aggressive patients & neurologic dx & cognitive impaired CI in hepatic dx; safe in renal dx Level 17-54 umol/l -trough	↑ Carbamazepine level by: cimetidine, danazol, diltiazem, erythromycin, felodipine, fluoxetine, grapefruit juice, isoniazid, ketoconazole, lamotrigine, metronidazole, nefazodone, phenobarbital, propoxyphene, verapamil & valproate ↓ Carbamazepine level by: phenytoin, phenobarb, St. John's wort, theophylline Carbamazepine ↓'s levels of: BCP's ~40%, lamotrigine, phenytoin, theophylline, topiramate, valproate & warfarin . INDUCES P450 3A4 System 	100mg bid ↑ 200mg/d q5-7day (to ↓ rash rate) ~2800mg/day (autoinduction of P450 system complete in 4 weeks)	200mg po tid 400mg po tid 600mg po bid (some clinicians give regular release bid in select situations) 400mg CR bid (600-1600mg/d) Peds: 10-20→35mg/kg/d Mainly an enzyme inducer	35 64 64 97
Clobazam FRISIUM/generic (10 ^s mg tab)	B e n z o Common: Drowsiness (tolerance develops), dizziness, ↓ concentration, anterograde amnesia, ↑ traffic accidents. Rare: skin rash, paradoxical anger, thrombocytopenia & depression.	? Platelets 	Alt: generalized tonic-clonic, myoclonic & atonic, partial & absence Sz Broad spectrum→tolerance develops	Few drug interactions ↓ clobazam level by: carbamazepine clobazam ↑ level of: phenytoin	5-10mg od 80mg/day	10mg po bid 30mg po hs (20-30mg/d) Peds: 0.5-1.5mg/kg/d	50 72
Clonazepam RIVOTRIL/generic (0.5 ^s ;1,2 ^s mg tab; 0.25 ^s ▼mg tab)	Other Benzo's used for status epilepticus etc... Diazepam VALIUM 2 ^s ;5 ^s ;10 ^s mg tab; 10mg/2ml amp; 5mg/ml rectal gel DIASTAT ; 10mg/2ml emulsion DIAZEMULS . Lorazepam ATIVAN 0.5,1 ^s ;2 ^s mg po /sl ^x tab; 4mg/ml amp	? Platelets 	√ Myoclonic Sz; Alt→tonic & atonic, absence & infantile spasms  ; Panic attack Option: sedative, social phobia, akathisia, acute mania, restless leg syndrome & neuralgic pain	Few drug interactions . Tolerance in 1/3 pts in 6 months. ? ↑ Generalized tonic clonic Sz. Level clonazepam 40-230nmol/l -useful for compliance, not efficacy	0.5mg po tid ↑ 0.5-1mg/d q3d 20mg/day	0.5mg po tid 1mg po tid 2mg po tid (4-8mg/d) Peds: 0.01-0.3mg/kg/d	36 74 54
Divalproex (DVA) EPIVAL/generic (125,250,500mg EC tab); 1000mg/10 ml vial  -prodrug of VPA; see valproic acid below	Common: nausea, diarrhea, dizziness, sedation, somnolence, essential tremor ≤20%, ataxia, fatigue, confusion, headache, abdominal cramps, hair loss ^{often temp.} , hyperammonemia, menstrual disturbances & ? ↑ osteoporosis. Rare: ↓ platelets (↓ dose helps) & WBC , hepatotoxic, pancreatitis , ↑ blood insulin, neural tube defects→spina bifida 1-2%. Caution: polycystic ovaries WEIGHT GAIN= ++ (up to 59%, more common in ♀; mean ↑ of 8-14kg) Pregnancy registry: heart defect & spina bifida 10.7vs2.9% in control gp ↑ malformations with valproate ^{Antama05} esp >1g/d ⁶¹	CBC, Platelets, LFT Valproic level Correct levels up for low albumin 	√ 1st Generalized tonic-clonic , Absence, Partial, Myoclonic & Atonic . Juvenile myoclonic & LGS √ BPAD acute mania, rapid cycle , mixed, prophylaxis & depression √ migraine prophylaxis; Option: for aggression; Acute Mania -Oral LD 20mg/kg CI in hepatic dx ADV: safe in renal dx, ↓ rash & less cognitive impairment. Level 350-830 umol/l -trough	↑ Valproic acid level by: aspirin, cimetidine, erythromycin, felbamate, fluoxetine, isoniazid & salicylates ↓ Valproic acid level by: carbamazepine, cholestyramine, lamotrigine, phenobarbital, phenytoin, primidone, rifampin & topiramate Valproic acid ↑'s levels of: amitriptyline, carbamazepine ^{epoxide} (ie. ↑ SE), clonazepam, diazepam, ethosuximide, lamotrigine lorazepam, phenobarbital & warfarin Does not ↓ effect of BCP's	250-500mg bid ↑ 250mg/d q1 week 3-5g/day	250mg po tid cc 500mg po bid cc 500mg po tid cc (1-3g/day) cc= with food Peds: 10-15→60mg/kg/d Mainly an enzyme inhibitor	75 97 142
Ethosuximide ZARONTIN (250mg cap; 50mg/ml syrup)	Common: nausea, diarrhea, anorexia, drowsiness, hiccups & headache . Rare: skin rash ^{Stevens-Johnson} , blood dyscrasias, lupus & behavioral changes esp. in kids.	CBC, Platelets, Level 	√ Only for uncomplicated Absence Sz . Does not protect for generalized tonic clonic Sz. Level 280-710umol/l -trough	↓ ethosuximide levels by: carbamazepine ↑ ethosuximide levels by: ritonavir & valproic acid	250mg od/bid ↑ 250mg/d q1week 2000mg/day	250mg po bid 500mg po bid (750-1500mg/d) Peds: 10-15→20-40mg/kg/d	80 154
Gabapentin  NEURONTIN/generic (100,300,400mg cap) (600,800mg tab  ▼, ↑ cost) Pregabalin LYRICA  75-300mg bid  ⁸⁵³³⁰⁻⁴⁹⁰ -for use in diabetic neuropathy & post herpetic neuralgia (New 2005)	Common: somnolence, dizziness, ataxia, headache, nystagmus, nausea, vomiting, blurred vision, tremor, slurred speech, edema, rash ~1%, behavioral changes in kids & ↓ WBC ≤1%. WEIGHT GAIN= + (appears dose related)	Scr 	Alt: Partial & 2nd generalized Sz. not for generalized Sz such as juvenile myoclonic. Option: Neuropathic pain & Anxiolytic in severe Panic dx & social phobia, restless leg & migraine Well tolerated in the elderly ³⁹ ADV: ↓ rash & safe in liver failure DIS: Myoclonus may be ↑ 3-25umol/l for compliance, not efficacy	Antacids ↓ by 20% absorption (space by 2hr) NO other signif. interactions With doses >600mg less is absorbed since mechanism is saturated Does not ↓ effect of BCP's	100-300mg tid (↑ 300mg q1day) 3.6-4.8g/d	400mg po tid 600mg po tid 800mg po tid ↓dose in renal dysfx (900-3600mg/d) Peds: 10-15→25-40mg/kg/d	207 321 387
Lamotrigine LAMICTAL/generic (25 ^s ;100 ^s ;150 ^s mg tab; 5 ^s mg chewable tab) (2mg chewable tab  ▼)	Common: dizziness, nausea, vomiting, ataxia, asthenia, headache, somnolence, fatigue, ↑ alertness, diplopia, abd pain, rash (1 st month→gen. red morbilliform) & ↓ hair. Rare: Stevens-Johnson syndrome ⁸ & toxic epidermal necrolysis, ? hepatotoxic, tics in kids & leukopenia. WEIGHT GAIN=neutral effect Broad spectrum of Sz activity Not teratogenic in animals, but ↑ risk of fetal death. Pregnancy: ↓ levels & ↑ levels in breast milk.	CBC, LFT, Scr to ↓ dose if necessary 	√ Mono→ Partial & LGS . Alt: Generalized tonic-clonic , Absence, Partial, Myoclonic & Atonic Option: BPAD I acute depression & Bipolar II rapid cycling FDA Jun03 Option in new onset geriatric Sz ³⁹ Rash 5-10%→life threatening 0.3% ⁸³³ (If drug related→ D/C at first sign of rash) ADV: ↓ hormonal dysfx & more alert 4-39 umol/l for compliance, not efficacy	↑ Lamotrigine level by: sertraline & valproate ↓ Lamotrigine level by: BCP's, carbamazepine, oxcarbazepine, phenytoin, phenobarb., primidone, rifampin, topiramate NO EFFECT ON P450 enzyme system With carbamazepine: ↑ dizziness. Rarely ↓ effect of BCP's ⁵⁹ & folic acid	25-50mg bid ↑ by 50mg/day every 1-2weeks (to ↓ rash rate) Peds: 0.15-0.6 mg/kg/d start 5-800mg/day	100mg po bid 150mg po bid (100-500mg/d) Peds: 1-15mg/kg/d If with valproate: 25mg hs ^{↑12.5mg/wk} → 100mg po hs (50-200mg/d) Peds: 1-5mg/kg/d	208 299 32 107

Levetiracetam KEPPRA 250, 500, 750 mg tab	Common: drowsy, dizzy, asthenia, fatigue, depression, psychosis & rarely ↓ WBC/Hg.	CBC, Scr 	Adj: Partial Sz → adults & kids ≥4yr ADV: ↓ rash. Dose ↓ if renal dysfx.	Few drug interactions Does not ↓ effect of BCP's	500mg bid ↑ 1g/d q2week	500mg po bid 1000mg po bid (1-3g/d) Ped: 10-60 mg/kg	420 800
Methsuximide CELONTIN (300mg cap)	Common: nausea, diarrhea, drowsiness, hiccups & headache. Rare: skin rash, blood dyscrasias, lupus & behavioral changes especially in kids.	CBC, Platelets, Level 	√ Only for Absence Sz. Does not protect for generalized tonic clonic Sz. Level 53-212 umol/l -trough	methsuximide ↑s levels of: phenobarbital, phenytoin & primidone methsuximide ↓s levels of: lamotrigine ↓ methsuximide levels by: carbamazepine, phenobarbital & phenytoin	300mg od ↑ 300mg/d q1week 1200mg/day	300mg po tid 300mg po qid (300-1200mg/d) Peds: 10-30mg/kg/d	146 192
Oxcarbazepine TRILEPTAL 150 ^o , 300 ^o , 600 ^o mg tab; 60mg/ml susp	Common: GI upset, sedation, diplopia, ↓ sodium ~3% & rash. Rare: skin → SJS & TEN Convert CBZ → this drug by 1.5x CBZ dose	As per CBZ 	√ Mono → Partial Sz in adults & ≥6yr ? Generalized Sx ADV: ? ↓ CNS SE & rash vs CBZ	Similar DI's as per CBZ but less. (BCP's levels ↓; phenytoin levels ↑) Cross sensitivity with CBZ of 25%	150mg bid ↑ 300-600mg/d q1week	600mg po bid 900mg po bid (600-2400mg/d) Peds: 8 → 10-50 mg/kg/d	698 1033
Nitrazepam MOGADON/generic (5, 10mg tab)	Common: Drowsiness (tolerance develops), dizziness, anterograde amnesia, ↑ traffic accidents, dependence & paradoxical anger. Rare: skin rash & thrombocytopenia.	? Platelets 	√ myoclonic & infantile spasms & sedative/hypnotic	Few drug interactions. Tolerance in 1/3 pts in 6 months. ? ↑ Generalized tonic clonic Sz.	5mg po hs 60mg	2.5mg po tid 5mg po tid Peds: 0.25-1.2mg/kg/d	23 38
Phenobarbital generic (15, 30 ^o , 60, 100mg tab; 5mg/ml soln; 30 ^o , 120mg/ml ^o amp) Special access: 60mg/ml inj	Common: sedation, rash 5-10%, ataxia, dizzy, ↓ concentration & cognition, sleep problems, nystagmus, hyperactive, ↓ Vit D, & behavioral changes esp. in kids. Rare: blood dyscrasias & liver toxicity.	CBC, LFT Level Pregnancy registry: malformations 6.5vs2.9% in control gp	√ Partial seizures (1-12months) neonatal Sz ^{Drug of choice} ↑ breast milk levels Generalized tonic-clonic (1mo-6yr) LD 20mg/kg IV @ 50-75mg/min Level 65-150 umol/l -trough	↑ phenobarbital level by: cimetidine, felbamate & valproate phenobarbital ↓s levels of: acetaminophen, BCP's , carbamazepine, cyclosporin, estrogen, lamotrigine, theophylline, verapamil & warfarin	60-90mg hs ↑ 30mg/d q1month 240mg/day	60mg po hs 90mg po hs (90-180mg/d) Peds: 2-8mg/kg/d	19 25
Phenytoin DILANTIN (30, 100mg cap; 50 ^o mg chew tab; 6 & 25mg/ml susp; 100mg/2ml vial (92% phenytoin → cap & inj; 100% phenytoin → tab & susp)	Common: nausea, diarrhea, dizzy, ataxia, ↓ coordination, ↓ concentration, sedation, somnolence, tremor, rash 5-10% (rarely serious), ↑ LFT, blood dyscrasias, gingival hyperplasia ~50%, nystagmus, ↑ body hair , acne, ↓ folic acid, ↓ vitamin D levels & osteomalacia. Fosphenytoin ^{CEREBYX} IV friendly 150mg Fosphenytoin=100mg Phenytoin	CBC, LFT, Level Folate level 	√ Generalized tonic-clonic & Partial (Not for absence Sz) LD 15-20mg/kg IV @ 50mg/min Saturable kinetics ↑ dose → ↑ level IV → Purple glove syndrome occurs Correct levels up for low albumin (Alb = 20g/l → 100%; 30g/l → 40%; >36g/l → none) Level 40-80 umol/l -trough	↑ phenytoin level by: amiodarone, cimetidine, ciprofloxacin, clobazam, disulfiram , fluconazole, isoniazid , methsuximide, oxcarbazepine, propoxyphene, SSRIs & topiramate ↓ phenytoin level by: antacids, carbamazepine, folic acid, nasogastric feeds , valproate & vigabatrin phenytoin ↓s levels of: amiodarone, BCP's , CBZ, dexamethasone, folic acid, itraconazole , lamotrigine, methadone , mexiletine, quinidine, theophylline, topiramate, vitamin D & warfarin	300mg hs ↑ 50-100mg/d q1month 400-600mg/d	300mg po hs 200mg po bid (300-400mg/d) Peds: 4-8 mg/kg/d IM → crystallization Caps → like SR product	33 41
Primidone MYSOLINE/generic (125 ^o , 250 ^o mg tab; 125mg chew tab)	Common: sedation, rash ~5%, depression, nausea, dizzy, ↓ Vit D levels & ↓ libido. -metabolized to phenobarbital & PEMA	CBC, LFT Level 	√ Partial & Generalized tonic clonic (less effective vs partial Sz than phenobarbital) √ Essential tremor CI: porphyria, ↑ breast milk levels Level 28-55umol/l -trough	↑ primidone level by: isoniazid & valproate ↓ primidone level by: acetazolamide, carbamazepine, phenobarbital (but ↑ phenob. conversion) & phenytoin primidone ↓ levels of: BCP's , chlorpromaz., furosemide, lamotrigine, quinidine, steroids & TCA	125mg hs ↑ 125mg/d q3d 2000mg/day	125mg po tid 250mg po tid (500-1250mg/d) Peds: 50mg start, 10-25mg/kg/d	25 34
Topiramate TOPAMAX/generic (25, 100, 200mg tab; 15, 25mg sprinkle cap) Caution: metabolic acidosis & ↓ sweating esp. in kids	Common: nausea, dizzy, tremor, ataxia, somnolence, cognitive dysfunction , headache, paresthesias -fingers & toes, behavioral changes, fatigue, diarrhea, ↓ word finding, nephrolithiasis & glaucoma . WEIGHT GAIN= neutral/ loss possible (seems dose & duration dependent & > in ♀) Renal stones 1.5% thus ↑ fluid intake.	CNS SE ↑ with agents such as DVA. Adjust dose for Scr Hypospadias in male infants	√ Mono → Partial & 1 ^o GTC ≥6yrs Alt: 1 ^o Generalized tonic-clonic & Partial ≥2yr, Atonic & Lennox-Gastaut (LGS) → Age 2-16 ? √ myoclonic & absence Sz √ Migraine prophylaxis Weight loss ~4kg ? dose related Broad spectrum of Sz activity	↓ topiramate level by: carbamazepine & phenytoin (~40%), valproate (~15%) ↑ renal stones with topiramate &: Acetazolamide, dorzolamide & methazolamide topiramate ↓s level of: BCP's ~30% esp. >200mg/d, lamotrigine & dva. + dva → ↓ platelet & ↑ encephalopathy	25mg bid ↑ 25-50mg/d q1week 400-1000mg/d	100mg po bid 200mg po bid (200-600mg/d) Peds: 0.5 mg/kg/d start → 5-9 mg/kg/d	329/492 506/763 generic/Trade
Valproic acid -VPA DEPAKENE/generic (250mg cap; 500mg EC cap; 250mg/5ml syrup)	As per divalproex above Depakene generally has more GI side effects than Epival.	CBC, Platelets, LFT Level Pregnancy registry: heart defect & spina bifida 10.7vs2.9% in control gp. ↑ malformations with valproate Artama 05, esp >1g/d ⁶¹	divalproex & valproic acid are therapeutically, but not technically interchangeable meds since they are distinct generic products As per divalproex above			500mg po bid 500mg po tid (1-3g/d)	131 193
Vigabatrin SABRIL (500 ^o mg tab, 500mg sachet)	Common: drowsy, dizzy, weight gain, fatigue, tremor, psychosis & depression ≤2%, ↑ behavioral changes in kids, tremor & peripheral vision changes .	Adjust dose for Scr Visual field	Alt: Complex partial & infantile spasms . May worsen absence & myoclonus. ADV: No skin, blood or liver SE.	vigabatrin ↓s levels of: phenytoin ~30% Does not ↓ effect of BCP's	500mg bid ↑ 1g/d q1week 4000mg/d	1000mg po bid 1500mg po bid (2-3g/d) Peds: 30-100 mg/kg/d	422 620
Tiagabine GABITRIL 4, 12, 16, 20mg tab	Common: ↓ coordination, drowsy, dizzy, headache, fatigue, asthenia, tremor, stupor & depression.		Adj: Partial Sz (≥ 12yr) May ↑ generalized & absence Sx ADV: low incidence of rash	↓ tiagabine levels by: carbamazepine, phenobarbital & phenytoin Does not ↓ effect of BCP's	2mg bid ↑ 4-8mg/d q1week	16mg po bid cc 16mg po tid cc (32-56mg/d) Peds: 0.25-1 mg/kg/d	
Zonisamide ZONEGRAN 100mg cap (Special Access)	Common: drowsy, ataxia, dizzy, anorexia, fatigue, rash <2% → sulfa med , hyperthermia, renal stones ~4%, ↓ WBC & ↑ LFT.	CBC, LFT, Scr -harm animal fetus	Adj: Partial Sz (≥ 16yr) ?/ Generalized, infantile spasms & myoclonic Sz. Dose ↓ if renal dysfx	↓ zonisamide levels by: carbamazepine, phenobarbital & phenytoin ↑ renal stones with topiramate	100mg od/bid ↑ 100mg/d q2week	200mg po bid (100-600mg/d) 300mg po bid (od/bid) Peds: 1-2 → 6-8mg/kg/d	

▲ **Carbamazepine** ↓ level of: alprazolam, bupropion, clonazepam, cyclosporine, dexamethasone, diazepam, doxycycline, ethosuximide, fentanyl, haloperidol, levethyroxine, phenobarbital, phenothiazines, pregnancy tests, steroids, theophylline, triazolam, tricyclic drugs & **warfarin**. Consider using ACTH

PREGNANCY category: C=possible risk to fetus (evident in animals) D=fetal risk in humans U=unknown. Risk if on multiple agents & doses; try for monotherapy, split doses & ↓ serum levels check levels each trimester. Try to **avoid** in 1st trimester. **Vit K** in last month.

GENERAL: If stopping Sz meds taper ≥2-3months, to ↓ risk of Sz relapse. Consider stopping Sz meds if: Kids Sz free for 2 yr OR Adults Sz free for 3-5yr. New onset Sz ³⁸: delaying tx not ↑ risk of chronic Sz. Consider surgical options for refractory Sz. ▼=covered NIHb

Rash: ↑ dose, ↑ too quickly, if with valproic or in kids → ↑ rash rate. **Absence Sz** ethosuximide, valproate, clonazepam, lamotrigine, topiramate, clobazam. **Myoclonus** valproate, clonazepam, lamotrigine, clobazam & topiramate. **Generalized tonic-clonic:** valproate, carbamazepine, phenytoin, lamotrigine, clobazam & topiramate. **Partial Sz** CBZ, phenytoin, lamotrigine, oxcarbazepine, valproate, levetiracetam, clobazam, gabapentin, topiramate, phenobarbital, primidone & vigabatrin. **Young females:** use **↑ BCP** ^{50ug dose} / alternate contraception; give **folic acid** ~5mg/day.

√ Useful for/in ADJ=adjunctive ADV=advantage Alt=alternate BCP=birth control pill CI=contraindication CNS=central nervous system CR=control release DIS=disadvantage DX=disease EC=enteric coated fx=function LD=loading dose LGS=Lennox-Gastaut LFT=liver function test N/A=not applicable Peds=pediatric dose SE=side effect

DRUG induced Sz: amoxapine, amphetamines, antipsychotics, benzodiazepine withdrawal, bupropion, cocaine, imipenem, lithium, meperidine, quinolones & theophylline. **SR**=sustained release **Sz**=seizure =exception drug status **X** = Non formulary Sask. =not covered NIHb =↓ dose for renal dysfx =scored tab

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