

**HOW TO USE THIS TABLE:** Formulary medications are listed first followed by non-formulary medications in alphabetical order. When selecting from multiple options in the table, consider individual patient characteristics and co-morbidities. Please refer to reference table for additional guidance. Providers may choose a drug from the reasonable alternative list or non-formulary list without necessarily having failed any or all formulary drugs in the commonly used column if the provider determines it is appropriate for the individual patient and submits an NFDR consult. Providers may consult their local neurologist or regional ECoE for additional guidance through referral, e-consult, or SCAN ECHO if desired. This is recommended if considering items marked with an asterisk\*. (Revised June 2014)

|  | Commonly Used   | Reasonable alternatives   | Drugs to avoid                                      |
|--|---|---|---|
| Partial onset (focal) seizures +/- secondarily generalized convulsions | Carbamazepine<br>Lamotrigine<br>Levetiracetam<br>Oxcarbazepine<br>Topiramate<br>Zonisamide<br>Lacosamide (NF) | Felbamate*<br>Gabapentin<br>Phenobarbital<br>Phenytoin<br>Valproate<br>Clobazam* (NF)<br>Eslicarbazepine (NF)<br>Ezogabine* (NF)<br>Perampanel (NF)<br>Pregablin (NF)<br>Rufinamide* (NF)<br>Vigabatrin* (NF) |   |
| Primary generalized epilepsy (or unknown classification)               | Lamotrigine<br>Levetiracetam<br>Topiramate<br>Valproate<br>Zonisamide   | Carbamazepine<br>Clonazepam<br>Phenytoin<br>Oxcarbazepine<br>Clobazam* (NF)<br>Felbamate* (NF)  | Gabapentin<br>Pregabalin<br>Tiagabine<br>Vigabatrin |
| Elderly patients with focal epilepsy                                   | Lamotrigine<br>Levetiracetam  | Carbamazepine (extended release preferred)<br>Gabapentin<br>Other drugs may be used if needed*  |   |
| Women of child bearing potential*                                      | Lamotrigine<br>Levetiracetam<br>Zonisamide  | Carbamazepine<br>Other drugs may be used if needed*   | Valproate*  |

NF Non Formulary \*Recommend consultation with epilepsy specialist

The proposed recommendations made in this document are based on available medical evidence and suggestions made by the Epilepsy Centers of Excellence (ECoE) and the Pharmacy Benefits Management (PBM) Services, including input from subject matter experts as well as position statements, recommendations and guidelines from the International League Against Epilepsy (ILAE), the American Epilepsy Society (AES) and the American Academy of Neurology (AAN.) The content of this document will be dynamic and revised as new information becomes available. The purpose of the document is to assist practitioners in clinical decision-making and improve the quality of patient care. The clinician will be expected to use and interpret the final version of this guidance in the clinical context of the individual patient. These are general recommendations and suggestions, and should not supersede the clinical judgment of the treating provider.

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| Drug (Class if scheduled)<br>Formulations<br>*Indicates non-formulary                    | Total daily dose<br>FDA Recommended |                          | Dosing Interval      | Preferred in                                 | Avoid in   | Special Considerations (interactions, titration tips)  | Potentially serious ADRs  | Common SE   |
|--|-------------------------------------|--------------------------|----------------------|--|--|--|---|---|
|  | Initial                             | Maintenance              |                      |  |  |  |   |   |
| "Carbamazepine chewable tablet, tablet, extended release tablet* and liquid suspension " | 200 mg                              | 400-1600 mg              | TID or Q6h; BID (XR) | Bipolar, neuralgia                           | Cross-reaction allergic rash to phenytoin, phenobarb, oxcarb, lamotrigine  | Consider sending HLA B*1501 test prior to initiation (Asian ancestry, cross-AED allergy), p450 inducer-Interacts with warfarin and many drugs##                                      | Liver dysfxn, hyponatremia, rash, agranulocytosis, Stevens Johnson Syndrome   | Sedation, dizziness, blurry/diplopia, headache, GI upset, sun sensitivity     |
| Clobazam (Schedule IV) Tablet*   | 10 mg                               | 20-40 mg                 | QD-BID               |  | Abuse potential, use with etoh and other benzos regarding overdose/death   | Ideal if dose-limiting SE with other effective chronic benzodiazepines   | Rash (SJS), anemia, LFT increases   | Lethargy, sedation, ataxia  |
| Clonazepam (Schedule IV) tablet  | 0.5 mg                              | 2-8 mg                   | TID                  | Myoclonic seizures and subcortical myoclonus | Elderly, abuse potential   | Withdrawal from clonazepam may induce status epilepticus or exacerbation of seizures. Psychiatric withdrawal also may occur, manifested as insomnia, anxiety, psychosis, and tremor. | Nausea, vomiting, aplastic anemia, idiosyncratic rash, cardiovascular or respiratory depression                     | Sedation, ataxia, hyperactivity, restlessness, irritability, depression       |
| Clorazepate (Schedule IV) tablet*  | 7.5 mg                              | up to 90 mg              | TID                  | Myoclonic seizures and subcortical myoclonus | Elderly, narrow angle glaucoma, abuse potential, use with etoh and other benzos increases risk of overdose/death | Has an active metabolite, start with lower dose in elderly (7.5mg daily), may cause development of rage reaction, do not give with phenytoin   | Decrease in hematocrit, decrease in systolic blood pressure   | Sedation, dizziness, blurred vision, dry mouth, anxiety                       |
| Eslicarbazepine tablets*   | 400 mg                              | 800-1200 mg              | QD                   |  |  | Active metabolite of ox-carbazepine  | Eosinophilia and systemic symptoms (DRESS) reported   | Dizziness, sedation, nausea, headache, and diplopia.                          |
| Ethosuximide Capsule*, liquid solution*  | 15 mg/kg                            | 15-40 mg/kg              | BID-QID              | Absence seizures only                        | Worsens myoclonic and all other sz types; allergic to succinimides   | Primarily for children/teens with absence epilepsy   | Idiosyncratic rash, hallucinations, depression  | GI upset, anorexia, diarrhea, sleep disturbance, sedation, hyperactivity      |
| Ezogabine (V) tablet*  | 100 mg three times daily            | 400 mg three times daily | TID                  | Adjunctive treatment of partial seizures     |  | Falsely elevates serum and urine bilirubin tests. Reduced dose required in elderly, renal and hepatic disease.   | Retinal pigment abnormalities and vision loss urinary retention, QT prolongation, nephrolithiasis, thrombocytopenia | Dizziness, sedation, constipation, weight gain, diplopia, tremor, parasthesia |
| Felbamate Tablets, liquid suspension   | 1200 mg/day                         | 3600 mg                  | TID, QID             | Only for severe refractory epilepsy          | Comorbid autoimmune disorders  | Consider checking ANA prior to initiation; consult with epilepsy center due to high risk##   | Liver failure, irreversible fatal aplastic anemia   | Insomnia, headache, ataxia, weight loss, anorexia                             |

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|---|--|--------------|-----------------|--|---|--|---|---|
|   | Initial  | Maintenance  |                 |  |   |  |   |   |
| Fosphenytoin<br>Injectable solution   | 15-20 mg PE/<br>kg load                              | 4mg-6mg/kg   | QD, BID,<br>TID | IV only<br>--preferred<br>over IV<br>phenytoin | Cardio-vascular<br>problems                                 | P450 inducer (warfarin interaction)##; perineal paresthesia with loading doses (side effect)   | Rash, liver dysfunction   |   |
| "Gabapentin<br>Tablets,<br>Capsules "   | 300 mg   | 900-4800 mg  | TID, QID        | Chronic pain, neuropathy                       |   | Renal excretion--minimal interactions, absorption impaired for doses over 1200 mg  |   | Sedation, dizziness, ataxia, weight gain  |
| "Lacosamide (V)<br>Tablets*<br>injectable solution*"                                | 50 mg  | 400 mg       | BID             |  | 3rd degree heart block                                      | Renal excretion--minimal interactions  | AV conduction abnormalities   | Ataxia, dizziness, diplopia, headache, nausea, vomiting   |
| Lamotrigine<br>Tablets; chew tablets*; ODT*, XR tablets*                            | 12.5-50 mg   | 200-600mg    | BID, QD (XR)    | MDD, bipolar                                   | Tremor, myoclonus   | Slow titration to avoid rash--rate varies if on concurrent enzyme inducers or inhibitors; levels lowered by carbamazepine, oral contraceptives, phenytoin, phenobarb; levels raised by valproate | Rash (SJS/TEN)  | Dizziness, tremor, ataxia, headache, vivid dreams, insomnia   |
| "Levetiracetam<br>Tablets,<br>XR tablets*, injectable solution"                     | 250-500 mg   | 1000-3000 mg | BID, QD (XR)    | Dialysis/renal failure, polypharmacy           | May worsen MDD, PTSD, anxiety, thought disorders            | Renal excretion--minimal interactions  | Rash  | Sedation, irritability, agitation, anxiety, depression  |
| Oxcarbazepine<br>Tablets, tablet ER*, liquid suspension*                            | 600 mg   | 600-2400 mg  | BID             | Bipolar  |   | Weak-mod CYP3A4 inducer##, check serum Na within 7 days if high risk hyponatremia  | Rash, hyponatremia  | Sedation, vertigo, ataxia, diplopia, pancytopenia, agranulocytosis  |
| Perampanel (III)<br>tablet*   | 2 mg for patients not on enzyme inducing medications | 8-12 mg      | QD              |  | Active psychosis and unstable recurrent affective disorders | Expensive, renal excretion   | Serious psychiatric and behavior reactions  | Weight gain, sedation, irritability, falls, aggression, mood alteration   |
| "Phenobarbital (III)<br>Tablets<br>Elixir*; injectable solution*"                   | 1-4 mg/kg  | 60-200 mg    | QD, BID         |  |   | Strong CYP3A4 inducer (may reduce warfarin efficacy)##   | Rash (SJS/TEN), liver dysfunction   | Behavioral changes, tolerance, dependence, altered sleep cycles   |
| Phenytoin extended release capsule; liquid suspension, injectable, chewable tablets | Oral load 15-20 mg/kg in divided doses Q6 hours      | 300-600 mg   | QD, TID         |  | Diabetes, can increase blood sugar levels, absence seizures | Use fosphenytoin for IV infusion. P450 inducer (warfarin interaction)##, monitor free phenytoin in pregnancy, elderly, or low albumin, divide doses of greater than 400 mg                       | Gingival hypertrophy, rash (SJS/TEN), liver dysfunction, purple glove and cardiovascular effects with IV infusion, teratogen, lupus like reactions, aplastic anemia | Confusion, slurred speech, diplopia, ataxia, sedation<br>Long term use may be associated with cerebellar atrophy or peripheral neuropathy |
| Pregabalin (V)<br>Capsules*   | 100-150 mg   | 150-600 mg   | BID, TID        | Neuropathy, chronic pain                       | Pre-existing cognition issues                               | Renal excretion  |   | Somnulence, dizziness, ataxia, leg edema, weight gain   |

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|---|---|--------------------------------|-------------------------------|---|--|---|--|--|
|   | Initial                                   | Maintenance                    |                               |   |  |   |  |  |
| Primidone Tablet  | 100-125 mg                                | 750-2000mg                     | TID, QID                      | Essential tremor  |  | P450 inducer (warfarin interaction)##   | Megaloblastic anemia, rash, liver dysfxn, teratogen  | Sedation, slurred speech, diplopia, ataxia, impotence  |
| Rufinamide Tablet*  | 400-800 mg                                | 3200 mg                        | BID                           |   | Familial short QT syndrome   | Adjunctive therapy, do not use in severe liver impairment, modestly induces CYP 3A4##   | Nausea, vomiting, status epilepticus   | Sedation, dizziness, headache, ataxia  |
| Tiagabine Tablet*   | 4 mg                                      | 32-56 mg                       | BID, QID                      | Bipolar, PTSD   | High risk of increased seizures or status epilepticus in patients with generalized epilepsy or in overdose | Take with food, plasma level lower when given with enzyme inducing drugs, may need higher dose. If on no enzyme inducing meds slower titration and lower initial dose. Avoid abrupt withdrawal. | Associated with new-onset seizures and status epilepticus in patients without epilepsy. Withdrawal seizures                        | Somnolence, nausea, dizziness, impaired cognition  |
| Topiramate sprinkle capsules*; tablets; XR*   | 25 mg/ increase by 25-50 mg every 2 weeks | 100-400 mg                     | BID                           | Migraine, chronic pain, obese   | Pre-existing cognition issues, metabolic acidosis with concomitant metformin use                           | Moderate p450 inducer##; slow titration to avoid cognitive SE, dose adjust in CrCl < 70 ml/min  | Weight loss, renal stones, acute closure in narrow angle glaucoma, hyperthermia and oligohidrosis, metabolic acidosis              | Fatigue, nervousness, difficulty concentrating, confusion, language problems, anxiety, tremor, paresthesia |
| Valproate delayed release sprinkle capsule*, delayed release tablet*; SA 24 hr tablet, immediate release capsules | 500-1000 mg                               | 1000-3500 mg, max 60 mg/kg/day | BID (ER), TID(EC), Q6h (caps) | Bipolar, Migraine   | Women of childbearing potential, mitochondrial POLG mutations, urea cycle disorders                        | XR tabs should be dosed BID in epilepsy, p450 inhibitor (warfarin interaction), care when concurrent use of lamotrigine   | Thrombocytopenia, weight gain, liver dysfunction (esp. in mitochondrial Disease), teratogenic, SIADH, hyperammonemia, pancreatitis | Tremor, dizziness, hair loss   |
| Vigabatrin Tablet*; powder packet*  | 1000mg increase by 500mg/week             | 2000-3000 mg                   | BID                           |   |  | Requires eye exams q3months, SHARE program registration   | Progressive and permanent bilateral peripheral visual constriction   | Sedation, fatigue, weight gain, blurred vision   |
| Zonisamide Capsule*   | 100 mg                                    | 100-600 mg                     | QD                            | Tremor, women of child bearing potential, elderly, 1st line choice for pregnant women | Sulfa allergy  | Dose efficacy may plateau at 400 mg   | Weight loss, renal stones, Rash, metabolic acidosis  | Sedation, ataxia, confusion, depression, difficulty concentrating, language difficulties                   |

**Rescue medications--consultation with neurology and/or epilepsy specialist is recommended for prescribing rescue medications**

|                                     |           |  |  |  |  |  |  |  |
|-------------------------------------|-----------|--|--|--|--|--|--|--|
| Diazepam (Schedule IV) rectal gel** | 0.2 mg/kg | A second dose can be given 4-12 hrs after the first dose if needed |  |  |  | It is recommended that diazepam rectal gel be used to treat no more than 5 episodes per month and no more than 1 episode every 5 days. <b>See Note**</b> |  |  |
| Lorazepam (Schedule IV) tablet      | 2mg       | Do not exceed 4mg  |  |  |  | Oral tablet can be used sublingual or buccal   |  |  |

\*\*Strongly recommend patient education by prescribing provider and/or pharmacist prior to dispensing new Rx by mail or window  
##Causes decreased estrogen component of oral contraceptives. Be sure to use at least 30 mcg of estrogen component.

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