Epilepsy and Seizure Care Guide

March 2026

CALIFORNIA CORRECTIONAL
HEALTH CARE SERVICES

Information contained in the Care Guide is not a substitute for a health care professional's clinical judgment. Evaluation and treatment should be tailored to the individual patient and the clinical circumstances. Furthermore, using this information will not guarantee a specific outcome for each patient. Refer to "Disclaimer Regarding Care Guides" for further clarification.

https://cchcs.ca.gov/clinical-resources/

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GOALS

- ✓ **Accurately diagnose epilepsy and classify by seizure type in the electronic health record system (EHRS) Problem List**
- ✓ **Avoid drug-drug interactions**
- ✓ **Minimize burden of seizures with a goal of seizure freedom through appropriate therapy**
- ✓ **Ensure antiseizure medication (ASM) adherence**
- ✓ **For patients on ASM, monitor adverse effects, mental health, ASM blood levels, and bone health, as clinically indicated**
- ✓ **Identify patients with epilepsy who would benefit from eConsult vs. referral to neurology and/or epileptology**

ALERTS

- **Consider work up after an initial seizure**
- **Transfer to higher level of care (HLOC) in high-risk scenarios, such as first unprovoked seizure, seizure-related injury, status epilepticus, etc.**
- **After a seizure, evaluate for occupational restrictions, safety, and injury prevention**
- **Discuss teratogenicity associated with certain ASM, contraception, and family planning with patients with epilepsy of childbearing potential (PWECP)**

INTRODUCTION

Epilepsy is one of the most common neurological diseases. Approximately 1.2% of the United States population (3 million adults) have epilepsy, and seizures affect 8-10% of the population over a lifetime with increasing incidence in patients older than 55.[1]

The International League Against Epilepsy (ILAE) defines epilepsy for any of the following conditions:

- At least two unprovoked (or reflex) seizures occurring >24 hours apart
- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures occurring over the next 10 years
- Diagnosis of an epilepsy syndrome

Epilepsy is considered to be in remission for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years with no seizure medicines for the last 5 years. Conversely, intractable epilepsy or treatment-resistant epilepsy is diagnosed when a patient fails to achieve and maintain seizure freedom after two appropriately chosen ASMs at therapeutic doses.

CLASSIFICATION

Essential in the evaluation of patients with epilepsy is accurate documentation of classification, which:

- Provides a framework for understanding the type of seizures that the patient has as well as the other seizure types that are more likely to occur in that patient.
- Incorporates etiology along each stage and emphasizes the need to consider etiology at each step of diagnosis, as it often carries significant treatment implications.
- Helps identify potential triggers for a patient's seizures.
- Prognosticates and guides the selection of ASM.
- Informs the risks of comorbidities including learning difficulties, intellectual disability, psychiatric features such as autism spectrum disorder, which can be associated with certain epilepsy syndromes.
- Informs mortality risk such as sudden unexpected death in epilepsy (SUDEP).[2,3]

CLASSIFICATION, Cont'd

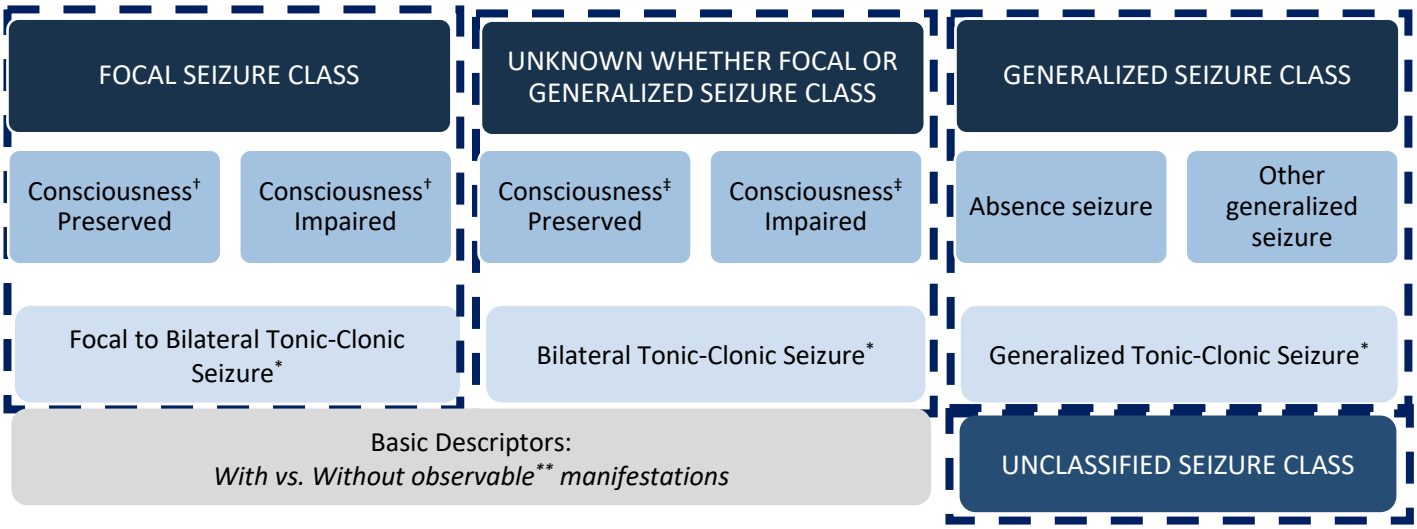

Figure 1: *The 2025 ILAE Classification of Epileptic Seizures comprises four main seizure classes: Focal, Generalized, Unknown, and Unclassified*

†*Operationally defined by awareness and responsiveness. If the state of consciousness is unknown, classify as "focal seizure" (without specifying the subclassification).*

‡*Operationally defined by awareness and responsiveness. If the state of consciousness is unknown, classify as "unknown whether focal or generalized seizure" (without specifying the subclassification).*

**Bilateral tonic-clonic seizures are associated with the highest morbidity and mortality.*

***Observable manifestations are readily recognized by an eyewitness. These may be motor, sensory, cognitive and language, autonomic, affective, and postictal. Impaired consciousness qualifies as an observable manifestation.*

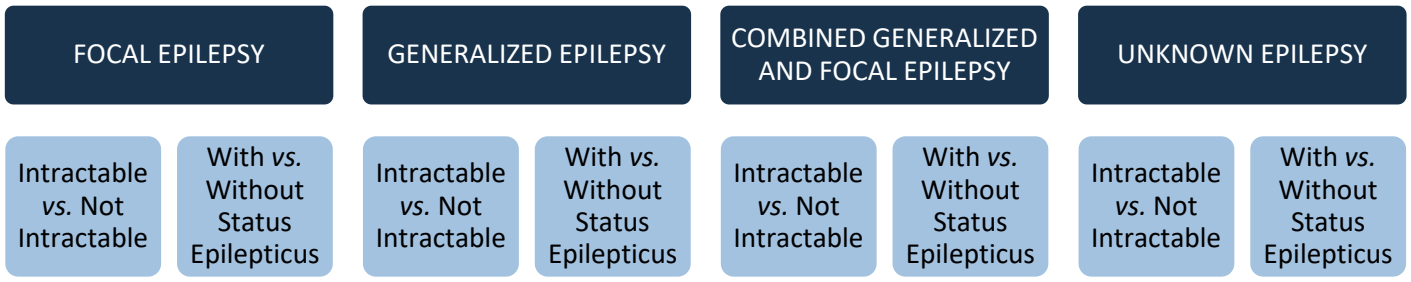

Figure 2: *The 2017 ILAE Classification of the Epilepsies comprises four main epilepsy types: Focal, Generalized, Combined Generalized and Focal, and Unknown*

CLASSIFICATION

At each stratum (seizure type to epilepsy type to epilepsy syndrome, if applicable), consider etiology as part of the diagnostic workup because of the treatment implications.

- Structural
- Post-traumatic
- Genetic
- Infectious
- Metabolic
- Immune
- Unknown[2,3]

Additionally, it is of prognostic and therapeutic importance to identify patients who have intractable epilepsy as well as patients who have ever had status epilepticus. Status epilepticus occurs when a continuous seizure lasts more than 5 minutes or when shorter seizures occur frequently, preventing return to neurological baseline between seizure events. Status epilepticus is a medical emergency associated with significant morbidity and mortality. Morbidity is defined as severe neurological or cognitive sequelae and deterioration of functional status. Mortality among adults is as high as 30%.[4,5]

Ultimately, the prognosis is most strongly related to the etiology, duration of status epilepticus, and the age of the patient. The goal of therapy is the rapid termination of both clinical and electrical seizure activity, since appropriate and timely therapy of status epilepticus reduces the associated mortality and morbidity.[5] (See Health Equity Alert)

HEALTH EQUITY ALERT

Status epilepticus is associated with high morbidity and mortality, both in the acute phase and over the long term. Complex and multifactorial factors that influence long-term outcomes depend on patient characteristics, status epilepticus etiology, seizure type (bilateral tonic-clonic seizures have the highest morbidity and mortality), treatment, complications, and social determinants of health.

In a 2024 publication, status epilepticus prevalence was highest among non-Hispanic (NH) Black patients. Minority populations (NH-Black, NH-Other, Hispanic) had higher odds of tracheostomy and gastrostomy vs. NH-White patients. The highest odds of intubation, tracheostomy, and gastrostomy were among older patients. Older age and lower income are associated with increased mortality.

SEIZURE MIMICS

When a patient presents with a possible seizure or a history of possible seizure, determine whether the paroxysmal event(s) are indeed a seizure versus convulsive syncope, behavioral event, parasomnia, movement disorder, or other nonepileptic event. Obtain a complete description of the seizure including behaviors, movements, duration, level of awareness, etc. (both ictal & postictal), from the patient and observers.

Seizure is more likely if tongue biting, limb jerking, or urinary incontinence occurred. Epileptic seizures are more likely to demonstrate forced and sustained (versive) head turning. Functional seizures (FS), previously known as psychogenic nonepileptic seizures, demonstrate different versions of head turning, classically side-to-side. Prodromal symptoms, such as déjà vu, mood changes, hallucinations, confusion, or post-event amnesia, also increase the likelihood of seizure. Factors that suggest diagnoses other than seizure include chest pain, nausea, dyspnea, palpitations, and presyncopal symptoms such as lightheadedness, tunnel vision, and dizziness.[6]

After confirming a probable seizure, evaluation focuses on identifying provoking factors such as tumor, metabolic derangement, infectious disease, transient ischemic attack (TIA) or stroke, traumatic brain injury (TBI), medications, or substance misuse.[1,2] Assess for history of medication or substance use that can provoke seizures through normal use, withdrawal, overdose, drug-drug interaction, or impaired metabolism due to comorbidities.[6,7]

HEALTH EQUITY ALERT

FS are highly debilitating. People with FS commonly experience childhood trauma and other adverse life events, particularly sexual trauma. Using principles of trauma-informed care, identify when a patient with FS is having a trauma response. By identifying the patient's prior adverse life events and coping mechanisms, providers can better individualize care for people with FS.

Consider how the diagnosis with FS will be communicated to the patient since this can improve symptom severity and decrease medical utilization.

1) Reassure the patient that the symptoms are genuine and not considered fake or volitional.
2) Define FS.
3) Explain how a diagnosis is confirmed.
4) Describe the mechanism of FS, which is an involuntary habit developed, usually in response to an initially stressful context, that has automatized over time.
5) Offer a biopsychosocial formulation that considers predisposing, precipitating, and perpetuating factors.
6) State there are helpful treatments.
7) Consider referral to Mental Health.

ACUTE SEIZURE

Consider the following etiologies for patients that present with a seizure:

- Cerebrovascular disease, such as ischemic stroke, intracranial hemorrhage, etc.
- Central nervous system infection, such as meningitis, encephalitis, neurocysticercosis, etc.
- Neurodegenerative diseases, such as Alzheimer's dementia, frontotemporal dementia, etc.
- Intracranial tumor, such as meningioma, metastases, etc.
- Head trauma
- Cerebral hypoxia or anoxia
- Metabolic disturbance, such as glucose imbalance, renal failure, hepatic encephalopathy, etc.
- Substance-related intoxication or withdrawal
- Withdrawal from, or low levels of, ASM, which may be due to non-adherence[2,4]

DURING AN ACUTE SEIZURE

STEP 1: CLINICAL STABILITY

During a seizure, assess the patient's vital signs and clinical stability. Then check for injuries and provide seizure first aid by staying with the patient to keep them safe from harm during seizure and turning them to the side if they are not awake and aware. Consider possible correctable systemic problems such as an acute medical condition (e.g., hypoglycemia, hyponatremia), syncope, arrhythmia, neurologic illness, or injury (e.g., TIA, stroke, TBI, movement disorder, meningitis, anoxic encephalopathy).

STEP 2: INITIATION OF THERAPY DURING EVALUATION

Upon seizure onset, if the patient has a Vagus Nerve Stimulation (VNS) device, usually implanted on the left upper chest wall below the clavicle, swipe the device with the VNS magnet every 60 seconds while seizures persist. Check the patient's wrists for their VNS magnet, if applicable. Between swipes remove the magnet from the VNS device completely. Provide supplemental oxygen, if clinically indicated.

Administer seizure rescue medication, lorazepam 4 mg IV/IO push over two minutes. Alternatively, use diazepam 10 mg IV/IO. Midazolam 10 mg intramuscular (IM) is the preferred benzodiazepine in patients without IV/IO access. Rectal diazepam is also reasonable initial therapy alternative, if IV/IO is not accessed. IM lorazepam and IM diazepam are **not** recommended due to erratic absorption and a slow time to peak drug levels.

After 5 minutes of continuous seizure activity after seizure rescue medication administration, consider the following:

- Administer another dose of lorazepam 4 mg IV/IO; alternatively, administer another dose of diazepam 10 mg IV/IO
- Send the patient to higher level of care (HLOC)

Since the majority of seizures are brief (lasting <5 minutes), status epilepticus protocols have used a 5-minute definition to minimize both the risk of morbidity and mortality from status epilepticus and the adverse outcomes associated with needlessly intervening on brief, self-limited seizures.

Convulsive status epilepticus occurs when:

- Active convulsions of a tonic-clonic seizure lasts 5 minutes or longer
- Patient has 2 or more tonic-clonic seizures without recovering awareness for a period of longer than 5 minutes

Nonconvulsive status epilepticus is used to describe a single or repeated absence seizures or focal impaired awareness seizures during which the person is not able to respond but is not displaying any movement or shaking of the body for longer than 10 minutes. This can begin as convulsive and then become nonconvulsive because of persistent seizures. Suspect nonconvulsive status epilepticus if the patient lacks awareness and is not able to respond for more than 10 minutes.

Patients with a diagnosis of epilepsy may be managed at the institution if there is no concern for status epilepticus and no injuries were sustained during the seizure.

ACUTE SEIZURE Cont'd

STEP 3: OBSERVATION AND DOCUMENTATION

Seizure observation and documentation is vital to accurate seizure classification (See Appendix 1).[1,5]

- Remove items on the patient (e.g. eyeglasses) or near the patient that can cause injury
- Loosen clothing around patient's neck
- Time seizure onset
- Place patient in left lateral decubitus position, and maintain patent airway
- Monitor vital signs
- Record the type of seizure, the level of awareness of the patient, and the length of time the seizure lasts
- Check electrocardiogram (ECG)
- Check point-of-care (POC) glucose. For hypoglycemia in the setting of seizure, consider placing order to administer 100mg thiamine IV/IO with dextrose solution. Hypoglycemia can provoke seizures and convulsive status epilepticus.

Patients who present with short convulsive (or tonic-clonic) seizures that only last a couple of minutes often have decreased awareness for several minutes because of the seizure's postictal phase. This means that even though the convulsions have stopped, patients remain very sleepy and difficult to rouse during the period that follows the seizure. Most patients gradually regain consciousness within 15-20 minutes, but the postictal phase can last hours for older patients. The postictal phase can make it difficult to tell when a seizure begins and ends.

STEP 4: POSTICTAL EVALUATION

During the postictal phase, complete a neurologic examination when the patient is alert and no longer disoriented to identify a neurologic provoking factor, such as lateralizing cortical deficits (i.e., unilateral weakness or aphasia). Other provoking factors include signs of infection, cerebrovascular disease, or metabolic derangement.[1,6,7]

Check appropriate lab tests, which include:

- Complete blood count (CBC)
- Complete metabolic panel (CMP)
- Magnesium level
- Serum ASM level, if applicable
- Urine toxicology screening
- Serum prolactin measurement, if clinically indicated as an adjunct to clinical assessment
    - Prolactin elevation at least twice baseline value, measured 10-20 minutes after a suspected event, is a useful adjunct to differentiate tonic–clonic seizures or focal impaired awareness seizures from a functional seizure (FS), also known as psychogenic nonepileptic seizure. A normal serum prolactin by itself is insufficient to make a diagnosis of FS or to exclude the possibility of tonic–clonic seizure or focal impaired awareness seizure because of its low sensitivity and low negative predictive value. Furthermore, serum prolactin has not been established in the evaluation of status epilepticus and repetitive seizures.
    - Prolactin elevation does not distinguish seizure from syncope.[1,6,7]

STEP 5: INDICATIONS FOR HIGHER LEVEL OF CARE

Consider sending patients to HLOC for the following:

- Patient with known anticoagulant use
- Patient with known immunocompromised state
- Patient with known malignancy
- Patient who is pregnant
- Patient who is clinically unstable
- Patient presenting with an unprovoked first seizure
- Patient presenting with serious injury like acute head trauma
- Patient who sustained injury during seizure
- Patient presenting with fever, persistent headache, and/or other meningeal signs
- Seizure lasts longer than 5 minutes after rescue medication administration
- Repetitive seizures or seizure clusters longer than 5 minutes without recovering awareness between seizures

- Patient with persistent neurologic deficits
- Patient with difficulty breathing after a seizure[1,5,7]

ACUTE SEIZURE Cont'd

STEP 6: DOCUMENTATION

When documenting an acute seizure, include the following information (See Appendix 1):

- Date and time of seizure onset
- Duration of seizure, and duration of postictal phase
- Activity or other potential triggers at time of seizure onset
- Presence of aura, if known
- Body part of first movement at onset of seizure, as well as pattern or progression to other body parts
  - Face: twitching, grimacing, teeth/jaw clenched
  - Eyes: check pupillary size, reaction to light, open/closed eyelids
  - Mouth: frothing, bleeding from tongue or cheek bite
  - Neck: extended/flexed, deviation to one side
  - Extremities: rigid, jerking, symmetrical/asymmetrical, rhythmic, extended/flexed
  - Posture: stiff, relaxed, writhing, tremulous, arching back
  - Automatisms: lip-smacking, chewing, swallowing, picking at clothes, rubbing hands, tapping feet
- Level of awareness during seizure: no change vs. decreased level of awareness with GCS score
- Vital signs during seizure
- Speech difficulty during seizure
- Change in skin color and sweating during seizure
- Urinary or bowel incontinence during seizure
- Any injuries sustained that may have caused or resulted from seizure
- Postictal neurologic examination findings
- Rescue medication or VNS therapy used during seizure, if applicable
- Name, dosage, and last dose taken of ASM(s), if applicable
- Date of most recent appointment with neurology and/or epileptology
- Date of most recent EEG and/or neuroimaging[8]

ACUTE SEIZURE Cont'd

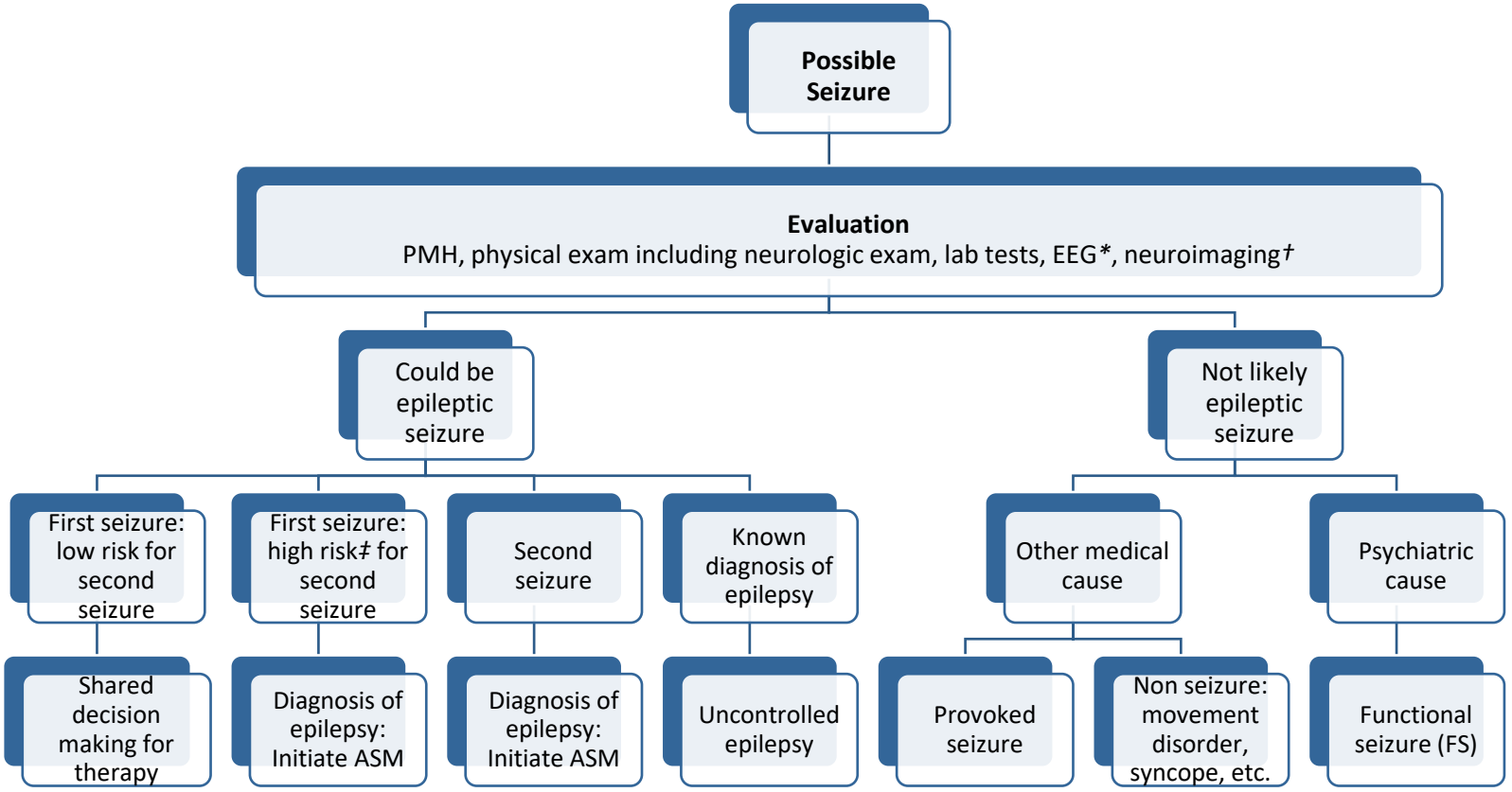

Figure 3: *A patient can have a seizure from an acute medical illness or trauma that begins before observable manifestations of seizure. It could also be related to substance intoxication or withdrawal. In these cases, seizures are "provoked.". These seizures are not diagnosed as epilepsy, and treatment addresses the underlying cause that provoked the seizure. There are also physical or medical events that may mimic or look like seizures. These are not the same as provoked seizures. They are also not due to changes in electrical activity in the brain seen in an epilepsy seizure. Since these are not seizures, they are often called nonepileptic events.*

**For patients presenting with unprovoked first seizure, recommend EEG if not done at HLOC. Otherwise, see INDICATIONS FOR EEG on page 14.*

†For patients presenting with unprovoked first seizure, recommend neuroimaging with MRI if not done at HLOC. Otherwise, see INDICATIONS FOR NEUROIMAGING on page 15.

‡High-risk if two unprovoked seizures more than 24 hours apart or abnormal EEG or abnormal neuroimaging or epilepsy syndrome or seizure out of sleep.

FOLLOW-UP MANAGEMENT

FOLLOW-UP APPOINTMENT FOR PATIENTS WHO HAD A FIRST SEIZURE

PAST MEDICAL HISTORY

Review past medical history (PMH) including current pregnancy. Inquire about prior seizure(s)/paroxysmal event(s) and attempt to obtain pre-incarceration history and medical records.

Ask about behaviors or triggers immediately before seizures. In addition to the patient's recollection of events, observer statements are useful. Provoking factors may be inflammatory, infectious, structural, toxic, or metabolic in nature and are found in 40% of first seizures.[1,7]

Identify seizure type (see Figure 1).

MEDICATIONS

Many medications can contribute to having a seizure. Evaluation should include a comprehensive history of medication and substance use, including medications recently started or stopped. Common medications associated with an increased risk of seizure include clozapine, bupropion, venlafaxine, diphenhydramine, and cephalosporins. Seizures can be caused by use of or withdrawal from substances including alcohol, opioids, stimulants, and cocaine.[7]

PHYSICAL EXAM

Perform and document appropriate physical exam. Include a complete neurologic exam, which includes mental status, cranial nerves, motor, sensory, reflexes, cerebellar, and gait assessments. Pay attention to signs of traumatic injuries to any part of the body, especially a tongue bite, which is highly specific in epileptic seizures.

DIAGNOSTIC TESTING

If not already done at HLOC, check appropriate tests

- CBC
- CMP
- Serum magnesium
- Urine toxicology screening, if clinically indicated
- Pregnancy test, if clinically indicated
- INR, for patients prescribed warfarin
- *HLA-B*1502* allele in patients at increased risk of developing serious cutaneous adverse drug reactions (CADR) from aromatic ASMs, especially **carbamazepine**, **oxcarbazepine**, and phenytoin (i.e., those of Asian ancestry, including South Asian Indian patients)
  (See Health Equity Alert)
  (See Primary Care Dermatology Care Guide)
- Recommend ECG prior to prescribing
  - **Lamotrigine**
  - **Carbamazepine**
  - Lacosamide
  - Phenytoin[6,7]

HEALTH EQUITY ALERT

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening conditions affecting the skin and mucous membranes. The *HLA-B*1502* allele is associated with **carbamazepine**-induced SJS/TEN. The US Food and Drug Administration (FDA) published an alert to providers that severe allergic skin reactions can be caused by **carbamazepine** use in patients with the *HLA-B*1502* allele and recommended screening for the allele before initiation of **carbamazepine** therapy in patients of Asian ancestry. Further studies have demonstrated a signification association between *HLA-B*1502* and phenytoin- or **lamotrigine**-induced SJS/TEN. *HLA-A*3101* allele is also implicated.

This overgeneralization as an impact of race is based on data collected from just two Asian countries. A large study of nearly 29,000 patients suggested that screening based on ethnicity assumptions may miss a high number of at-risk individuals. Screening United States patients for *HLA-B*1502* without ethnicity-based preselection identifies more than twice the number of carriers at risk of **carbamazepine**-related adverse events than screening patients of Asian ancestry alone. Although risk assessment based on ethnicity assumptions may not identify a large portion of at-risk patients in the ethnically diverse US population, to date, there are no updates on recommendations to expand *HLA-B*1502* screening in other populations.

FOLLOW-UP MANAGEMENT Cont'd

FOLLOW UP APPOINTMENT FOR PATIENTS WHO HAD A FIRST SEIZURE

Patients with clinical factors associated with an increased risk for seizure recurrence include prior brain insult like a stroke or trauma, EEG with epileptiform abnormalities, significant neuroimaging abnormality, and nocturnal seizure.

EEG

Review EEG from HLOC. If no EEG was done at HLOC for unprovoked first seizure, refer for routine EEG. A diagnosis of seizure is made if the patient has an EEG capturing epileptiform activity, but a normal/negative routine EEG does not "rule-out" epilepsy because the sensitivity of an initial routine EEG is only 17.3%. Sensitivity can be increased to 80-90% with use of three serial routine EEGs done on different days. *Not all patients who present with a provoked seizure need an EEG.*[8]

- Photic stimulation (to detect any light/visually triggered epileptic response) and hyperventilation are usually part of the standard EEG assessment.
- When initial routine EEG results are normal, a follow-up study, such as sleep-deprived EEG or prolonged ambulatory EEG, can capture epileptiform activity.
- Presence of EEG abnormalities doubles recurrence risk of seizure, impacting the decision to initiate ASM.[1,6,7]

NEUROIMAGING

Up to 30% of patients with a first seizure have abnormalities on neuroimaging, so review any prior neuroimaging, if available. If no neuroimaging was done at HLOC for unprovoked first seizure, then order "MRI BRAIN (Seizure) W/-W/O CONTRAST", which is the modality of choice for neuroimaging in most patients with epilepsy. The ILAE Neuroimaging Task Force recommends use of this epilepsy protocol, also known as Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNESS-MRI) Protocol, which is generalizable, regardless of the clinical setting. The HARNESS-MRI Protocol includes thin slices to improve sensitivity for lesions associated with epilepsy. Even if regular MRI imaging was performed, HARNESS-MRI Protocol is recommended. CT head has a role in the urgent assessment of seizures or when MRI is contraindicated. *Not all patients who present with a provoked seizure need neuroimaging.*[6,7,8]

DOCUMENTATION

When documenting an ambulatory clinic note for a patient who is following up for a first seizure:

- Date of recent seizure
- Duration of seizure, especially if seizure lasted more than 5 minutes
- Known or suspected seizure triggers
- Presence of aura
- Semiology of seizure
- Level of awareness during seizure
- Any injuries sustained that may have caused or resulted from seizure
- Name and dosage of rescue medication, if applicable
- Name, dosage, and last dose taken of ASM, if applicable
- Any adverse effects from ASM, including changes in mood and/or behavior
- Any other medications recently started or discontinued that could affect seizure threshold or drug interactions
- Date of most recent EEG and/or neuroimaging
- Identify seizure type (see Figure 1)[1,6,7]

HEALTH EQUITY ALERT

EEG requires adherence between the electrode and scalp. Hair types characterized as curly and tightly coiled hair are more susceptible to damage, so patients with this hair texture often wear protective hairstyles, such as locs, braids, twists, or cornrows. Certain hair textures and hairstyles may impede proper adherence to the scalp and affect the quality of EEG, mostly affecting Black patients. This can lead to misdiagnoses, underdiagnoses, and inappropriate therapy.

Hair holds significant cultural and identity-based importance for many Black patients. Requiring Black patients to adhere to Eurocentric hair standards to facilitate EEG data collection can have negative cultural implications, cause physical discomfort, and induce emotional distress. Therefore, schedule EEG to coincide with the patient's wash day or when one hairstyle is to be undone for a new one.

Advise patients to clean scalp and hair the day prior to the scheduled EEG. During the EEG, hair needs to be dry, and scalp needs to be product free, including no conditioner or oils. Conditioner can be applied only to the tips of the hair. Hair can be natural. For easier access to the scalp, keep hair stretched and detangled, or place into low braids or low twists.

After the EEG, patients can wash their hair to remove the electrode adhesive, then hair styled as desired.

FOLLOW-UP MANAGEMENT Cont'd

FOLLOW UP APPOINTMENT FOR PATIENTS WITH EPILEPSY

Past Medical History

Review past medical history (PMH) including current pregnancy. Attempt to obtain pre-incarceration history and medical records, which should include prior EEG and neuroimaging reports.

Inquire about semiology of seizures. Ask about behaviors or triggers immediately before seizures. In addition to the patient's recollection of events, observer statements are useful.[1,6]

Identify seizure type (see Figure 1) and/or epilepsy type (see Figure 2), inquire about the number and frequency of seizures over the past day, week, or month, and assess for changes in seizure control. Determine if patient was sent to HLOC for seizure in the past 24 months and why HLOC was necessary. [1,6]

Medications

Many medications can contribute to having a seizure. Evaluation should include a comprehensive history of medication and substance use, including medications recently started or stopped. Common medications associated with an increased risk of seizure include clozapine, bupropion, venlafaxine, diphenhydramine, and cephalosporins. Seizures can be caused by use of or withdrawal from substances including alcohol, opioids, stimulants, and cocaine.[6]

Ask patient about their adherence to ASM, including when the last dose was taken. Since many ASMs are nursing administered (NA), review the MAR to assess for adherence prior to any new seizure event. Additionally, serum ASM levels can be used to assess adherence.[1]

Physical Exam

Perform and document appropriate physical exam. Include a complete neurologic exam. For patients prescribed ASM, look for adverse effects, such as:

- Rashes or mucosal bullae from hypersensitivity reactions
- Neurologic changes, such as slurred speech, difficulty concentrating, ataxia, tremor, or nystagmus
- Vision loss or visual field defect from glaucoma, uveitis, or choroidal detachment
- Mood changes such as depression or suicidal ideation
- Behavioral changes such as aggression or agitation, which may result in Rules Violation Reports (RVRs)
- Irregular rhythm from arrhythmia
- Petechiae or ecchymoses from thrombocytopenia or anemia
- Abdominal findings from pancreatitis or hepatotoxicity

Onsite Testing

Check appropriate tests, which include:

- CBC
- CMP
- Serum magnesium
- Serum phosphate
- Serum ASM level, if applicable
- Serum 25-hydroxyvitamin D (25[OH]D), if on ASM for ≥2 years
- Urine toxicology screening, if clinically indicated
- Pregnancy test, if clinically indicated
- INR, if clinically indicated for patients prescribed warfarin
- *HLA-B*1502* allele in patients at increased risk of developing serious CADR from aromatic ASMs, if not already completed
- Consider ECG prior to prescribing
  - **Lamotrigine**
  - **Carbamazepine**
  - Lacosamide
  - Phenytoin[1,6,7]

FOLLOW-UP MANAGEMENT Cont'd

FOLLOW UP APPOINTMENT FOR PATIENTS WITH EPILEPSY

EEG

Review EEG report(s) in EHRS. See INDICATIONS FOR EEG on page 14.[1,6]

NEUROIMAGING

Review neuroimaging report(s) in EHRS. See INDICATIONS FOR NEUROIMAGING on page 15. If new neuroimaging is clinically indicated, order "MRI BRAIN (Seizure) W/-W/O CONTRAST", which is the modality of choice for neuroimaging in most patients with epilepsy. The ILAE Neuroimaging Task Force recommends use of this epilepsy protocol, also known as Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNESS-MRI) Protocol, which is generalizable, regardless of the clinical setting. The HARNESS-MRI Protocol includes thin slices to improve sensitivity for lesions associated with epilepsy. Even if regular MRI imaging was performed, HARNESS-MRI Protocol is recommended. CT head has a role in the urgent assessment of seizures or when MRI is contraindicated.[6,7,8]

DOCUMENTATION

When documenting an ambulatory clinic note for a patient with epilepsy

- Epilepsy type
- Date of most recent seizure, and date of most recent tonic-clonic seizure, if applicable
- Usual duration of seizures
- Frequency of seizures per day/week/month/year, and frequency of tonic-clonic seizures, if applicable
- Known or suspected seizure triggers
- Presence of aura
- Semiology of seizures/seizure type(s)
- Level of awareness during seizures
- Any history of seizures lasting more than 5 minutes
- Any injuries sustained that may have caused or resulted from seizures
- Name, dosage, and last dose taken of rescue medication, if applicable
- Name, dosage, and last dose taken of ASM(s), if applicable
- Any adverse effects from ASM(s), including changes in mood and/or behavior
- Any other medications recently started or discontinued that could affect seizure threshold or drug interactions
- Last serum ASM level, if clinically indicated
- Date of most recent appointment with neurology and/or epileptology
- Date of most recent EEG and/or neuroimaging
- Identify seizure type (see Figure 1) and/or epilepsy type (see Figure 2)[1,6,7]

FOLLOW-UP MANAGEMENT Cont'd

INDICATIONS FOR EEG

EEG is a safe, noninvasive, and inexpensive test of neurological function, and a routine EEG is the cornerstone in providing objective support for a clinical diagnosis of epilepsy. In people with epilepsy, routine EEG is also used for the classification, quantification, and characterization of interictal epileptiform abnormalities to aid in the initiation or withdrawal of ASM. Video-assisted EEG is now readily available in many settings and is used to correlate behavioral activity with electrocerebral activity to provide even greater yield.[9]

A 'positive' EEG is defined by the presence of interictal epileptiform discharges (IED). Among adult routine EEGs, which records approximately 30-60 minutes of data, the sensitivity is only 17.3%. Sensitivity can be increased to 80-90% with use of three serial routine EEGs separated by time.[10]

Alternatively, a 24-hour ambulatory continuous EEG has increased sensitivity when compared with routine EEG and repeated routine EEG. Ambulatory EEG has a sensitivity of 72%.[11]

Possible Indications for Routine EEG	Conclusions
Recommended for unprovoked first seizure	Presence of unequivocal IED diagnoses new-onset epilepsy
Classification of focal and generalized epilepsy ***if indicated per eConsult guidance***	IED help in the choice of ASM for the seizure type(s) and epilepsies
Selection of ASM and monitoring response to treatment *if indicated per eConsult guidance*	Reduction in spike burden or seizure burden may represent a response to therapy
Head injury *if indicated per neurology guidance*	IEDs may occur that suggest untreated seizures
Brain tumor *if indicated per neurology guidance*	Focal slowing correlates with location of abnormality, and IEDs suggest a greater potential for seizures
Stroke *if indicated per neurology guidance*	Presence of IEDs helps to predict a higher incidence of post-infarction seizures
Paroxysmal neurological events *if indicated per eConsult guidance*	IEDs suggest seizures independent of bizarre paroxysmal behavior
Behavioral conditions, such as functional seizure *if indicated per eConsult guidance*	May provide a definitive diagnosis when suggestion during routine EEG provokes a habitual attack to differentiate them from epileptic seizures
Episodic anxiety or mood disturbances *if indicated per eConsult guidance*	May occur in temporal lobe seizures suggested by anterior lobe IEDs
Cognitive and memory problems *if indicated per eConsult guidance*	May help suggest seizures when IEDs present
Sleep disorder *if indicated per eConsult guidance*	Presence of IEDs suggest nocturnal seizures versus parasomnia

FOLLOW-UP MANAGEMENT Cont'd

INDICATIONS FOR NEUROIMAGING

According to American College of Radiology Appropriateness Criteria®, the following are indications for neuroimaging:

Indications for Neuroimaging	Appropriate Use Criteria
New-onset seizures	• Initial imaging with MRI brain [preferred by American Academy of Neurology (AAN) and American Epilepsy Society (AES)] • Initial imaging with CT head has a role in the urgent assessment of seizures or when MRI is contraindicated
Known epilepsy with change in seizure semiology or new neurologic deficit or no return to previous neurologic baseline	• Imaging with MRI brain (preferred by AAN and AES) • Imaging with CT head • Neurology may also recommend PET/CT brain
Known epilepsy with history of tumor	• Imaging with MRI brain (preferred by AAN and AES) • Imaging with CT head • Neurology and/or oncology may also recommend PET/CT brain
Known epilepsy for surgical planning in patient with intractable epilepsy	• Imaging with MRI brain • Neurology may also recommend PET/CT brain, MRI functional brain, among other imaging studies

MRI serves multiple purposes for new-onset seizures, including identifying and characterizing focal causative lesions as well as assessing progression. MRI is an important tool for determining prognosis as well as a treatment strategy. In the nonemergent situation, MRI is the imaging study of choice when indicated. For example, if a patient returns from HLOC after a seizure and only had a CT head done, order MRI brain non-emergently. Priority for obtaining imaging for those patients who have focal findings on neurologic examination, persistent headache, recent history of head trauma, and abnormalities on EEG are correlated to have a high probability of finding structural abnormalities.[12]

FOLLOW-UP MANAGEMENT Cont'd

INDICATIONS FOR ECONSULT TO NEUROLOGY

Utilization of eConsults safely improves access to neurologic expertise and prevents the need for some face-to-face visits. Neurologists performing eConsults can triage patients to telemedicine or to face-to-face consultation, particularly when diagnosis is uncertain or when the neurologic examination may help guide appropriate testing.

Consider eConsult to neurology for the following scenarios, if needed:

- Guidance to aid in the workup and diagnosis of seizure-like events as epileptic seizure, provoked seizure, or non-seizure event (e.g., syncope, movement disorder, sleep disorder, FS, etc.)
- Guidance to accurately classify epilepsy type or epilepsy syndrome
- Guidance to appropriately select ASM by epilepsy type
- Guidance to appropriately select ASM, adjust ASM dosage, or switch to a different ASM if there are concerns of drug interaction(s) (e.g., avoiding enzyme-inducing ASM for patients prescribed antiretroviral therapy)
- Guidance to adjust ASM dosage perioperatively, if clinically appropriate
- Guidance to taper one ASM when switching to another ASM, such as switching from phenytoin to lamotrigine
- Guidance to initiate ASM taper for a patient with seizure freedom for more than 2 years who is low risk of seizure recurrence (i.e., possible candidate for ASM discontinuation)[13]

INDICATIONS FOR REFERRAL TO NEUROLOGY

Many uncomplicated patients with epilepsy can be managed by PCP, particularly uncomplicated new-onset epilepsy and patients who have maintained seizure freedom on a stable ASM regimen. Select patients may benefit from comanagement with neurology. The ILAE Telemedicine Task Force promotes utilizing telemedicine to reduce the treatment gap for patients with epilepsy, with "consideration given to utilizing a hybrid model of both face-to-face visits and telemedicine" as clinically appropriate.[14]

Consider referring to neurology via telemedicine for most scenarios, including but not limited to the following:

- Recommendation from eConsult
- Patient has abnormal findings on EEG
- Patient has been managed by PCP but has adverse effect(s) to ASM
- Patient has been managed by PCP but continues to have seizures that are unchanged or worsening despite a trial of two different ASMs for at least 3 months
- Patient has unknown etiology of their epilepsy
- Patient has a known epilepsy syndrome, such as Lennox-Gastaut Syndrome and Juvenile Myoclonic Epilepsy
- Patients with epilepsy of childbearing potential (PWECP), especially patients who are pregnant

Consider referring to neurology face-to face for the following scenarios:

- Recommendation from eConsult
- Provider has concerns for abnormal findings on neurologic examination
- Patient had seizures freedom as managed by PCP but now has unexplained seizure recurrence despite adherence to ASM and no drug interactions
- Patient has change in seizure semiology
- Patient has change in behavior or cognition or has other signs of disease progression or deterioration
- Patient has new abnormal findings on neuroimaging[13]

INDICATIONS FOR REFERRAL TO EPILEPTOLOGY

Consider referring to epileptology for the following scenarios:

- Recommendation from eConsult or from neurologist
- Patient has been comanaged with neurology for 12 months and is adherent to ASM regimen but continues to have seizures, since these patients are potential candidates for epilepsy surgical intervention due to uncontrolled epilepsy
- Patient has been comanaged with neurology for 12 months and is adherent to ASM regimen but continues to have adverse effects to ASM[15]

TREATMENT

Medication selection is dependent in part on seizure type and epilepsy syndrome. Seizure freedom and remission is the desired outcome for patients with epilepsy and has been linked to improved quality of life. Avoid drug interactions by utilizing the Drug-Drug Interaction Checker. Certain ASM are sometimes substances of misuse in CDCR/CCHCS. All ASMs confer an elevated risk of suicidal ideation and behavior and an increased risk of teratogenesis.[16]

PROVOKED SEIZURE

Long-term use of ASM is usually not indicated for provoked seizures. Treat the underlying cause of a provoked seizure, if possible. Discontinue prophylactic ASM unless seizures recur.[16]

UNPROVOKED FIRST SEIZURE

For a patient with an unprovoked first seizure, the chance for a seizure recurrence can be estimated and stratified on the basis of clinical factors, with greater risk associated with a prior brain insult or lesion as the cause of the seizure, an EEG with epileptiform abnormalities, a significant neuroimaging abnormality, or a nocturnal seizure. The chance for a recurrent seizure is greatest within 2 years after a first seizure (21-45%).[6,7]

- When choosing among ASM, carefully consider specific therapeutic and adverse event profiles on an individualized basis.
- ASM selection also depends on seizure type, so accurate classification is crucial.
  - ☐ If focal seizure is suspected, then most ASMs are appropriate for first-line therapy.
  - ☐ If generalized seizure is suspected, then broad-spectrum ASMs are recommended.
  - ☐ If the seizure type is not known, then usually a broad-spectrum ASMs is recommended first.
- Advise patients that their risk for ASM adverse events ranges from 7-31% and that these adverse events are predominantly mild and reversible.[6,7,9]
- Some ASMs can be started more quickly while others need to be started at low doses and slowly increased over days, weeks or sometimes months. Starting an ASM quickly may be preferred if the risk for more seizures is high or if the person's lifestyle requires it. Yet, side effects are more likely to occur when an ASM is started at a large dose or the full dose right away or if the dose is increased quickly. Some ASMs have unique advantages and disadvantages that:
  - ☐ Treat comorbid migraine or other pain syndromes
  - ☐ Treat depression or anxiety
  - ☐ Cause weight gain or weight loss
  - ☐ Require serum ASM levels
  - ☐ Increase risk of birth defects in patients with epilepsy of childbearing potential (PWECP)[6,7,9,10,16]
- Avoid drug interactions by utilizing the Drug-Drug Interaction Checker.
  - ☐ Consider drug interactions when new medications are added, when ASMs are added or dosage changes, and when seizure control changes.
- Measure baseline labs, if not already done.
  - ☐ CBC
  - ☐ CMP
  - ☐ Magnesium
  - ☐ 25-hydroxyvitamin D (25[OH]D)
- When a stable dose is achieved for certain ASMs, consider obtaining ASM level to establish a serum baseline.
  - ☐ Drug levels can be used to monitor adherence, especially when seizure control changes.

TREATMENT Cont'd

ETIOLOGIES OF EPILEPSY

- Structural
  - Epilepsy is said to have a structural cause if there is a distinct abnormal structural cause present in the brain that is known to substantially increase the risk of seizures.
- Post-traumatic
  - Seizures which occur early after TBI (within the first week) are felt to be a symptom of the recent injury and are provoked.
  - Seizures which occur in the late period (more than a week) after TBI are more likely to recur and result in post-traumatic epilepsy (PTE).
  - About 1 in 50 people who have TBI will go on to develop PTE, usually within 2 years of TBI.
  - Approximately 25-40% of patients will have remission of their epilepsy with initial treatment, so initiate ASM for patients with early seizure after TBI to decrease the likelihood of progression to status epilepticus.
  - Because of the high rate for repeat seizures, long-term treatment with ASM is recommended for people who have even one late seizure, especially if abnormalities are seen on neuroimaging.[17]

High Risk for Early Seizure	High Risk for Post Traumatic Epilepsy
Cerebral contusion	Same risk factors for early seizure
Cerebral hemorrhage	Had early seizure(s)
Penetrating injury	History of depressed skull fracture
Cerebral edema	TBI related to alcohol use
Focal neurologic exam	Neurosurgery was required
Loss of consciousness for more than 30 minutes	EEG abnormalities post-TBI
	Age >65 years old
	Family history of epilepsy

Table 3: Risk factors after TBI for early seizures (within the first week of head trauma) and post-traumatic epilepsy

- Genetic
- Infectious
  - Central nervous system (CNS) infection is the most common cause of acquired epilepsies worldwide but is more common in the developing world, where the risk of developing epilepsy after a CNS infection is between 6.8-8.3%.
  - Common infections associated with epilepsy are:
    - Neurocysticercosis, cerebral malaria, and other parasitosis
    - CNS mycoses
    - HIV
    - Viral encephalitis
    - CNS tuberculosis
    - Post-bacterial encephalitis
    - Post-intracranial abscess
    - Post-intracranial empyema[17]
- Metabolic
- Immune
- Unknown[2,3]

TREATMENT Cont'd

CHRONIC MANAGEMENT OF EPILEPSY

Once epilepsy is diagnosed, start/continue ASM because the risk for additional seizures is very high (57% by one year and 73% by four years).

- When choosing among ASM, carefully consider specific therapeutic and adverse event profiles on an individualized basis.
- ASM selection also depends on seizure type and epilepsy syndrome, so accurate classification is crucial.
  - ☐ If focal seizure is suspected, then most ASMs are appropriate for first-line therapy.
    - Consider **lamotrigine**, **levetiracetam**, and **zonisamide** for patients with new-onset focal epilepsy
    - Consider **lamotrigine** and gabapentin for patients ≥60 y/o with new-onset focal epilepsy[5,18]
  - ☐ If generalized seizure is suspected, then broad-spectrum ASMs are recommended.
  - ☐ If the seizure type is not known, then usually a broad-spectrum ASMs is recommended first.[14,16,18]
- Advise patients that their risk for ASM adverse events ranges from 7-31% and that these adverse events are predominantly mild and reversible.[6,7,9]
- Some ASMs can be started more quickly while others need to be started at low doses and slowly increased over days, weeks or sometimes months. Starting an ASM quickly may be preferred if the risk for more seizures is high or if the person's lifestyle requires it. Yet, side effects are more likely to occur when an ASM is started at a large dose or the full dose right away or if the dose is increased quickly. Some ASMs have unique advantages and disadvantages that:
  - ☐ Treat comorbid migraine or other pain syndromes
  - ☐ Treat depression or anxiety
  - ☐ Cause weight gain or weight loss
  - ☐ Require serum ASM levels
  - ☐ Increase risk of birth defects in patients with epilepsy of childbearing potential (PWECP)[6,7,9,10,16]
- Avoid drug interactions by utilizing the Drug-Drug Interaction Checker
  - ☐ Consider drug interactions when new medications are added, when ASMs are added or dosage changes, and when seizure control changes.
- Measure baseline labs, if not already done
  - ☐ CBC
  - ☐ CMP
  - ☐ Magnesium
  - ☐ 25-hydroxyvitamin D (25[OH]D)
- When a stable dose is achieved for certain ASMs, consider obtaining ASM level to establish a serum baseline
  - ☐ Drug levels can be used to monitor adherence, especially when seizure control changes.
- ASM are sometimes substances of misuse in CDCR/CCHCS.[16,18]
- Optimize monotherapy before considering a second agent.
  - ☐ If seizures are uncontrolled because patient is not seizure free at the maximally tolerated dose of initial ASM, consider changing to a different first-line ASM.
  - ☐ Titrate new medication to therapeutic level prior to tapering initial ASM.[6,16,18]

TREATMENT Cont'd

PATIENTS WITH EPILEPSY OF CHILDBEARING POTENTIAL

The overarching goals of care for patients with epilepsy of childbearing potential (PWECP) are to optimize clinical outcomes for patients and future pregnancies.

- Counsel all PWECP at least once a year about how epilepsy and its treatment may affect contraception and pregnancy. A shared decision-making process leads to more informed choices, a better understanding of available options, a more accurate risk perception, and improved decision quality grounded in individual values.
- Recommend ASMs, such as **lamotrigine**, **levetiracetam**, or **oxcarbazepine**, and dosages that optimize both seizure control and fetal outcomes should pregnancy occur, at the earliest possible opportunity preconceptionally (e.g., at the time of starting an ASM in a person postmenarche).
- Avoid the use of **valproic acid**, phenobarbital, and topiramate in PWECP to minimize the risk of major congenital malformations (MCMs), adverse perinatal outcomes, and adverse neurodevelopmental outcomes, if clinically feasible.
- Prescribe at least 0.4 mg of **folic acid** supplementation daily to any PWECP treated with an ASM.
- Refer to neurology for comanagement of PWECP.[19]

PATIENTS WITH EPILEPSY WHO ARE PREGNANT

Seizure freedom for at least 9 months prior to pregnancy is associated with a high rate (84%-92%) of remaining seizure-free during pregnancy. During pregnancy, the goal is to minimize the occurrence of convulsive seizures (generalized tonic-clonic seizures and focal-to-bilateral tonic-clonic seizures), which minimizes the potential risks to the birth parent (e.g., seizure-related mortality) and to the fetus.

- Providers should exercise caution in attempting to remove or replace an ASM that is effective in controlling generalized tonic-clonic or focal-to-bilateral tonic-clonic seizures, even if it is not an optimal choice with regards to the risk to the fetus (e.g., **valproic acid**).
- Monitor ASM levels for **lamotrigine**, **levetiracetam**, **oxcarbazepine**, **carbamazepine**, and phenytoin in PWECP throughout pregnancy as guided by individual ASM pharmacokinetics and patient clinical presentation.
- Prescribe at least 0.4 mg of **folic acid** supplementation daily preconceptionally and during pregnancy to any PWECP treated with an ASM.
- Recommend fetal screening for MCMs (e.g., a detailed anatomical ultrasound, where available) for PWECP who are treated with any ASM during pregnancy.
- Refer to neurology and high-risk obstetrics for comanagement of patients with epilepsy who are pregnant.[19,20]

TREATMENT Cont'd

INTRACTABLE EPILEPSY

According to ILAE, treatment-resistant epilepsy, also known as intractable epilepsy, meets the following criteria:

- A patient fails to become (and stay) seizure-free after achieving steady state therapeutic levels on ≥2 ASMs.
- The ASMs prescribed are appropriate for the seizure type and were tried alone and together with other ASMs.
- The patient taking ASMs is able to tolerate treatment (i.e., ASM does not cause any serious adverse effects).

To determine if a patient is a candidate for epilepsy surgery, refer to epileptology (See **Figure 4**) for an extensive evaluation, which includes workup with video-EEG, anatomical (MRI) and functional (PET, SPECT, MEG) imaging, and neuropsychological testing. Consider epilepsy surgery for the following groups.[15,21,22]

- Intractable epilepsy, which affects a third of patients living with epilepsy
- Severe medication side effects are also an indication for epilepsy surgery
- Any patient with epilepsy due to tumor, vascular malformation, or other brain lesion[21]

Epilepsy surgery options:

- Resective surgery – the most common type of resection is anterior temporal lobectomy. For patients with temporal lobe epilepsy, it is now widely accepted that surgery is superior to prolonged medical therapy. Frequently with this type of surgery, more than 70% of eligible patients will be seizure-free.
- Laser interstitial thermal therapy (LITT) – a minimally invasive alternative to surgical resection of an epileptic focus. Most patients may be discharged after a day.
- Other less common surgeries include multiple subpial transections (MST) and corpus callosotomy. These surgeries are palliative, not curative, since they simply interrupt the propagation of the seizures. Despite that, these surgeries can improve the patient's quality of life by decreasing the frequency and intensity of the seizures.
- For patients with epilepsy who are not epilepsy surgery candidates, electrode and stimulator neuromodulation (Vagus Nerve Stimulation or VNS, Deep Brain Stimulation or DBS, Responsive Neurostimulation or RNS®) have been shown to decrease seizure frequency by 40-70%.[21,22,23]

Choosing Antiseizure Medications by Seizure Type or Epilepsy Syndrome		
Seizure Type or Epilepsy Syndrome	**First Line Antiseizure Medications**	**Monotherapy Alternatives**
Focal onset (aware or unaware)	**Lamotrigine** (*slower dosage titration*) **Levetiracetam** (*behavioral changes*) Lacosamide **Oxcarbazepine** (*HLA-B*1502 testing*) **Carbamazepine** (*HLA-B*1502 testing*) **Zonisamide** (heat risk) Gabapentin (*for age ≥ 60 y/o*)	Topiramate (*avoid for PWECP, heat risk*) **Valproic acid** (*avoid for PWECP*) Phenytoin Phenobarbital Brivaracetam
Generalized onset tonic-clonic	**Valproic acid** (*avoid for PWECP*) **Levetiracetam** (*behavioral changes*)	**Lamotrigine** (*slower dosage titration*) Topiramate (*avoid for PWECP, heat risk*)
Generalized onset myoclonic	**Valproic acid** (*avoid for PWECP*) **Levetiracetam** (*behavioral changes*)	
Generalized onset absence	**Valproic acid** (*avoid for PWECP*) Ethosuximide	**Lamotrigine** (*slower dosage titration*) **Levetiracetam** (*behavioral changes*)
Epilepsy Syndrome	Consider referral to neurology* for comanagement of epilepsy syndromes	

Table 4: *First-line ASMs and alternatives by seizure type or epilepsy syndromes.* ***BOLD*** *= CCHCS formulary*

** See INDICATIONS FOR ECONSULT and INDICTATIONS FOR REFERRAL on page 16.*

TREATMENT Cont'd

Antiseizure Medication Characteristics		
Drug	**Daily Dose for Adults**	**Other Characteristics**
BROAD SPECTRUM		
Clonazepam		**Other indications:** anxiety
Diazepam	10 mg IV, maximum rate of 5 mg/min; may repeat at 3-5 min	**Other indications:** alcohol withdrawal, anxiety
Lamotrigine	75-200 mg twice daily	**Other indications:** bipolar disorder, refractory depression
Levetiracetam	1500 mg twice daily	
Lorazepam	4 mg, maximum rate of 2	**Other indications:** agitation, alcohol withdrawal, anxiety
Midazolam	0.2 mg/kg/dose (Max: 10	
Topiramate	120-200 mg in 2 doses	**Other indications:** alcohol withdrawal, alcohol use disorder,
Valproic acid	60 mg/kg/day in 2-3 doses IR	**Other indications:** bipolar disorder, migraine
Zonisamide	400-600 mg/day	Once daily dose
NARROW SPECTRUM		
Carbamazepine		**Other indications:** agitation, bipolar disorder, impulsivity,
Clobazam	Up to 20 mg/day in 2 doses	
Gabapentin	600 mg 3 times a day	**Other indications:** alcohol use disorder, anxiety, migraine,
Lacosamide	150-200mg in 2 doses	
Oxcarbazepine	1200-2400 mg/day in 2-3 doses	**Other indications:** aggression, bipolar disorder, impulsivity
Phenobarbital	Maximum 240 mg/day	**Other indications:** alcohol withdrawal
Phenytoin	300-400 mg/day in 3-4 doses	
ABSENCE SEIZURES		
Ethosuximide		

Table 5: *Characteristics of broad spectrum and narrow spectrum ASMs.* ***BOLD*** *= CCHCS formulary*

TREATMENT Cont'd

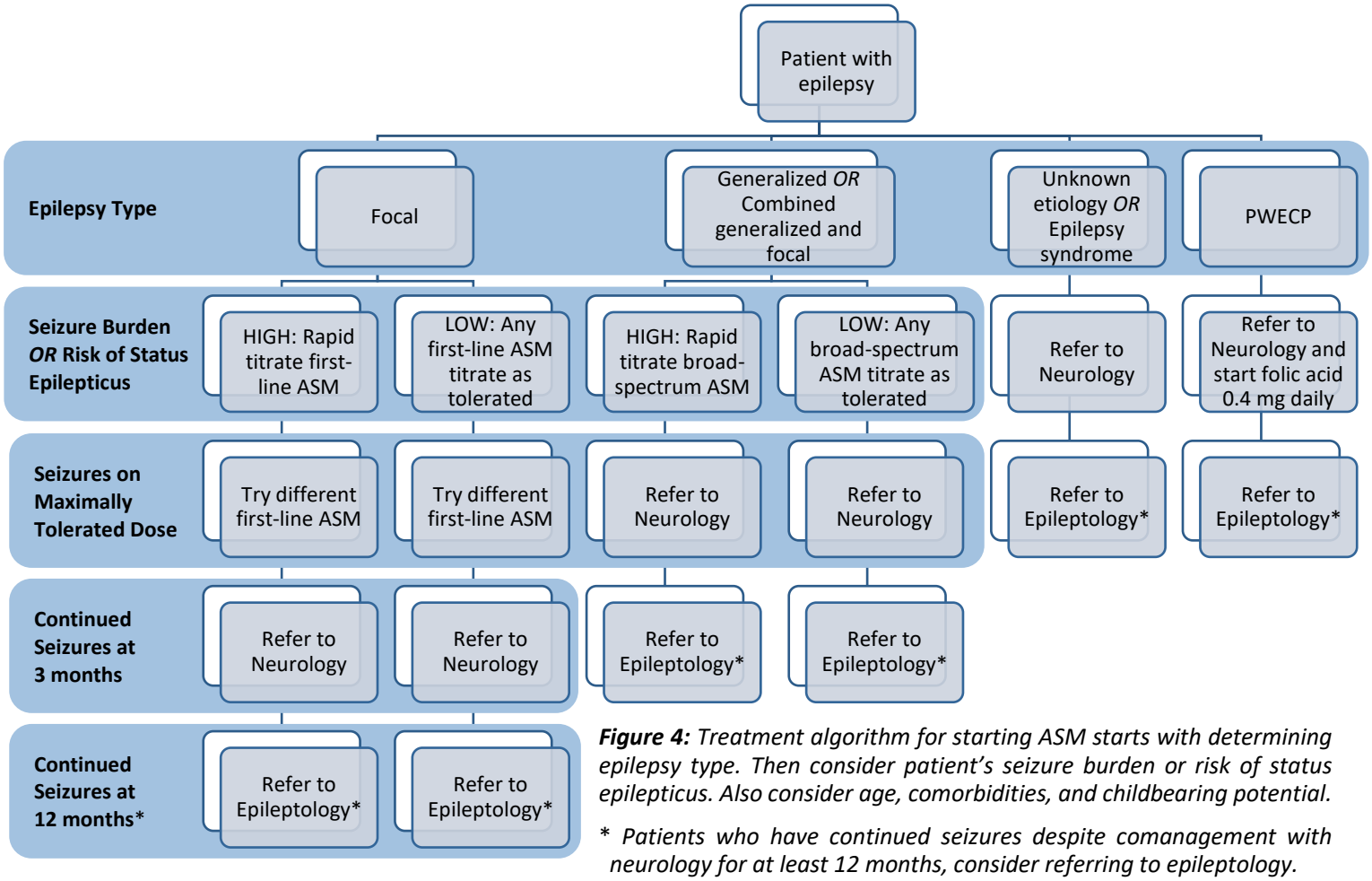

Figure 4: *Treatment algorithm for starting ASM starts with determining epilepsy type. Then consider patient's seizure burden or risk of status epilepticus. Also consider age, comorbidities, and childbearing potential.*

** Patients who have continued seizures despite comanagement with neurology for at least 12 months, consider referring to epileptology.*

See INDICATIONS FOR ECONSULT and INDICATIONS FOR REFERRAL on page 16.

MEDICATION TABLES

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Carbamazepine Tegretol® **IR (Immediate release):** **100 mg chewable tablet,** **200 mg tablet** $-$$	**Indications:** Focal onset seizures, tonic-clonic seizures, and mixed seizure patterns **IR tablets** **Initial Dose:** 200 mg orally twice daily **Titration:** Increase dose weekly by 200 mg/day to max 1600 mg/day in divided doses, three to four times a day. **Usual dose:** 800 to 1200 mg/day. **Max dose:** 1600 mg/day **Give with food** **Half-Life:** 25-65 hours initial doses, 12-17 hours after repeated doses (3 to 5 weeks) due to autoinduction **100 mg chewable tabs:** Only for half tablet dosing of carbamazepine 200 mg (100 mg dose). Do not use multiple tabs to make up higher doses. **Drug levels:** Therapeutic: 4-12 mcg/ml Drug levels not routinely indicated unless to assess adherence or suspected toxicity. Dosage based on seizure control & side effects. Toxic levels: >15 mcg/ml Timing: Just before morning dose Time to steady state: >1 month	Drowsiness, dizziness, blurred or double vision, lethargy, headache, nausea, vomiting, diarrhea, hyponatremia, agranulocytosis, ataxia, thrombocytopenia, increased LFTs, rash, pruritus, AV block, gingival hyperplasia, gingival bleeding, increased caries risk, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** Rare severe reactions including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and Eosinophilia and Systemic Symptoms (DRESS). **Drug interactions:** Appropriate Use Be familiar with prescribing information, particularly regarding use with other drugs. (1) Level is decreased by enzyme-inducing drugs (e.g., phenytoin, phenobarbital, others). (2) Level is increased by many drugs, (e.g., erythromycin, propoxyphene, isoniazid, cimetidine, fluoxetine, others). (3) HCV drugs, HIV drugs, warfarin	**Contraindications:** Hypersensitivity to drug/class/component. Hypersensitivity to TCAs. History of bone marrow suppression. Use with an MAOI or use within 14 days of discontinuing a MAOI. Concomitant use of nefazodone or delavirdine or other nonnucleoside reverse transcriptase inhibitors. **Renal Impairment:** Dose reduction not required. HD: Supplemental dose not needed. **Hepatic Impairment:** Use with caution. Consider dose reduction. **Pregnancy:** Positive evidence of fetal risk. **Lactation:** Probably safe. Usually compatible with breastfeeding per American Academy of Pediatrics. Monitor infant for side effects. **Black Box Warnings** **Asian ancestry:** Perform Human Leukocyte Antigen (HLA) B*1502 allele test prior to initiation. Those testing positive should not be treated unless benefit clearly outweighs risk. (Increased risk of development of Stevens-Johnson syndrome or toxic epidermal necrolysis), monitor CBC, LFT's, and electrolytes periodically. **Blood dyscrasias:** Potentially fatal blood cell problems have occurred. Possibly increased risk in those with low WBC counts. Monitor CBC (baseline, every 12 weeks for 12 months, then annually). Check vitamin D if on carbamazepine for ≥2 years.

Bold = Formulary *See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions, and contraindications.
The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment. *See prescribing information for complete description of dosing, adverse effects and drug interactions.
Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Lamotrigine Lamictal® **IR (Immediate-release) Tablet: 25 mg, 100 mg, 150 mg, 200 mg** $	**Indications:** Focal onset seizures, tonic-clonic seizures, or Lennox-Gastaut syndrome (Adjunctive) **Adjunctive—(IR):** Weeks 1-2: 25 mg/day; Weeks 3-4: 50 mg/day. Maintenance: Titrate dose to effect; after week 4, increase daily dose every 1-2 weeks by 50 mg/day. Usual maintenance dose: 225-375 mg/day in 2 divided doses. **Adjustment for ASM regimens containing valproate (IR):** Weeks 1-2: 25 mg every other day; Weeks 3-4: 25 mg/day. Maintenance: Titrate dose to effect; after week 4, increase daily dose every 1-2 weeks by 25-50 mg/day. Usual maintenance dose: 100-400 mg/day in 1-2 divided doses. (**Note:** For patients taking lamotrigine with valproic acid alone, usual maintenance dose is 100-200 mg/day). **Adjustment for enzyme-inducing ASM regimens (e.g., carbamazepine, phenytoin, phenobarbital, primidone) without valproate (IR):** Weeks 1-2: 50 mg/day; Weeks 3-4: 100 mg/day in 2 divided doses. Maintenance: titrate dose to effect; after week 4 increase daily dose every 1-2 weeks by 100 mg/day. Usual maintenance dose: 300-500 mg/day in 2 divided doses **Half-Life:** 12 - 59 hours **Drug Levels** The value of monitoring plasma concentrations of lamotrigine has not been established.	Rash, drowsiness, nausea, dizziness, ataxia, blurred vision, aplastic anemia, pancytopenia, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts** Rare severe reactions including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and Eosinophilia and Systemic Symptoms (DRESS). **Drug interactions:** (1) Level is increased by many drugs (e.g., valproic acid, others). (2) Level is decreased by enzyme-inducing drugs (e.g., phenytoin, carbamazepine, phenobarbital, others).	**Contraindications:** Hypersensitivity to lamotrigine or any component of the formulation. **Renal Impairment** Use caution. **Hepatic Impairment** Mild impairment**:** No adjustment required. Moderate-to-severe impairment without ascites: Decrease doses by ~25%; adjust as clinically indicated. Moderate-to-severe impairment with ascites: Decrease doses by ~50%; adjust according to clinical response. **Pregnancy** Positive evidence of fetal risk. **Lactation** Probably safe. Usually compatible with breast-feeding per the American Academy of Pediatrics. Monitor infant for side effects. **Black Box Warning** Skin rashes which may be severe and potentially life-threatening have been reported; risk may be increased by coadministration with valproic acid.

Bold = Formulary *See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions, and contraindications.
The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment. *See prescribing information for complete description of dosing, adverse effects and drug interactions.
Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Levetiracetam Keppra® **IR (Immediate-release) Tablet: 250 mg, 500 mg, 750 mg, 1000 mg** Cost $$$	**Indications:** Focal onset seizures, tonic-clonic seizures (adjunctive), myoclonic seizures (adjunctive) **Focal Onset Seizures (IR tablets):** Initial dose: 500 mg orally twice daily; may increase dose by 1000 mg/day every 2 weeks **Adjunctive – Tonic-clonic seizures, myoclonic seizures (IR tablets):** Initial dose: 500 mg orally twice daily Maintenance: increase dose by 1000 mg/day every 2 weeks to a dose of 1500 mg twice daily **Max dose:** 3000 mg/day **Half-Life:** 6-8 hours **Drug Levels** No recommended target level and no clear correlation between trough and therapeutic response. Usual level associated with response 12-46 mcg/ml. Measurement useful to assess adherence.	Dizziness, headache, anorexia, vomiting, asthenia, abnormal behavior, irritability, psychosis, somnolence, fatigue, cough, ataxia, syncope, impaired coordination, vertigo, depression, diarrhea, diplopia. Behavioral disturbances such as aggressive behavior, agitation, hostility, mood symptoms, nervousness, and suicidality have also been reported. **Monitor patients for suicidal behavior and thoughts** Rare severe reactions including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and Eosinophilia and Systemic Symptoms (DRESS). **Drug interactions:** Methotrexate, carbamazepine	**Contraindications** Hypersensitivity to drug/class/component. There are no contraindications listed in manufacturer's labeling. **Renal Impairment** Dose adjustments are based on CrCl adjusted for body surface area (BSA) CrCl 50-80 mL/minute/1.73m^2: 500-1000 mg every 12 hours CrCl 30- 49 mL/minute/1.73m^2: 250- 750 mg every 12 hours CrCl < 30 mL/minute/1.73m^2: 250- 500 mg every 12 hours HD: 500-1000 mg every 24 hours with a supplemental 250-500 mg dose after dialysis **Hepatic Impairment** No adjustment **Pregnancy** Crosses placenta. Fetal risk cannot be ruled out **Lactation** Excreted in human milk. Infant risk cannot be ruled out

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Lorazepam Ativan® **Injectable:** **2 mg/mL – 1 mL** $	**Indication:** Status epilepticus Dosing: 4 mg IV given at a maximum rate of 2 mg/minute; may repeat dose once in 5 minutes if needed	Respiratory depression, hypotension, somnolence, respiratory failure **Drug Interactions:** CNS depressants, opioids, scopolamine, valproate, oral contraceptives, probenecid	**Contraindications:** Hypersensitivity to drug/class/component; acute narrow angle glaucoma **Renal/hepatic Impairment:** No dose adjustment for acute doses **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death; use of benzodiazepines, including lorazepam, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death; continued use of benzodiazepines for several days to weeks may lead to clinically significant physical dependence **Pregnancy** May cause fetal damage when administered to pregnant women. Should not be used during pregnancy except in serious or life-threatening conditions where safer drugs cannot be used or are ineffective **Lactation** Excreted in human milk. Infant risk is minimal

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Oxcarbazepine Trileptal® **IR (Immediate-release) Tablet: 150 mg, 300 mg, 600 mg** $$-$$$ **Oral suspension: 300 mg/5 ml** $$$$-$$$$$	**Indications:** Monotherapy or adjunctive therapy in the treatment of focal onset seizures **Dosing:** **Initial:** 300 mg twice daily **Titration:** **Monotherapy (patients not receiving prior ASMs):** Increase dose every third day by 300 mg/day to a dose of 1200 mg/day in two divided doses. Dose may be increased up to 2400 mg/day to enhance efficacy as tolerated. **Adjunctive therapy:** Increase by a maximum of 600 mg/day at weekly intervals up to 1200 mg/day in two divided doses. **Conversion to monotherapy – Initially:** 300 mg twice daily while simultaneously reducing the dose of concomitant ASMs. Concomitant ASMs should be completely withdrawn over 3-6 weeks, while the maximum dose of oxcarbazepine should be reached in about 2-4 weeks. **Half-Life:** 4-9 hrs. **Drug Levels** Monitoring drug levels is not generally indicated. Maximum dose is determined by side effects and/or adequacy of seizure control. **Time to peak, serum:** 4.5 hours (tablets)	Dizziness, somnolence, headache, ataxia, fatigue, vertigo, abnormal gait, tremor, diplopia, nystagmus, abnormal vision, vomiting, nausea, abdominal pain, fatigue, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** Rare severe reactions including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and Eosinophilia and Systemic Symptoms (DRESS). **Hyponatremia:** Clinically significant hyponatremia (sodium <125 mmol/L) can develop during use; monitor serum sodium, particularly during the first three months of therapy or in patients at risk for hyponatremia. **Drug interactions:** (1) Level is decreased by enzyme-inducing drugs (phenytoin, phenobarbital, verapamil, valproate). (2) May increase phenytoin and phenobarbital levels, may reduce efficacy of oral contraceptives and felodipine and other CCBs. (3) HCV drugs, HIV drugs, warfarin (4) Avoid alcohol due to increased sedative effects of combination.	Contraindications Hypersensitivity to oxcarbazepine or any component of the formulation. Renal Impairment CrCl ≥30 ml/min: No adjustment CrCl <30 ml/min: Start at ½ usual starting dose and increase slowly to achieved desired clinical response Hepatic Impairment Mild-moderate hepatic impairment: No adjustment Severe hepatic impairment: Not recommended Pregnancy Crosses placenta. Fetal harm has been demonstrated Lactation Excreted in human milk. Infant risk cannot be ruled out Important Note: Avoid use in patients with the genetic marker HLA-B*1502 allele as there is an increased risk for Stevens-Johnson syndrome or toxic epidermal necrolysis during treatment. Consider genotyping for HLA-B*1502 allele before starting therapy in patients with lineage to genetically at-risk populations.

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Valproic acid Depakene® **Capsule: 250 mg** **Oral solution: 250 mg/5 ml** $$-$$$ **Divalproex sodium** Depakote ® Tablet DR (delayed-release): 125 mg, 250 mg, 500 mg **Tablet ER (extended-release): 250mg, 500mg** $$-$$$$$	**Indications:** Focal onset with impaired awareness seizures: monotherapy or adjunctive therapy. Absence seizures: monotherapy or adjunctive therapy. **Initial Oral Dose:** Seizures: 10-15 mg/kg/day Administer doses >250 mg/day in divided doses (regular and delayed usually one to three times/ day, ER, usually once daily). **Titration:** Increase by 5-10 mg/kg/day at weekly intervals until therapeutic levels are achieved; maintenance 30- 60 mg/kg/ day. Maximum dose: 60 mg/kg/day Swallow whole, take with a full glass of water. If needed, take with food to reduce GI effects. **Half-Life:** 9-16 hours **Drug Levels** Therapeutic: Epilepsy: 50-100 mcg/ml (valproic acid), seizure control may improve at levels >100 mcg/ml, some patients may experience control with higher or lower serum levels, but toxicity may occur at levels of 100-150 mg/ml. Monitor levels primarily for adherence. Dosage of drug based on seizure control and side effects. Toxic levels: >175 mcg/ml	Significant: (>10%): headache, somnolence, dizziness, insomnia, nervousness, pain, alopecia, nausea, vomiting, diarrhea, abdominal pain, dyspepsia, anorexia, thrombocytopenia, diplopia, blurred vision, infection, flu-like syndrome. Life threatening low incidence: Stevens- Johnson syndrome, TEN, bone marrow suppression, Eosinophilia and Systemic Symptoms (DRESS). **Monitor patients for suicidal behavior and thoughts.** **Drug interactions:** (1) Level is decreased by enzyme-inducing drugs (phenytoin, phenobarbital, carbamazepine and others). (2) Level is increased by erythromycin, aspirin, and amitriptyline. (3) Warfarin	**Contraindications** Hypersensitivity to drug/class/component. Contraindicated with hepatic impairment, mitochondrial disorders, urea cycle disorders. **Renal Impairment** No adjustment needed **Hepatic Impairment** Contraindicated for use in patients with hepatic disease or significant hepatic dysfunction **Pregnancy** Crosses placenta. Positive evidence of fetal risk. Do not administer to patients who are pregnant or of childbearing age unless absolutely necessary. **Lactation** Excreted in human milk. Caution should be exercised when administered to a nursing patient. Of note, usually compatible with breast-feeding per the American Academy of Pediatrics. **Black Box Warnings** **Hepatotoxicity:** Serious or fatal hepatotoxicity, usually occurring in the first 6 mo of treatment, may be preceded by malaise, weakness, facial edema, anorexia and vomiting. **Pregnancy:** Teratogenic (weigh benefits vs. risks). **Pancreatitis:** Life threatening, may occur at start of use or after many years. **Bone health:** Check vitamin D if patient has been on valproic acid for ≥2 years.

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Zonisamide Zonegran® **Capsule:** **25 mg, 50 mg, 100 mg** $$-$$$ Oral suspension: 20 mg/mL $$$$$	Indication (Adjunctive): Focal onset seizure Dosing Initial: 100 mg orally daily in 1-2 divided doses Titration: May increase dose by 100 mg/day every 2 weeks as needed Note: No additional benefit has been demonstrated with dosages above 400 mg/day Max Dose: 600 mg/day Half-Life: 63 hours (plasma) 105 hours (erythrocytes) Drug Levels: 10 to 40 mg/L	Somnolence, anorexia, dizziness, ataxia, agitation/irritability, difficulty with memory and/or concentration, serious hematologic events (aplastic anemia, agranulocytosis), metabolic acidosis, acute myopia, secondary angle closure glaucoma, depression, suicidal ideation, and decreased sweating **Monitor patients for suicidal behavior and thoughts.** Rare severe reactions including toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and Drug Reaction with Eosinophilia and Systemic **Symptoms** (DRESS) **Drug Interactions:** P-gp substrates (e.g., digoxin, quinidine), carbonic anhydrase inhibitor (e.g., topiramate, acetazolamide or dichlorphenamide), methenamine, rifampin, colchicine	**Recommended Use Criteria** • Patient has no contraindications to zonisamide AND • Patient prescribed zonisamide for focal onset seizures **Contraindications:** Hypersensitivity to sulfonamides or zonisamide **Renal Impairment** Slower titration and more frequent monitoring may be required. No quantitative recommendations are available **Hepatic Impairment** Slower titration and more frequent monitoring may be required. No quantitative recommendations are available **Pregnancy** Crosses placenta. Fetal harm has been demonstrated **Lactation** Excreted in human milk. Infant risk cannot be ruled out Heat Alert Medication

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Cenobamate Xcopri® Tablets: 12.5 mg, 25 mg, 50 mg, 100 mg, 150 mg, 200 mg $$$$$	Indication: Focal onset seizures **Dosing** **Initial:** Week 1 & 2: 12.5 mg orally once daily **Titration:** Week 3 & 4: 25 mg orally once daily Week 5 & 6: 50 mg orally once daily Week 7 & 8: 100 mg orally once daily Week 9 & 10: 150 mg orally once daily **Maintenance:** Week 11 and thereafter: 200 mg once daily; dose may be further increased based on response and tolerability by 50-mg increments once daily every 2 weeks to 400 mg daily **Max Dose:** 400 mg once daily **Half-Life:** 50-60 hours	Somnolence, dizziness, fatigue, diplopia, and headache, shortened QT interval, hyperkalemia, diplopia, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** **Drug Interactions:** CNS depressants, opioids Phenytoin: Gradually decrease phenytoin dosage by up to 50% Phenobarbital, Clobazam, CYP2B6 and CYP3A Substrates: Reduce dosage as needed Lamotrigine, Carbamazepine, CYP2C19 Substrates: Increase dosage as needed Oral Contraceptives: Effectiveness of hormonal oral contraceptives may be reduced. Women should use additional or alternative non-hormonal birth control	**Contraindications:** Hypersensitivity to any component of formulation; familial short QT syndrome **Renal Impairment** CrCl <90 mL/min: Use with caution, may consider dosage reduction HD: Not recommended **Hepatic Impairment** Mild-moderate impairment (Child-Pugh A or B): Maximum dose is 200 mg once daily and additional dosage reduction may be considered Severe impairment (Child-Pugh C): Not recommended **Pregnancy** No adequate data on the developmental risk associated with use of this drug in pregnant women; based on animal data, this drug may cause fetal harm **Lactation** No data available on the presence of cenobamate in human milk, the effects on the breastfed infant, or the effects of the drug on milk production. Infant risk cannot be ruled out

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Clobazam Onfi® Tablet: 10 mg, 20 mg $ Suspension: 2.5 mg/mL $$$	**Indication** (Adjunctive): Seizures associated with Lennox-Gastaut syndrome **Dosing** Individualize dose based on clinical efficacy and tolerability **Initial:** 5 mg orally twice daily **Titration:** 10 mg orally twice daily on Day 7, then 20 mg orally twice daily on Day 14 **Poor Metabolizers of CYP2C19** **Initial:** 5 mg orally once daily **Titration:** 5 mg orally twice daily on Day 7, 10 mg orally twice daily on Day 14, then 20 mg orally twice daily on Day 21, as tolerated **Geriatric:** **Initial:** 5 mg orally once daily **Titration:** >30 kg**:** 5 mg orally twice daily on Day 7, 10 mg orally twice daily on Day 14, then 20 mg orally twice daily on Day 21 if required ≤30 kg**:** 5 mg orally twice daily on Day 14, then 10 mg orally twice daily on Day 21 if required **Max Dose:** 40 mg/day (>30 kg); 20 mg/day (≤30 kg) **Half-Life:** 36-42 hours (clobazam); 71-82 hours (N-desmethylclobazam [active metabolite]) **Drug Levels** Clobazam: 30-300 ng/mL N-desmethylclobazam: 300-3000 ng/mL	Constipation, somnolence or sedation, pyrexia, lethargy, drooling, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** Dermatological Reactions (including Stevens-Johnson syndrome and toxic epidermal necrolysis): Discontinue at first sign of rash unless the rash is clearly not drug-related Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multiorgan Hypersensitivity: Discontinue if no alternative etiology **Drug Interactions:** CNS depressants, opioids, hormonal contraceptives, strong CYP2C19 inhibitors (e.g., fluconazole, fluvoxamine, ticlopidine), moderate CYP2C19 inhibitors (e.g., omeprazole)	**Contraindications:** Hypersensitivity to any component of formulation **Renal Impairment** Mild-moderate impairment: No adjustment Severe impairment/ESRD: No recommendation, no data **Hepatic Impairment** Mild-moderate hepatic impairment (Child-Pugh 5-9): >30 kg: Initially 5 mg once daily and titrate to 5 mg twice daily on Day 7, 10 mg twice daily on Day 14, then 20 mg twice daily on Day 21, as tolerated ≤ 30 kg: Initially 5 mg once daily and titrate to 5 mg twice daily on Day 14, then 10 mg twice daily on Day 21, as tolerated **Pregnancy Category: Not assigned** Crosses placenta. In-utero exposure to benzodiazepines has the potential to cause harm to the fetus. **Lactation** Excreted in human milk **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death; use of benzo-diazepines exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death; continued use of benzodiazepines may lead to clinically significant physical dependence.

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Clonazepam Klonopin® Tablet: 0.5 mg, 1 mg, 2 mg $	**Indication:** Lennox-Gastaut syndrome, atonic seizures, myoclonic seizures, absence seizures **Dosing** **Initial:** 1.5 mg/day orally divided into 3 equal doses **Titration:** May increase by 0.5-1 mg every 3 days until seizures are controlled **Usual maintenance dose:** 2-8 mg/day Lower initial dosages and slower titration may be needed in debilitated or elderly adults **Max Dose:** 20 mg/day **Half-Life:** 30-40 hours **Drug Levels:** 0.02 to 0.07 mg/L	Drowsiness, ataxia, dizziness, behavior problems, upper respiratory infection, fatigue, depression, suicidal thoughts **Monitor patients for suicidal behavior and thoughts.** **Drug Interactions:** CNS depressants, opioids, phenytoin, carbamazepine, lamotrigine, phenobarbital, fluconazole, vigabatrin	**Contraindications:** History of sensitivity to benzodiazepines; Significant liver disease; Acute narrow angle glaucoma **Renal Impairment:** No dosage adjustments provided in the manufacturer's labeling; **use** with caution **Hepatic Impairment** Mild-moderate hepatic impairment: No dosage adjustments provided in the manufacturer's labeling; use with caution Severe hepatic impairment (Child-Pugh C): Contraindicated **Pregnancy** Crosses placenta. Fetal harm has been demonstrated **Lactation** Excreted in human milk. Infant risk cannot be ruled out **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death; use of benzo-diazepines exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death; continued use of benzodiazepines may lead to clinically significant physical dependence. Some loss of effect may occur during the course of clonazepam treatment

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ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Diazepam Valium® Diastat® Injectable: 5 mg/mL $$$ Tablet: 2 mg, 5 mg, 10 mg $ Rectal: 10 mg, 20 mg $$$$-$$$$$	**Indication** (Adjunctive)**:** Status epilepticus, focal onset seizures, tonic-clonic seizures, acute repetitive seizures, seizure clusters **Dosing:** **Status epilepticus:** IV: 0.15-0.2 mg/kg/dose (Max: 10 mg/dose) IV as a single dose; may repeat dose once in 5 minutes if needed. Alternatively, 5 to 10 mg IV every 10 to 15 minutes as needed up to a maximum of 30 mg. May repeat in 2 to 4 hours if needed. Rectal: 0.2 to 0.5 mg/kg/dose (round up to the nearest 2.5 mg increment; Max: 20 mg/dose) rectally as a single dose **Adjunctive treatment: focal onset seizures, tonic-clonic seizures:** Oral: 2-10 mg orally 2-4 times daily Older adults: 2-2.5 mg orally 1-2 times daily; increase dose gradually as needed and tolerated **Acute repetitive seizures, seizure clusters:** IV: 5 to 10 mg IV every 10 to 15 minutes as needed up to a maximum of 30 mg. May repeat in 2 to 4 hours if needed. Rectal: 0.2 mg/kg/dose rectally once; round dose upward to the next available dosage strength. May give a second dose 4 to 12 hours after the first dose if needed. Do not treat more than 1 episode every 5 days and more than 5 episodes/month **Max Dose:** Oral: 40 mg/day IV: 20 mg/dose Rectal: 0.2 mg/kg/dose **Half-Life:** IV: 35 to 45 hours; Desmethyldiazepam (active metabolite): 87 hours Oral: 44 to 48 hours; Desmethyldiazepam (active metabolite): 100 hours Rectal: 45 to 46 hours; Desmethyldiazepam (active metabolite): 71 to 99 hours	Drowsiness, fatigue, ataxia, muscle weakness, headache, dizziness, diarrhea, depression, venous thrombosis and phlebitis at the site of injection **Monitor patients for suicidal behavior and thoughts.** **Drug Interactions:** Opioids, phenothiazines, antipsychotics, anxiolytics, sedatives, hypnotics, anticonvulsants, narcotic analgesics, anesthetics, sedative antihistamines, narcotics, barbiturates, MAO inhibitors, antidepressants, phenytoin cimetidine, ketoconazole, fluvoxamine, fluoxetine, omeprazole	**Contraindications:** History of sensitivity to diazepam, myasthenia gravis, severe respiratory insufficiency, severe hepatic insufficiency, sleep apnea syndrome, acute **narrow**-angle glaucoma **Renal Impairment:** No dosage adjustments provided in the manufacturer's labeling; use with caution **Hepatic Impairment:** No adjustment required; however, daily dose reduction of 50% is warranted in cirrhosis **Pregnancy** Crosses placenta. Fetal harm has been demonstrated **Lactation** Excreted in human milk. Infant risk cannot be ruled out **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death; use of benzo-diazepines exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death; continued use of benzodiazepines may lead to clinically significant physical dependence

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Midazolam Versed® Seizalam® Injectable: 5 mg/mL $	**Indication:** Status epilepticus Dosing: 0.2 mg/kg/dose (Max: 10 mg/dose) IM as a single dose	Upper airway obstruction, agitation, pyrexia, decreased tidal volume and/or respiratory rate decrease **Drug Interactions:** CNS depressants, opioids, cimetidine, erythromycin, diltiazem, verapamil, ketoconazole, itraconazole	**Contraindications:** Hypersensitivity to drug/class/component; acute narrow angle glaucoma **Renal impairment:** Midazolam eliminated more slowly, which may result in prolonged drug exposure **Hepatic Impairment:** No dose adjustment for acute doses **Congestive Heart Failure:** Midazolam eliminated more slowly, which may result in prolonged drug exposure **Black Box Warning:** Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death; use of benzodiazepines, including midazolam, exposes users to risks of abuse, misuse, and addiction, which can lead to overdose or death; if used more frequently than recommended, abrupt discontinuation or rapid dosage reduction of midazolam may precipitate acute withdrawal reactions, which can be life-threatening **Pregnancy** Midazolam crosses the placenta. Teratogenic effects have been observed with benzodiazepines in some studies; however, a clear association has not been reported and additional data are needed. Exposure to late in pregnancy may cause neonatal sedation and/or symptoms of neonatal withdrawal **Lactation** Excreted in human milk. Infant risk is minimal

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Drug-Drug Interaction Checker

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ANTISEIZURE MEDICATIONS

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MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Ethosuximide Zarontin® Capsule: 250 mg $-$$	**Indication:** Absence seizure **Dosing** **Initial:** 250 mg orally twice daily **Titration:** Increase 250 mg/day every 4-7 days, based on clinical response, serum level, and tolerability **Max Dose:** 1.5 g/day in divided doses **Half-Life:** 30 to 60 hours **Drug Levels:** 40 to 100 mcg/mL	Anorexia, nausea, upset stomach, vomiting, ataxia, dizziness, headache, somnolence, agranulocytosis, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** Rare severe reactions including Stevens-Johnson syndrome (SJS) and Eosinophilia and Systemic Symptoms (DRESS). **Drug Interactions:** phenytoin, valproic acid, phenobarbital, ritonavir, hydroxychloroquine, nevirapine	**Contraindications:** History of hypersensitivity to succinimides **Renal Impairment** No dosage adjustments provided in the manufacturer's labeling; use with caution **Hepatic Impairment** No dosage adjustments provided in the manufacturer's labeling; use with caution **Pregnancy** Crosses the placenta. Birth defects have been reported **Lactation** Excreted in human milk. Infant risk cannot be ruled out

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Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Gabapentin Neurontin® Capsule: 100 mg, 300 mg, 400 mg Tablet: 600 mg, 800 mg $-$$	**Indication** (Adjunctive)**:** Focal onset seizures with and without secondary generalized tonic-clonic seizures **Dosing** **Initial:** 300 mg orally 3 times daily **Titration:** Increase dose based on response and tolerability; usual dose 300-600 mg orally 3 times daily **Max Dose:** 2400 mg/day (long-term), 3600 mg/day (short-term) **Half-Life:** 5 to 7 hours **Drug Levels:** 5.9 to 21 mcg/mL	Somnolence, dizziness, ataxia, fatigue, nystagmus, peripheral edema, weight gain, respiratory depression, suicidal ideation, depression **Monitor patients for suicidal behavior and thoughts.** Rare severe reactions including Stevens-Johnson syndrome (SJS), and Eosinophilia and Systemic Symptoms (DRESS). **Drug Interactions:** Opioids, antihistamines, benzodiazepines, antacids (magnesium or aluminum-containing), baclofen	**Contraindications:** Hypersensitivity to any component of formulation **Renal Impairment** CrCl ≥ 60 mL/min: No dose adjustment needed. CrCl 30- 59 mL/min: 400 to 1,400 mg/day daily in 2 divided doses. CrCl 15-29 mL/min: 200 to 700 mg/day once daily CrCl = 15 mL/min: 100 to 300 mg/day once daily given as 100, 125, 150, 200, or 300 mg. CrCl < 15 mL/min: Reduce daily dose in proportion to CrCl (e.g., CrCl = 7.5 mL/min should receive one-half the dose that an individual with CrCl of 15 mL/min receives) Hemodialysis (HD): maintenance doses based on CrCl as indicated. Give a supplemental post-HD dose ranging from 125 to 350 mg orally (based on maintenance dose and CrCl) after each 4 hours of hemodialysis **Hepatic Impairment** No dosage adjustments are needed **Pregnancy** Crosses the placenta. Inadequate data on the developmental risks associated with the use in pregnant women **Lactation** Excreted in human milk. Infant risk cannot be ruled out

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Lacosamide Vimpat® Tablet: 50 mg, 100 mg, 150 mg, 200 mg Oral solution: 10 mg/mL $$$	**Indication:** Focal onset seizures (monotherapy or adjunctive), primary generalized tonic-clonic seizures (adjunctive) **Dosing** **Initial:** Monotherapy: 100 mg orally twice daily Adjunctive Therapy: 50 mg orally twice daily **Titration:** Increase by 50 mg orally twice daily every week **Usual Dose**: Monotherapy: 150 mg to 200 mg orally twice daily Adjunctive Therapy: 100 mg to 200 mg orally twice daily **Max Dose:** 400 mg/day **Half-Life:** 13 hours (15 to 23 hours for metabolite)	Diplopia, headache, dizziness, nausea, somnolence, vomiting, diplopia, vertigo, blurred vision, tremor, ataxia, euphoria, fatigue, nystagmus, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** **Drug Interactions:** Medications affecting card (sodium channel blockers, beta-blockers, calcium channel blockers, potassium channel blockers, medications prolong PR interval (sodium channel blocking AEDs), strong inhibitors of CYP3A4 and CYP2C9	**Non-formulary Use Criteria** • Patient has no contraindications to lacosamide AND • Patient prescribed or recommended lacosamide use be initiated or continued by a consulting neurologist, epileptologist, or neurosurgeon **Contraindications:** Hypersensitivity to any component of formulation **Renal Impairment** CrCl ≥ 30 mL/min: No dosage adjustment necessary CrCl < 30 mL/min: A reduction of 25% of the maximum dosage is recommended **Hepatic Impairment** Mild to moderate impairment: A reduction of 25% of the maximum dosage is recommended Severe impairment: Use not recommended **Pregnancy** Crosses the placenta. Inadequate data on the developmental risks associated with the use in pregnant women **Lactation** Excreted in human milk. Infant risk cannot be ruled out Cardiac Rhythm and Conduction Abnormalities: Obtaining ECG before, beginning, and after titration to steady-state maintenance is recommended in patients with underlying proarrhythmic conditions or on concomitant medications that affect cardiac conduction; closely monitor these patients

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Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Phenytoin Dilantin ® Capsule ER (extended-release): 100 mg $-$$$ Oral suspension: 125 mg/5 ml $$-$$$	**Indications:** Tonic-clonic, focal onset seizures with impaired awareness, status epilepticus **Capsule ER:** **Initial dose:** 100 mg orally 3 times daily with dose adjustment at no less than 7-10 day intervals. **Maintenance dose:** 100-200 mg 3 times daily. May consider converting established patients on 100 mg 3 times a day to 300 mg ER once daily. **Loading dose ER capsules (excluding patients with renal or liver disease):** Reserve for patients in a setting where phenytoin levels can be monitored. 1 g divided into 3 doses (400, 300, 200 mg) orally at 2-hr intervals. Begin maintenance dosage 24 hrs after load. **Oral Suspension:** 125 mg 3 times daily, then individualized up to 625 mg/day divided into 3 doses. Shake well before use. Absorption impaired with continuous NG feeding. **Dosage adjustment in obesity** Use adjusted body weight (ABW) calculation. **Max loading dose:** 2000 mg **Half-Life:** Variable depending on dose and patient factors, 7-42 hrs. **Drug Levels** Therapeutic serum/plasma concentration: 10-20 mcg/ml (total), 1-2 mcg/ml (free); Note: Appropriate drug level informs seizure control with acceptable side effects (may be <10 mcg/ml or >20 mcg/ml); Toxic Levels: >20 mcg/ml (total), >2 mcg/mL (free) Timing: 24 hr after oral load or prior to next dose; Time to steady state: 7-10 days, highly variable; Titration (after a loading dose) If rapid therapeutic levels needed, initial levels may be drawn within 24 hr (oral loading dose) to determine maintenance dose or need to reload.	Neurologic: ataxia, drowsiness, confusion, headache, insomnia, slurred speech, twitching, vertigo, Nystagmus Dermatologic: bullous dermatitis, morbilliform rash, Stevens-Johnson syndrome, Toxic epidermal necrolysis. GI: constipation, dysgeusia, enlargement of lips, gingival hyperplasia, nausea, vomiting. Hematologic: agranulocytosis, leucopenia, pancytopenia, thrombocytopenia, porphyria, Dyscrasias. Hepatic: hepatitis, liver failure. Check vitamin D if patient has been on Phenytoin for ≥2 years. Dental: gingival hyperplasia, gingival bleeding, increased caries risk. Hypersensitivity: Eosinophilia and Systemic Symptoms (DRESS) Neuropsychiatric: depression, suicidal ideation. **Monitor patients for suicidal** behavior **and thoughts.** **Drug interactions:** (1) Level is decreased by enzyme-inducing drugs (e.g., carbamazepine, phenobarbital, others). (2) Level is increased by many drugs (e.g., isoniazid, sulfonamides, fluoxetine, others). (3) HCV drugs, HIV drugs, warfarin	**Non-formulary Use Criteria** • Patient prescribed or recommended phenytoin use initiated or continued by a consulting neurologist, epileptologist, neurosurgeon AND • Patient has no contra-indications to phenytoin AND • ASM on formulary at optimized doses have not resulted in seizure freedom AND/OR • ASM on formulary at optimized doses have been discontinued due to adverse effects Exceptions: • Patients seen at reception center have a 6-month grace period for referral to neurology to recommend continuation or co-manage a taper • Patients currently prescribed phenytoin will have a 6-month grace period to send patient to neurology to either recommend continuation or comanage taper **Contraindications:** Hypersensitivity to phenytoin, other hydantoins, or any component of the formulation. Concomitant use with delavirdine or rilpivirine. **Renal Impairment:** CrCl <25 mL/min—dosage adjustment. Monitor free phenytoin levels. **Hepatic Impairment:** Patients with hepatic disease or impaired liver function may show early signs of toxicity. Monitor free phenytoin levels closely. Dosage adjustments as needed. **Pregnancy:** Crosses placenta. Positive evidence of fetal risk. Maternal use of phenytoin should be avoided when possible **Lactation:** Excreted into human milk. Breastfeeding not recommended

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MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication. Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Pregabalin Lyrica® Capsule: 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg, 300 mg $-$$	**Indication** (Adjunctive)**:** Focal onset seizures **Dosing** **Initial:** 150 mg/day orally divided 2 to 3 times day **Titration:** Increase dose weekly based on efficacy and tolerability **Max Dose:** 600 mg/day **Half-Life:** 6 hours	Dizziness, somnolence, dry mouth, edema, blurred vision, weight gain, thinking abnormal (primarily difficulty with concentration/attention), ataxia, euphoria, headache, fatigue, peripheral edema, weight gain, Stevens-Johnson syndrome, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** **Drug Interactions:** Opioids, antihistamines, benzodiazepines, barbiturates, baclofen, pioglitazone	**Contraindications:** Hypersensitivity to any component of formulation **Renal Impairment** CrCl ≥ 60 mL/min: No dose adjustment needed. CrCl 30-60 mL/min: 75 to 300 mg/day divided 2 or 3 times daily CrCl 15-30 mL/min: 25 to 150 mg/day divided 1 or 2 times daily CrCl < 15 mL/min: 25 to 75 mg once daily Hemodialysis (HD): supplemental dose after every 4-hour HD treatment • 25 mg/day regimen: 25 or 50 mg supplemental dose • 25-50 mg/day regimen: 50 or 75 mg supplemental dose • 50- 75 mg/day regimen: 75 or 100 mg supplemental dose • 75 mg/day regimen: 100 or 150 mg supplemental dose **Hepatic Impairment** No dosage adjustments are needed **Pregnancy** Crosses the placenta. Inadequate data on the developmental risks associated with the use in pregnant women **Lactation** Excreted in human milk. Infant risk cannot be ruled out

Bold = Formulary *See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions, and contraindications.
The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment. *See prescribing information for complete description of dosing, adverse effects and drug interactions.
Drug-Drug Interaction Checker

MEDICATION TABLES Cont'd

ANTISEIZURE MEDICATIONS

Antiseizure medications (ASM) increase the risk of suicidal thought or behavior in patients taking these medications for any indication.

Monitor patients for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior.

MEDICATION	DOSING*	ADVERSE EFFECTS* DRUG INTERACTIONS	COMMENTS*
Topiramate Topamax® Tablet: 25 mg, 50 mg, 100 mg, 200 mg $-$$	**Indication:** Monotherapy: Focal onset seizure or primary generalized tonic-clonic seizures Adjunctive: Focal onset seizures, primary generalized tonic-clonic seizures, or seizures associated with Lennox-Gastaut syndrome **Dosing** **Initial:** Monotherapy: 25 mg orally twice daily Adjunctive: 25 to 50 mg orally 1 to 2 times daily **Titration:** Monotherapy: Increase dose by 50 mg increments at weekly intervals based on response and tolerability up to 200 mg/day in 2 divided doses; may further increase in 100 mg increments at weekly intervals up to 400 mg/day in 2 divided doses Adjunctive: Increase in 25 to 50 mg increments at weekly intervals based on response and tolerability up to 400 mg/day in 2 divided doses **Max Dose:** 400 mg/day **Half-Life:** 21 hours	Paresthesia, anorexia, weight loss, speech disorders/related speech problems, fatigue, dizziness, somnolence, nervousness, psychomotor slowing, abnormal vision, fever, metabolic acidosis, decreased sweating, hyperthermia, nephrolithiasis, depression, suicidal ideation **Monitor patients for suicidal behavior and thoughts.** Rare severe reactions including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS) **Drug Interactions:** Phenytoin, carbamazepine, valproic acid, carbonic anhydrase inhibitor (e.g., zonisamide dichlorphenamide, acetazolamide), HCTZ, oral contraceptives, pioglitazone, lithium, amitriptyline	**Nonformulary Use Criteria** • Patient has no contra-indications to topiramate AND • Patient prescribed or recommended topiramate use be initiated or continued by a consulting neurologist, epileptologist, neurosurgeon, psychiatrist, or addiction medicine specialist AND/OR • Patient prescribed topiramate for one of the following FDA indications: ▪ Focal, generalized, or combined focal and generalized epilepsy ▪ Migraine prophylaxis **Contraindications** Hypersensitivity to any component of formulation **Renal Impairment** CrCl ≥ 70 mL/min: No dosage adjustment necessary. CrCl < 70 mL/min: Reduce the dose to 50% of the usual dose Hemodialysis: Supplemental dose may be required **Hepatic Impairment** No dosage adjustments are needed **Pregnancy** Crosses placenta. Fetal harm has been demonstrated **Lactation** Excreted in human milk. Infant risk cannot be ruled out Heat Alert Medication

Bold = Formulary *See prescribing information for complete description of dosing, adverse effects, drug interactions, precautions, and contraindications.
The cost scale $-$$$$$ represents the relative cost of acquisition of medication only. Frequency and complexity of medication administration (institution workload, effect on adherence) should be considered when determining overall cost-effectiveness of treatment. *See prescribing information for complete description of dosing, adverse effects and drug interactions.
Drug-Drug Interaction Checker

MONITORING

Regular follow-up is essential to long-term monitoring of seizure control, ASM adherence, and adverse effects. The goal of therapy is seizure freedom with no to minimal adverse effects to therapy.[15]

SEIZURE CONTROL

Controlled seizures mean seizure freedom, no seizure in the past year. Active epilepsy, especially when seizures remain uncontrolled, poses substantial burdens because of somatic, neurologic, and mental health comorbidity; cognitive and physical dysfunction; side effects of ASMs; higher injury and mortality rates; and poorer quality of life. Among the 1.2% of U.S. adults with active epilepsy, 67% had seen a neurologist or an epilepsy specialist in the past year, and 90% of whom are prescribed ASM(s). However, only 44% of patients taking ASMs are seizure-free.[15,16]

The first step to ascertaining seizure control is to ask patients about their adherence to their ASM regimen. Then, ask about the date of their last seizure as well as the frequency of their seizures.

For patients who continue to have seizures despite their existing ASM regimen, optimize monotherapy before considering second agent. If seizures are uncontrolled because patient is not seizure free at the maximally tolerated dose of initial ASM, consider changing to a different first-line ASM. Titrate new medication to therapeutic level prior to tapering initial ASM. ASM dosing changes are based on seizure control and adverse effects, rather than drug levels.[15] Failure to respond to ASMs triggers a review of the patient's epilepsy diagnosis and their adherence to ASM.[6,7] See INDICATIONS FOR ECONSULT and INDICTATIONS FOR REFERRAL on page 16.

EEG has limited use in the management of epilepsy that is controlled. Consider EEG when a patient with epilepsy reports a change in seizure pattern or worsening mental status. Order neuroimaging for patients with a new focal deficit, persistent altered mental status, fever, acute head trauma, intractable headache, history of cancer, or suspected immune deficiency.

Remission is defined as being seizure-free for at least 10 years and off medication for at least 5 years. Patients with PTE and those diagnosed by structural brain abnormalities on neuroimaging are not good candidates for ASM withdrawal. Discontinuation of ASMs in patients with clearly established epilepsy syndromes is also not recommended due to the high risk of seizure recurrence, even after long seizure free intervals on therapy.

When discontinuation of ASM is considered (e.g., for patients in whom epilepsy diagnosis is unclear or those without structural brain abnormalities on neuroimaging who have been seizure-free for at least 2 years), most schedules aim for a 3-9-month taper, with dose reductions at 1-3-month intervals. More rapid tapers have been studied but are associated with higher rates of seizure recurrence.[15,16,21]

ASM ADVERSE EFFECTS

Every ASM, either older or newer generation, has been associated with the occurrence of adverse effects, which are very individual. The older generation ASMs tend to require more frequent laboratory monitoring than the newer drugs. Furthermore, studies in newly diagnosed patients with epilepsy have compared new generation ASMs to older ones and have demonstrated that the newer ASMs were less likely to cause patients to discontinue use than the older ones, which had more adverse effects.

Inquire about the following when starting ASM, titrating the dosage of ASM, or discontinuing dose of ASM:

- Rash
- Behavioral changes and/or new or more frequent RVRs
- Suicidality
- Mental status change, such as alertness, concentration, motor or cognitive function decline
- Excessive bleeding or bruising
- Signs and symptoms of hepatotoxicity
- Signs and symptoms of pancreatitis
- Signs and symptoms of secondary angle closure glaucoma for patients taking topiramate and **carbamazepine**
- Menstrual history and pregnancy status for PWECP[15,16,18,20]

MONITORING Cont.

Consider the following laboratory test to monitor for adverse effects:

- CBC with differential at least every 6 months
- For patients taking **carbamazepine**, ethosuximide, felbamate, phenytoin, and **valproic acid**, consider including
  - Reticulocytes
  - Serum iron
- CMP at least every 3-6 months, then every 6-12 months once stable
- INR/PT/PTT for patients taking **valproic acid** every 6 months and perioperatively, as clinically indicated
- Ammonia for patients taking **valproic acid** or topiramate with symptoms of lethargy, vomiting, hypothermia, or mental status change
- Serum calcium, especially for patients taking **carbamazepine**, phenytoin, primidone, **valproic acid** for ≥2 years
- Serum 25-hydroxyvitamin D (25[OH]D), especially for patients taking **carbamazepine**, **valproic acid**, phenytoin, primidone for ≥2 years
- Serum ASM concentration levels
  - **Carbamazepine**
  - **Valproic acid**
  - Ethosuximide
  - Felbamate
  - Phenytoin
- Lipid panel
  - **Carbamazepine**
- Thyroid function tests
  - **Oxcarbazepine**
  - **Carbamazepine**
- Urinalysis
  - **Carbamazepine**
  - Ethosuximide
- Consider ECG prior to prescribing and upon reaching steady state ASM dose
  - **Lamotrigine**
  - **Carbamazepine**
  - Lacosamide
  - Phenytoin

Include bone health and monitoring vitamin D for **carbamazepine**, phenytoin, primidone, and **valproic acid**. Monitor dental side effects of specific ASMs, i.e., gingival hyperplasia, periodontal disease, increase caries risk. Consider dental follow up at least annually.

ASM dosing changes are based on seizure control and adverse effects, rather than drug levels. Monitor for adverse effects and toxicity, drug interactions, efficacy, and ASM drug levels, when indicated.[8,15] See INDICATIONS FOR ECONSULT and INDICTATIONS FOR REFERRAL on page 16.

MENTAL HEALTH

Functional seizures (FS) are not caused by abnormal brain electrical activity. FS may look like epileptic seizures but have a physiologic and/or psychogenic etiology. They may happen suddenly or start gradually. They may include involuntary changes in behavior, movement, sensation, or awareness that usually last longer than epileptic seizures. A patient with FS lacks awareness of any psychological or distressing factors and is not consciously in control of their symptoms. About 80% of patients with FS have a history of mental health issues, such as depression, anxiety, post-traumatic stress disorder (PTSD), and personality disorders, as well as a history of sexual, emotional or physical abuse. Treatment for FS focuses on addressing underlying causes and helping the patient learn new coping skills and is comanaged with mental health services. FS do not respond to ASM.

MONITORING Cont.

Mood and anxiety disorders are relatively frequent comorbidities in epilepsy, with a lifetime history identified in one in three patients with epilepsy. Several epidemiological studies have suggested that the relationship between psychiatric disorders and epilepsy is not necessarily unilateral but rather bidirectional, and some patients can present with a psychiatric disorder before the emergence of seizures. Screen for depression and anxiety using PHQ-2 and GAD-7 for all patients. Both calculators are available in EBMCalc in EHRS.

Cognitive impairment is a more prevalent comorbidity that affects 70-80% of patients with epilepsy. Cognitive disturbances are multifaceted and are linked to the etiology and age of the beginning of epilepsy, seizure frequency, degree of education attained, and ASM therapy. Given the potential impact of cognitive impairment on daily functioning, it is crucial to assess and manage cognitive deficits in patients with epilepsy. The Montreal Cognitive Assessment (MoCA) can be used to screen for cognitive impairment in patients with epilepsy.[23,24]

DENTAL HEALTH

Patients with epilepsy have significantly more caries and missing teeth compared to the general population because patients with epilepsy generally experience difficulty with motor skills and coordination, which negatively influences tooth brushing ability. Furthermore, approximately half of patients taking phenytoin will experience gingival hyperplasia within 12–24 months of starting this medication. Lastly, seizures can cause minor oral injuries, such as tongue biting and tooth injuries. In some cases, maxillofacial trauma can occur. Therefore, consider referring patients with epilepsy to a dental provider, especially those with tonic-clonic seizures, those prescribed phenytoin, and those who have experience oral and/or facial trauma after a seizure.[25]

PATIENTS WITH EPILEPSY OF CHILDBEARING POTENTIAL

In addition to monitoring seizure control, ASM adherence, adverse effects of ASM, and comorbid mental health conditions, monitor the following for PWECP:

- Menstrual history and pregnancy status
- Pregnancy intention
- Contraception options
- Adherence to folic acid supplementation[19,20]

SUDEP

Patients who continue to have seizures are at greater risk of complications, which is why preventing seizures and other problems is so important. The most serious complications are injuries and death from seizures. Among deaths attributable to seizures, important causes include sudden unexpected death in epilepsy (SUDEP), status epilepticus, physical injuries, and drowning.

Counsel people with epilepsy of SUDEP, even when the probability of the event is low. In one year, SUDEP typically affects 1 in 1,000 adults with epilepsy, but the incidence is even higher among patients with uncontrolled epilepsy.

HEALTH EQUITY ALERT

Multiple population-based studies have reported an increased risk of premature mortality among people with epilepsy compared to the general population. SUDEP incidence is significantly higher among patients with epilepsy who have lower socioeconomic status. In fact, patients with epilepsy in the less advantaged communities are more than twice as likely to suffer SUDEP than their counterparts at the highest end of the socioeconomic spectrum. Not being free of GTCs, not adding ASM when the seizures are not well controlled, and decreased access to epilepsy surgery place patients at increased risk of SUDEP. Seizure control is directly affected by access to medical care.

A major risk factor for SUDEP is the presence and frequency of generalized tonic-clonic seizures (GTCS). Patients who have ≥3 GTCS per year have a 15-fold increased risk of SUDEP. Therefore, improved control of a patient's GTCS will result in a reduced risk of SUDEP, and a reduction in SUDEP risk is an additional benefit to the many benefits resulting from improved seizure control. Many factors that are indicators of uncontrolled epilepsy, including having GTCS, having frequent GTCS, nocturnal seizures, and the absence of seizure freedom, are strongly associated with SUDEP.[26]

ACCOMMODATIONS

CDCR Housing/Activity Restrictions:

- Having epilepsy does not automatically necessitate low bunk and low tier housing. Complete a CDCR 7410, Comprehensive Accommodation Chrono for low bunks for patients with witnessed seizures and/or uncontrolled seizures within the past year despite therapy.
- Lower tiers can be considered on a case-by-case basis.
- Issue restrictions on driving, operating heavy equipment, working with heat, and working at heights.

MONITORING Cont.

PERIOPERATIVE MANAGEMENT

Generally speaking, continue ASM perioperatively to decrease the risk of breakthrough seizures. An exception is when the surgical procedure is intended to capture abnormal electroencephalographic activity, such as for surface or depth electrode recording.

There is a potential decline in therapeutic drug concentrations required for seizure control during a brief period of cessation. Furthermore, some anesthetic agents can decrease the seizure threshold. For patients unable to take oral medications postoperatively, intravenous agents can be used if more than one dose is missed.[27]

ANTISEIZURE MEDICATIONS			
Newer Generation Antiseizure Medications (ASM) ***Levetiracetam*** ***Lamotrigine*** ***Oxcarbazepine*** ***Zonisamide*** *Gabapentin* *Lacosamide* *Pregabalin* *Topiramate* *Vigabatrin*	Continue ASM during the perioperative period. May increase or decrease the metabolism of anesthetic agents, such as neuromuscular blocking agents, so recommend referral to anesthesiology. Check preoperative ECG, CBC, CMP. If the patient has epilepsy with comorbid renal and/or hepatic impairment, consider checking serum drug concentration levels.	Continue ASM during the perioperative period. Patients with epilepsy have an increased risk for postoperative complications.	If the patient will be NPO for at least 24 hours after surgery/procedure, consider obtaining baseline preoperative serum drug concentration levels, if applicable. Furthermore, if there is no intravenous (IV) formulation available of regular antiseizure medication, consider preoperative conversion to one that does have IV formulation with neurology referral.
First Generation Antiseizure Medications ***Carbamazepine*** ***Valproic acid*** *Phenobarbital* *Phenytoin* *Primidone*	Continue ASM during the perioperative period. May increase or decrease the metabolism of anesthetic agents, such as neuromuscular blocking agents, so recommend referral to anesthesiology. Check preoperative ECG, CBC, CMP. If the patient has epilepsy with comorbid renal and/or hepatic impairment, consider checking serum drug concentration levels.	Continue ASM during the perioperative period. Patients with epilepsy have an increased risk for postoperative complications.	If the patient will be NPO for at least 24 hours after surgery/procedure, recommend obtaining baseline preoperative serum drug concentration levels. Furthermore, if there is no intravenous (IV) formulation available of regular antiseizure medication, consider preoperative conversion to one that does have IV formulation with neurology referral.
Benzodiazepines *Lorazepam (oral)* *Diazepam (oral)*	Continue ASM during the perioperative period. Seizure and/or withdrawal risk if abruptly discontinued or chronic dose significantly reduced. Check preoperative CBC, LFT	Continue ASM during the perioperative period. Monitor for CNS depression and delirium in older patients. Patients with epilepsy have an increased risk for postoperative complications.	If the patient will be NPO for at least 24 hours after surgery/procedure, parenteral diazepam and lorazepam are available. Comanage with mental health and/or neurology.

Table 6: *Perioperative medication guidance for ASM.* ***BOLD*** *= CCHCS formulary*

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Appendix 1

Epilepsy Foundation Tips for Seizure Observation and Recording

When watching a seizure, try to note what happens before, during, and after the event. Write down what happened as soon as you can. Include as much information as possible about the following areas:

Behavior Before the Seizure
- What was the person doing at the time of event?
- Were there any changes in mood or behavior hours or days before the event?
- Was there any 'warning' or 'aura' shortly before event?

When Event Occurs
- Date and time

Possible Triggers or Factors That May Make Event More Likely to Occur
- Time of day or month
- Menstruation, pregnancy, changes in contraception, or other hormonal treatment
- Missed, late, or changes in medicines
- Irregular sleep patterns, not enough sleep, other sleep problems
- Irregular eating patterns, specific foods
- During or after exercise or hyperventilation
- Alcohol or other drug use
- Emotional stress, worry, excitement
- Sounds, flashing lights, bright sunlight
- Other illnesses or infections

What Happens During the Event
- Change in awareness, alertness, confusion
- Ability to talk and understand
- Changes in thinking, remembering, emotions, perceptions
- Sensations - changes in seeing, twitching, eye blinking or rolling, drooling
- Changes in muscle tone - body becomes stiff or limp
- Movements - jerking or twitching movements, unable to move, body turning, falls
- Automatic or repeated movements - lip-smacking, chewing, swallowing, picking at clothes, rubbing hands, tapping feet, dressing or undressing
- Walking, wandering, running
- Changes in color of skin, sweating, breathing
- Loss of urine or bowel control

Parts of Body Involved
- Where did symptoms start?
- Where did symptoms spread?
- Which side of the body was affected, or was the effect symmetric?

What Happens After Event
- Response to voice or touch
- Awareness of name, place, time
- Memory of events
- Ability to talk or communicate
- Weakness or numbness
- Changes in mood or how person acts
- Tired, need to sleep

Duration
- Length of aura
- Length of seizure
- Length of postictal phase
- How long before patient returned to baseline/normal activity?

EPILEPSY FOUNDATION

Appendix 2

Epilepsy Algorithm

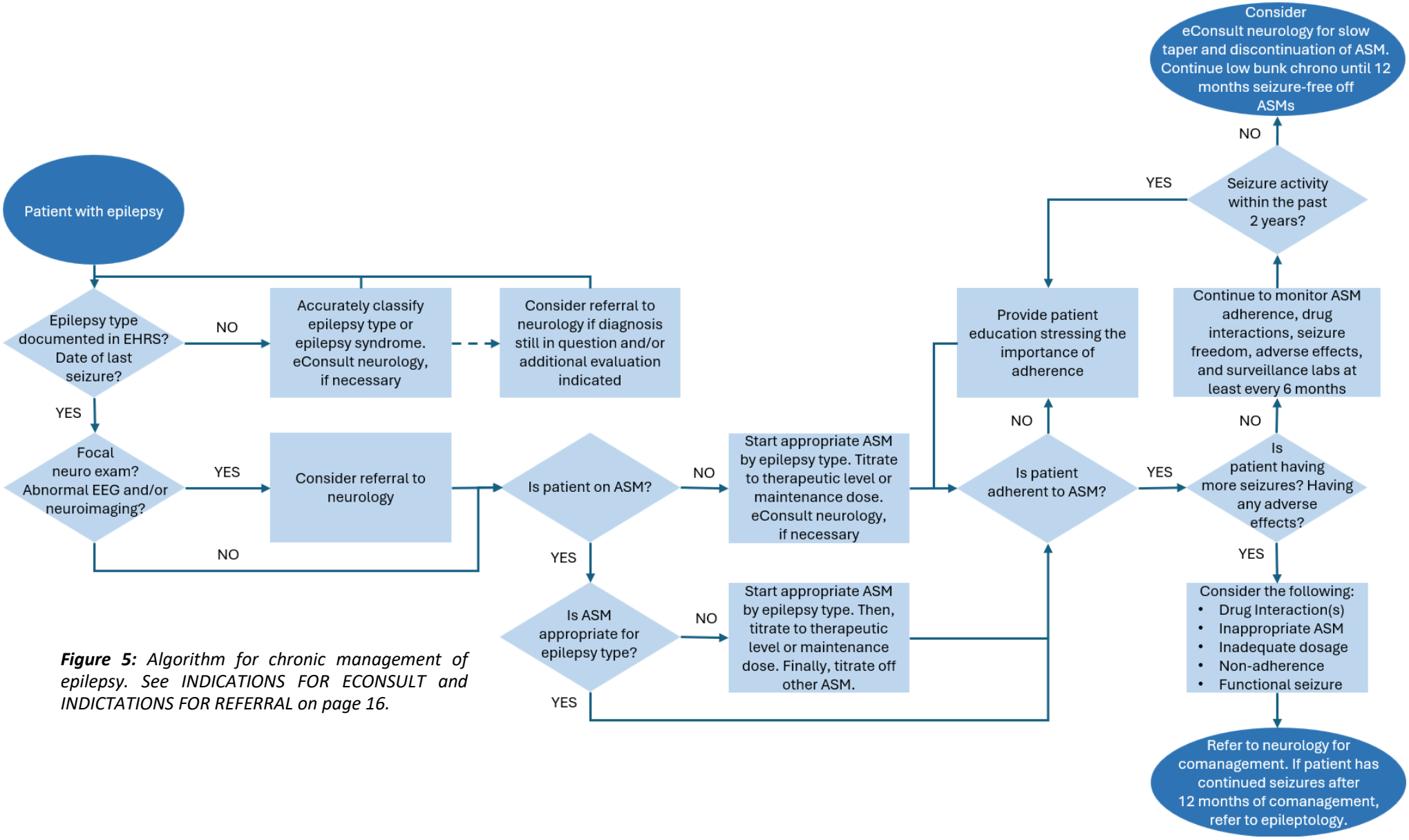


Figure 5: *Algorithm for chronic management of epilepsy. See INDICATIONS FOR ECONSULT and INDICTATIONS FOR REFERRAL on page 16.*

PATIENT EDUCATION

EPILEPSY: WHAT YOU SHOULD KNOW

Q: What is a seizure, and what is epilepsy?

A: A seizure occurs when brain cells—some of them or all of them—are abnormally overactive. Epilepsy is a condition where people are at increased risk for seizures. A person has epilepsy if they have had two or more seizures, without any known reason for them to happen.

An example of a reason not considered epilepsy is when someone has a seizure because of alcohol withdrawal. Level of awareness, body movement, sensation, speech, mood, memory, and emotions can be changed during the few minutes that the seizure lasts. Some people lose consciousness during a seizure.

Q: Do I need to take antiseizure medications?

A: It depends. Follow up with your PCP to see if you need antiseizure medications. Your PCP will probably order lab tests and imaging of the brain for you to do. There are many different types of epilepsy, and some antiseizure medications treat different types of epilepsy.

Q: What do antiseizure medications do?

A: Antiseizure medications decrease the chance that you will have more seizures in the future. They can help patients with epilepsy lead completely seizure-free lives, so it is really important that you take your antiseizure medication as ordered by your PCP. Patients have complete control of seizures with the first antiseizure medication about 50-60% of the time. If the first medication does not control seizures, a second antiseizure medication might help. In about 10-20% of cases, there is an additional chance of seizure freedom. If the second medication fails to stop seizures, another might be tried. This may bring seizure freedom in only 1-3% of patients.

Your PCP will likely refer you to a brain doctor called a neurologist if seizures cannot be controlled on antiseizure medications.

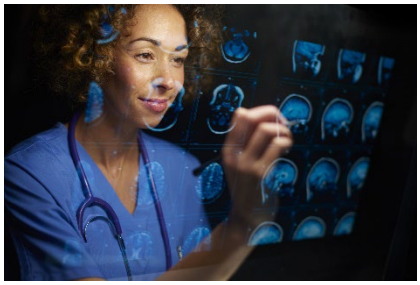
Q: How can antiseizure medications affect me?

A: It depends. Some antiseizure medications can have interactions with other medicines you are taking, so your PCP may need to adjust your other medicines if you start a new antiseizure medication.

Some antiseizure medications have side effects that are short-term. Others continue as long as the medication is taken. Some side effects are linked to dosage. Side effects are different for each antiseizure medication. Ask your PCP if there are any serious side effects. Together, you and your PCP can choose which of the many antiseizure medication will be the safest and most tolerable for you. It is important that your PCP check your progress at regular visits, especially during the first few months of your treatment with antiseizure medication. This will allow your PCP to adjust your dose or switch to a different antiseizure medication, if needed.

Q: I have epilepsy. How do I stay safe?

A: It is really important that you take your antiseizure medication(s) as ordered by your PCP. When you see your PCP at your follow-up visit, tell them when you had your last seizure and how many seizures you have in a week. If you have uncontrolled seizures, be very careful around heat or flames. If your seizures are not in control, avoid working on ladders or unprotected heights, especially if you are alone.



It is rare for people to die from a seizure, but it can happen. The most common cause of death in people with epilepsy is SUDEP, or sudden unexpected death in epilepsy. Since uncontrolled seizures play a role, it is important for you to pay attention to your seizure control.

- Do not suddenly stop your antiseizure medication; it is dangerous and increases your risk of SUDEP.
- If antiseizure medications are not working, let your PCP know.

EDUCACIÓN DEL PACIENTE

EPILEPSIA: LO QUE DEBE SABER

P: ¿Qué es una convulsión y qué es la epilepsia?

R: Una convulsión ocurre cuando las células cerebrales, algunas de ellas o todas ellas, están anormalmente hiperactivas. La epilepsia es una condición en la que las personas tienen un mayor riesgo de sufrir convulsiones. Una persona tiene epilepsia si ha tenido dos o más convulsiones, sin que se conozca ninguna razón para que ocurran.

Un ejemplo de una razón que no se considera epilepsia es cuando alguien tiene una convulsión debido a la abstinencia de alcohol. El nivel de conciencia, el movimiento corporal, la sensación, el habla, el estado de ánimo, la memoria y las emociones pueden cambiar durante los pocos minutos que dura la convulsión. Algunas personas pierden el conocimiento durante una convulsión.

P: ¿Necesito tomar medicamentos anticonvulsivos?

R: Depende. Consulte con su médico de atención primaria (PCP) para ver si necesita medicamentos anticonvulsivos. Es probable que su médico de atención primaria ordene análisis de laboratorio e imágenes del cerebro. Existen muchos tipos diferentes de epilepsia, y algunos medicamentos anticonvulsivos están diseñados para tratar tipos especificos de epilepsia.

P: ¿Qué hacen los medicamentos anticonvulsivos?

R: Los medicamentos anticonvulsivos disminuyen la probabilidad de que tenga más convulsiones en el futuro. Pueden ayudar a las personas con epilepsia a llevar una vida completamente libre de convulsiones, por lo que es muy importante que tome su medicamento anticonvulsivo según las indicaciones de su médico de atención primaria (PCP).

Los pacientes logran un control total de las convulsiones con el primer medicamento anticonvulsivo en aproximadamente el 50-60% de los casos. Si el primer medicamento no controla las convulsiones, un segundo medicamento podría ayudar. En alrededor del 10-20% de los casos, existe una posibilidad adicional de lograr la ausencia de convulsiones. Si el segundo medicamento tampoco funciona, se puede Añadir otro más. Esto puede lograr la ausencia de convulsiones en solo el 1-3% de los pacientes.

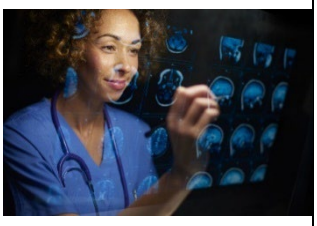
Si las convulsiones no se pueden controlar con medicamentos anticonvulsivos, es probable que su PCP lo dirige a un médico especialista en el cerebro llamado neurólogo.

P: ¿Cómo pueden afectarme los medicamentos anticonvulsivos?

R: Depende. Algunos medicamentos anticonvulsivos pueden tener interacciones con otros medicamentos que esté tomando, por lo que es posible que su PCP deba ajustar sus otros medicamentos si comienza a tomar un nuevo medicamento anticonvulsivo.

Algunos medicamentos anticonvulsivos tienen efectos secundarios a corto plazo. Otros continúan mientras se toma el medicamento. Algunos efectos secundarios están relacionados con la dosis. Los efectos secundarios son diferentes para cada medicamento anticonvulsivo. Pregúntele a su médico de atención primaria si hay algún efecto secundario grave. Juntos, usted y su PCP pueden elegir cuál de los muchos medicamentos anticonvulsivos será el más seguro y tolerable para usted. Es importante que su médico de atención primaria controle su progreso en visitas regulares, especialmente durante los primeros meses de su tratamiento con medicamentos anticonvulsivos. Esto le permitirá a su PCP ajustar su dosis o cambiar a un medicamento anticonvulsivo diferente, si es necesario.

P: Tengo epilepsia. ¿Cómo me mantengo a salvo?



R: Es muy importante que tome sus medicamentos anticonvulsivos según las indicaciones de su médico de atención primaria. Cuando vea a su médico de atención primaria en su visita de seguimiento, dígale cuándo tuvo su última convulsión y cuántas convulsiones tiene en una semana. Si tiene convulsiones incontrolables, tenga mucho cuidado con el calor o las llamas. Si sus convulsiones no están bajo control, evite trabajar en escaleras o alturas sin protección, especialmente si está solo.

Es raro que las personas mueran a causa de una convulsión, pero puede suceder. La causa más común de muerte en las personas con epilepsia es la SUDEP, o muerte súbita inesperada en la epilepsia. Dado que las convulsiones incontroladas juegan un papel, es importante que preste atención a su control de las convulsiones.

- No suspenda repentinamente su medicamento anticonvulsivo; es peligroso y aumenta el riesgo de SUDEP.
- Si los medicamentos anticonvulsivos no están funcionando, infórmeselo a su PCP.