NEW ONSET SEIZURE

SUMMARY
The purpose of the ‘Pediatric New Onset Seizure Clinical Care Guideline’ is to assist primary care providers to make appropriate healthcare decisions surrounding new onset seizures using the best available current evidence.

NEED REAL TIME HELP? CALL US!
- Children's Hospital Colorado Neurology Department has a neurologist on call, the "doc of the day," to assist with advice regarding patient care.
- For urgent calls, it is best to call ‘One Call’ at 720-777-3999. For non-urgent calls, please call the neurology office at 720-777-6985 ext. 2.

EVALUATION
- Obtain a detailed history and screening neurologic exam.

LABORATORY STUDIES
- Labs are rarely helpful to identify etiology during the initial presentation if the patient returns to baseline without intervention. Labs should be ordered based on individual clinical circumstances that include suggestive historic or clinical findings such as vomiting, diarrhea, dehydration, or failure to return to baseline alertness.

ELECTROENCEPHALOGRAM (EEG)
- The most useful test for the initial evaluation of seizures. Usually it is acceptable and practical to obtain EEGs on an outpatient basis.

IMAGING
- Magnetic Resonance Imaging (MRI) is sensitive for subtle findings related to developmental brain abnormalities and remote insult.
- Computed Tomography (CT) is useful to assess skull fractures and hydrocephalus.

TREATMENT
- Antiseizure medications are not usually recommended for first-time seizure but could be considered if history reveals a strong suspicion of absence seizures or previously unrecognized seizures – consult with a Children’s Hospital neurologist for pharmacotherapy options
- Caregiver Information: basic choking intervention, basic seizure safety information, seizure action plan
- Seizure Action Plan: for all settings in the child’s life (school, grandparents house, sleepovers, activities, etc.)

INDICATION FOR CONSULTATION WITH A NEUROLOGIST
Referral to a Children’s Hospital neurologist should happen at any point in which the practitioner feels the patient is beyond their comfort zone or scope of practice. In particular, consider referral for:
- new onset seizure under 3 years of age
- unclear etiology
- multiple neurologic diagnoses
- suspected infantile spasms
- type of seizure unclear
- refractory to medication
- complicated medication management
TARGET POPULATION

Inclusion Criteria

- Patients age 6 months to 21 years
- Patients with first-time seizure
- Patients with newly recognized seizure or epilepsy syndrome

Exclusion Criteria

- Age less than 6 months
- Patients with febrile seizures
- Patients with seizure disorder under the care of a neurologist
- Patients with seizures as a symptom of an acute traumatic brain injury (TBI), central nervous system (CNS) infection, or tumor
- Patients with status epilepticus
- Patients infantile spasms
GENERAL INFORMATION | TERMINOLOGY

Seizure: A transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. A seizure does not necessarily mean that a person has epilepsy\(^\text{1}\).

The recurrence risk following a single seizure is less than 50%. The risk increases with each of the following factors\(^\text{2}\):

1. An abnormal EEG
2. Developmental delay
3. Abnormal exam findings
4. Family history of epilepsy
5. Abnormal brain imaging

Epilepsy: Clinically defined as:

1. At least 2 unprovoked (or reflex to certain stimuli) seizures occurring more than 24 hours apart \(OR\)
2. One unprovoked (or reflex to certain stimuli) 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 \(OR\)
3. Diagnosis of an epilepsy syndrome

Note: Epilepsy is considered resolved for individuals who had an age-dependent epilepsy syndrome and are past the applicable age or those who have remained seizure-free for the past 10 years, with no seizure medicines for the last 5 years\(^3\).

Incidence of epilepsy: The estimated annual incidence in the U.S. is 48 cases of epilepsy for every 100,000 people. The incidence is higher in young children and older adults. When considered over a lifetime, approximately 1 in 26 people will develop epilepsy\(^4\).

COMMON SEIZURE TYPES

Note: In 2010, the International League against Epilepsy (ILAE) introduced new terminology\(^3,5\). Previous terms for etiology include "idiopathic", "symptomatic", and "cryptogenic". These terms have been replaced with "genetic", "structural/metabolic" and "unknown".

Focal seizures

- Affect one hemisphere or smaller area
- Formerly referred to as “simple partial,” “complex partial,” “partial seizures,” and “secondarily generalized”
  - Now referred to by ILAE 2010 as "focal seizure" followed by a description of the degree of impairment during the seizure, such as the following\(^2\):
    - Without impairment of consciousness or awareness
    - With observable motor or autonomic components.
      - This roughly corresponds to the concept of “simple partial seizure.” “Focal motor” and “autonomic” are terms that may adequately convey this concept depending on the seizure manifestations.
    - Involving subjective sensory or psychic phenomena only
      - This corresponds to the concept of an aura,
    - With impairment of consciousness or awareness.
      - This roughly corresponds to the concept of complex partial seizure.
      - “Dyscognitive” is a term that has been proposed for this concept\(^3\).
• Evolving to a bilateral, convulsive seizure (involving tonic, clonic, or tonic and clonic components)
  ○ This expression replaces the term “secondarily generalized seizure.”

Generalized seizures
• Involve bilateral neural networks
• Can be asymmetric
• Include the following types:
  ○ Generalized Tonic - Clonic Seizures (formerly called “grand mal” seizures): Generalized convulsive seizures, typically bilateral and symmetric, although variants with asymmetry including head and eye deviation can be seen.
    • A clonic seizure is a seizure involving bilaterally rhythmic jerking and may occur alone or in combination with tonic activity where there is bilaterally increased tone of the limbs typically lasting seconds to a minute.
    • A tonic-clonic seizure is a seizure consisting of a tonic and a clonic phase, typically in this order
  ○ Absence Seizures (formerly called “petit mal” seizures): Abrupt onset/offset of altered awareness that can vary in severity and have associated motor features.
    • Consider focal seizure if individual absence seizure last longer than 45 seconds or has a postictal phase.
    • Consider glucose transporter disorders if onset of absence seizures occurs in child less than 2 years old.
  ○ Myoclonic Seizures: Single or series of jerks (brief muscle contractions) and are not as prolonged or rhythmic as clonic seizures.
  ○ Atonic Seizures (formerly called “drop” seizures): Involves sudden loss or diminution of muscle tone without apparent preceding myoclonic or tonic features.
    • Very brief (less than 2 seconds) and may involve the head, trunk or limbs.
    • Atonic seizures often occur in individuals with intellectual impairment.

COMMON EPILEPSY SYNDROME
This list focuses on common syndromes and is not inclusive (references: epilepsy.com and epilepsydiagnosis.org)

1. Childhood epilepsy with centrotemporal spikes:
   (formerly called “benign childhood epilepsy with centrotemporal spikes” (BECTS) or “Rolandic epilepsy”)
   • Self-limiting epilepsy (remitting at predictable age)
   • Age: Onset is between 3 and 14 years (peak 8-9 years). Seizures usually resolve by age 15 years
   • Gender: Both sexes are affected.
   • History/Physical: Antecedent, birth and neonatal history is normal. A history of febrile seizure is seen in 5-15% cases.
   • Deficits: During the course of the active epilepsy, behavioral and neuropsychological deficits may be found, particularly in language and executive functioning.
   • Characteristics: Patients and their families often describe nocturnal and very early morning seizures with facial twitching, arrest of speech that the child often remembers. Seizures can include jerking of a limb or progress to a generalized seizure.
   • Treatment: Seizures are often sporadic and usually brief so treatment is not always indicated even after a second seizure depending on the family’s preference. Oxcarbazepine and zonisamide (among others) are reasonable first choice treatments.
   • Tip: if the EEG and story are diagnostic, imaging is not needed since it is typically normal.
2. **Childhood Absence Epilepsy (CAE):**
   - Typically self-limiting epilepsy
   - Age: Characterized by onset of frequent absence seizures between the ages of 2 to 12 years (peak 5 to 6 years)
     - Seizures usually resolve by puberty
   - Gender: Both sexes are equally affected.
   - History/Physical: Antecedent and birth history is normal. A history of febrile seizures is seen in 15-20% of cases.
     - Neurological examination and head size are normal. Development and cognition are typically normal.
   - Deficits: Attention deficit hyperactivity disorder and learning difficulty may occur.
   - Characteristics: A small percentage of patients have generalized convulsions — which should be included on the seizure action plan.
   - Treatment: Seizures respond well to medication for the majority of patients. Common treatment choices are ethosuximide (treat absence only) and valproic acid (treats absence and convulsions). Lamotrigine also treats absence and convulsive seizures but is often a second choice. Other options can be considered but have not been well evaluated, such as levetiracetam, topiramate and zonisamide.
   - Tips: Consider Juvenile absence epilepsy (JAE) with onset after age 8 and less frequent seizures. JAE has a lower likelihood of spontaneous remission.

3. **Juvenile Myoclonic Epilepsy (JME):**
   - myoclonic seizures and generalized tonic-clonic (formerly called “grand mal”) seizures and Absence (formerly called “petit mal”) seizures,
   - Age: characterized by onset between 8 to 25 years of age. A small number (approximately 5%) of cases evolve into this syndrome from childhood absence epilepsy. Seizures continue into adulthood.
   - Gender: Both males and females are equally affected.
   - History/Physical: Antecedent and birth history is normal. A history of febrile seizures is seen in 5-10% of cases.
     - Development and cognition are typically normal. Neurological examination and head size are normal.
   - Treatment: Valproic acid is the most effective anti-epileptic drug in the treatment of juvenile myoclonic epilepsy; however, it is not the appropriate first choice to treat women of childbearing years. Levetiracetam is another possible drug choice; however, it has not been well studied for all of the seizure types that occur within this syndrome. Levetiracetam is approved for use in the treatment of myoclonic seizures in juvenile myoclonic epilepsy. Lamotrigine is widely used for juvenile myoclonic epilepsy. However, it may lead to worsening of the myoclonic jerks even though it may be helpful for the generalized convulsions and absence seizures. (ref.epilepsy.com)
   - Tips: Ask about early morning jerky movements for teens presenting with generalized convulsions; many anti-seizure medications can worsen myoclonic seizures. Counsel patients on seizure triggers such as sleep deprivation and alcohol.
     - Imaging is typically normal and is not needed.

4. **Mesial Temporal Lobe Epilepsy:**
   - Behavioral arrest with loss of awareness (dyscognitive features). Automatisms are common and include oro-alimentary and/or gestural automatisms. Seizures often start with a subjective psychic or sensory phenomenon (aura) which can be experiential such as fear or déjà vu. Epigastric and auditory phenomena also occur.
     - Autonomic features are common including pallor and palpitations. Postictal confusion typically occurs.
     - Note: Temporal focal dyscognitive seizures need to be distinguished from absence seizures. While both may have automatisms, temporal lobe seizures are typically longer (> 30 seconds), associated with pallor, and followed by postictal confusion.
   - Deficits: Co-morbid mood and learning conditions can significantly affect quality of life.
Treatment: Oxcarbazepine, lamotrigine and other broad spectrum anti-seizure medications are reasonable first-line treatments.

Tips: These seizures can be difficult to treat so consider referral to a neurologist more quickly than you might other syndromes.

Brain imaging with MRI warranted.

5. Panayiotopoulos syndrome:

Age: Onset is between 1 and 14 years of age (majority between 3 and 6 years). Seizures usually resolve by age 11-13 years.

Seizures are characterized by autonomic, mainly emetic symptoms and often with unilateral deviation of the eyes or head deviation. About two thirds start in sleep; the child may wake up with similar complaints while still conscious or else may be found vomiting, conscious, confused, or unresponsive. Other autonomic manifestations include pallor, flushing or cyanosis, change in pupil size, coughing, incontinence of urine or feces. In most seizures children eventually become unresponsive and might manifest more easily recognizable seizure symptoms.

Gender: Both sexes are affected equally.

History/Physical: Antecedent and birth history is normal. Head size and neurological examination are usually normal. Development and cognition are normal. However, during active seizure periods, subtle neuropsychological deficits in language and executive functioning have been reported. EEGs are abnormal with occipital spikes but not slowing in the majority of cases. Imaging is not needed if the clinical picture and EEG are diagnostic.

Treatment: This disorder is not common, but is worth mentioning because the seizures are rare and often do not warrant treatment, even after a second seizure. If treated, oxcarbazepine, levetiracetam and zonisamide are reasonable first choices.

Tips: Seizures can be confused with migraine headache.

Imaging is not necessary if the clinical description and EEG support the diagnosis.

DIFFERENTIAL DIAGNOSES FOR SEIZURES

1. Breath-holding spells:

6 months through 6 years of age with most common from 1 to 3 years of age. Precipitating injury or surprise with a preceding cry and then long exhalation and respiratory pause is common. Children might stiffen or have clonic movements briefly as part of the syncopal event.

May take a few rounds of questioning to identify

2. Syncope:

Not unusual to have a few seconds of stiffening or jerking with a loss of consciousness

Helpful history includes:

- Preceding triggers such as standing up quickly
- Review of systems with presyncopal or other cardiac symptoms
- Quick return to alertness is less likely to be seizure.

3. Gastroesophageal reflux (GERD)/ Sandifer syndrome:

Age of patient typically in the first years of life. Sandifer syndrome refers to posturing/arching with reflux.

Timing with feeding and other reflux symptoms like spitting up are more suggestive of symptomatic reflux.
4. Nonepileptic events (pseudoseizures, psychogenic) should be considered with:
   - Eyes closed during the ictus
   - Other behavioral concerns in review of history
   - Flailing rather than rhythmic movement, pelvic thrusting
   - No change in color
   - Prolonged or stuttering course without a postictal period

5. Other nonepileptic events such as stereotypies:
   - If the events can be interrupted they are unlikely to be seizures. Calling someone’s name or waving a hand is not enough to interrupt a behavioral event.
   - Tip: Direct the family to immediately and physically stimulate the patient (such as picking the child up or giving a firm nudge) to assess future events.

**INITIAL CLINICAL EVALUATION**

Age at onset, cognitive and developmental antecedents and consequences, motor and sensory examinations, EEG features, provoking or triggering factors, and patterns of seizure occurrence with respect to sleep can help with the diagnosis of seizure type, epilepsy syndrome and possible etiology to direct testing and treatment.

**Event History**

It is critical to obtain as detailed a history as possible at the time of presentation. The determination that a seizure has occurred is typically based on a detailed history provided by a reliable observer. Keep in mind there might be multiple types of events, each of which should have its own description.

Components of event history should include the following when possible:

1. **Description: (see seizure descriptions above for the significance of these details)**
   - It is useful to note the term the family uses for an event if there is more than one type for ease of communication.
   - Include what is happening before the event starts – such as awake/asleep, crying, arising etc.
   - Ask in detail about preceding symptoms – such as fear behavior or sensation, autonomic symptoms like pupillary dilatation, drooling, change in respiratory or heart rate, incontinence, pallor, vomiting.
     - Ask in detail about the event from patient and all observers including details such as- eyes open/closed (closed eyes are less likely to be a seizure), automatisms such as lip smacking or hand fumbling, limp/stiff/jerking at different points in the event, incontinence and length.
     - Clear loss of consciousness from the onset suggests a generalized seizure. Inability to interact normally without complete loss of consciousness suggests focal seizure with dyscognitive features (previously called complex partial) or absence if brief.
     - Staring episodes are more likely to be a seizure when:
       - Spells noted in multiple environments (absence)
       - Spells interrupt activities (absence) or have postictal manifestations (focal)
       - Spells don’t stop with physical touch
       - Spells precipitated by hyperventilation during exam
       - Children sometimes describe a sense of “lost time” or people suddenly moving to a new location
     - Ask in detail about the post-ictal behaviors such as sleepiness, confusion, weakness and aggression.
2. Length of Time:
   • Note: For first-time seizures people often greatly overestimate the length, so it is helpful to compare to something familiar like the length of a commercial, getting in the car, or events that did occur like calling 911.

3. Classification:
   • This section helps you keep the different events separate so that you might efficiently obtain an update at future visits. Don’t box yourself into a classification if you are not sure. It is fine to note “parasomnia vs. focal seizure with dyscognitive features and excessive salivation.”

4. Onset:
   • Age of onset. To make the note useful in future encounters, try to avoid terms like “six months ago” but rather use age or actual dates. Sometimes there is the date of a recognized seizure an earlier date of possible similar event.

5. Triggers:
   • Common triggers are illness, fever, sleep deprivation and less often exposure to a medication or toxin. Trauma and crying as triggers may suggest breath-holding or syncope rather than seizures.

6. Frequency:
   • For subsequent visits it is useful to note the most severe frequency and the current frequency.

7. Last episode:
   • You sometimes need two dates- the most recent definite event and the most recent possible event.

Past Medical History and Review of Systems
1. Birth history: To suggest an in utero or perinatal insult, e.g. loss of fetal movement or a complicated delivery/abnormal placenta might suggest an acquired brain insult as a cause of seizures.
2. Bed-wetting in a child who is usually dry might be a sign of seizures.

Family history
In addition to asking about seizures and developmental disabilities in family members, also ask specifically about febrile seizures and unexplained injuries (one-car accidents or drowning) which might represent a seizure. Sometimes families have new family history at a follow up visit- so ask at follow up visits as well.

Examinations
1. General exam: A thorough general exam is important and should include:
   • Head size compared to body size. Limb asymmetry might suggest a remote insult or developmental brain malformation.
   • Skin markings (including Wood’s lamp examination in light-skinned children). Skin markings may suggest a phakomatosis, such as neurofibromatosis or tuberous sclerosis. Unusual moles or discolored hair patches in the scalp can overlay a cortical malformation. Dysmorphic features can be a clue to an underlying genetic condition.
     Tip: consider head imaging more strongly with such findings

2. Screening neurologic exam: May indicate new or old neurologic injury
   • Cranial nerves: Pupil reactivity, nystagmus, facial symmetry/strength, palate elevation, tongue protrusion
   • Motor: muscle bulk, tone, and strength (assess for asymmetries), reflexes including plantar response
   • Coordination: finger to nose movements (assess for focal tremors)
   • Gait: Look for asymmetry.
3. **Additional exams:**
   - Hyperventilation is helpful to reveal absence seizures during a visit. You might use a pinwheel or ask patients to blow forcefully on a piece of tissue to make it move for 2 minutes and observe during that time and for several minutes after.

**LABORATORY, IMAGING, AND OTHER STUDIES**

Note: Labs are rarely helpful to identify etiology during the initial presentation if the patient returns to baseline without intervention.

**Labs**

Laboratory tests should be ordered based on individual clinical circumstances that include suggestive historic or clinical findings such as vomiting, diarrhea, dehydration, or failure to return to baseline alertness.

1. **Urine toxicology:**
   - Consider if patient has prolonged post-ictal state or if there is any suspicion of drug exposure or substance abuse
2. **Complete blood count (CBC) and urinalysis (UA)**
   - If infection suspected
3. **Lumbar puncture (LP)**
   - If concern for possible meningitis or encephalitis based on the whole clinical picture; with a lower threshold to obtain for children under 6 months of age who are not returning to baseline.

**Electroencephalogram (EEG)**

Electroencephalogram (EEG) is the most useful test in evaluation of seizures. The ideal timing is unclear. Usually it is acceptable and practical to obtain EEGs on an outpatient basis. Although EEGs are more likely to be abnormal within the first 48 hours following a seizure, abnormalities such as slowing, need to be interpreted cautiously and are not of enough significant usefulness to routinely push for that period.

**NOTE: Consider urgent inpatient EEG for persistent mental status changes to rule out subclinical seizures.**

It is possible and common to have normal EEGs, even with definitive epilepsy. Inter-ictal EEG abnormalities are not uncommon and do not necessarily confirm a diagnosis of epilepsy, so it is important to confirm that the EEG findings support a specific diagnosis.

The EEG is usually diagnostically reliable with conditions such as:

- Absence epilepsy
- Juvenile myoclonic epilepsy
- Benign Rolandic epilepsy
- Infantile spasms and other epileptic encephalopathies (not in scope of this guideline)

**Imaging**

- Brain imaging uncovers abnormalities requiring acute intervention in only 2% of children at the time of first seizure.
- Abnormalities which affect prognosis and management are found in 10-20% of non-urgent studies for first seizures.

- Ophthalmoscopic exam for papilledema, especially if acutely ill
Infants are more likely to have seizures from a remote symptomatic etiology, such as perinatal stroke or focal cortical dysplasia\(^6\).

Brain imaging is often not needed for generalized seizures or recognizable self-limited epilepsy syndromes.

Brain imaging IS indicated for:

- Patients of any age with focal findings during the ictal or postictal period,
- Focal EEG abnormality (unless the features are consistent with a known epilepsy syndrome)
- Abnormal patient exam such as motor or limb size asymmetry or skin findings associated with brain abnormalities such as neurofibromatosis, tuberous sclerosis, and patches of discolored hair (which can be associated with underlying focal cortical dysplasia)
- Unclassified generalized seizures in the first year of life and in adulthood.

**Imaging Modalities**

- Magnetic resonance imaging (MRI):
  - If a neuroimaging study is obtained, MRI is the preferred modality for most cases
  - MRI is more sensitive for subtle findings such as developmental brain abnormalities and remote insult.
- Computed tomography (CT) scan
  - Useful to assess acutely for blood, bone windows for skull fracture, and is adequate to assess for hydrocephalus

**INITIAL CLINICAL MANAGEMENT**

The first phone call or visit after a first seizure should focus on:

1. Reassurance
2. Confirm all caregivers know basic choking intervention and seizure safety (see caregiver education)
3. Community resources (see section on community resources) and
4. Result in a seizure action plan for all settings of the child’s life, including: school, grandparents, sleep overs etc. (see section on caregiver education)
5. Treatment: Antiseizure medications are usually not indicated for first-time seizure. Consider medications after a first recognized seizure if history uncovers a strong suspicion of absence (petit mal) seizures or previously unrecognized seizures. (see section on pharmacotherapy)
6. Return and 911 precautions discussed.
   - For self-limited seizures a patient does not need to return to the emergency room for each similar event.
   - Education at the first visit or call can prevent unnecessary emergency room visits.

Tip: Epilepsy.com also has resources for providers
### Anti-seizure medications commonly used in pediatrics: side effects and pearls

<table>
<thead>
<tr>
<th>Generic (Brand)</th>
<th>Available Formulations</th>
<th>Side Effects</th>
<th>Monitoring and Clinical Pearls</th>
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<tbody>
<tr>
<td><strong>Levetiracetam</strong> (Keppra)</td>
<td>Solution: 100 mg/mL, Tablet IR: 250, 500, 750, 1000 mg, Tablet ER: 500, 750 mg</td>
<td>- Mood&lt;br&gt;- Sleep changes&lt;br&gt;- Irritability&lt;br&gt;- Behavior disturbance&lt;br&gt;- Increased blood pressure (diastolic)</td>
<td>Easy titration&lt;br&gt;Often first line&lt;br&gt;Monitor blood pressure in patients aged 1-4 years periodically</td>
</tr>
<tr>
<td><strong>Oxcarbazepine</strong> (Trileptal)</td>
<td>Suspension: 300 mg/5mL: Tablet IR: 150, 300, 600 mg, Tablet XR (Oxtellar brand only): 150, 300, 600 mg</td>
<td>- Unsteadiness&lt;br&gt;- Dizziness&lt;br&gt;- Blurry vision&lt;br&gt;- N/V&lt;br&gt;- Abdominal pain&lt;br&gt;- Diplopia&lt;br&gt;- Nystagmus</td>
<td>Laboratory monitoring:&lt;br&gt;- Serum Na if indicated clinically or if patient at high risk of hyponatremia (i.e. pt at risk for electrolyte imbalance)&lt;br&gt;Prodrug rapidly converted to active component 10-monohydrate derivative (MHD)&lt;br&gt;Drug interactions: Cyp 3A4 Inducer&lt;br&gt;Risk of SJS/TEN increased in Han Chinese, Thai, and Philippines populations due to association with HLA-B*1502</td>
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<tr>
<td><strong>Lamotrigine</strong> (Lamictal)</td>
<td>Chewable/Dispersible tablet: 5, 25 mg, Tablet: 25, 100, 150, 200 mg, Nonformulary for Kaiser: Chewable/Dispersible tablet: 2 mg (brand only), Tablet XR: 25, 50, 100, 200, 250, 300 mg</td>
<td>- N/V&lt;br&gt;- Diplopia&lt;br&gt;- Dizziness&lt;br&gt;- Unsteadiness&lt;br&gt;- Ataxia&lt;br&gt;- Headache&lt;br&gt;- Sedation</td>
<td>Black Boxed warning: Severe dermatologic reactions&lt;br&gt;- risk increased in pediatrics&lt;br&gt;- slow dose titration schedule must be followed&lt;br&gt;- discontinue if rash occurs&lt;br&gt;Drug interactions:&lt;br&gt;- <strong>Lower doses</strong> necessary if taking with Valproic Acid to prevent life threatening rash&lt;br&gt;- Higher dose adjustments if taking with enzyme inducers (carbamazepine, phenytoin, phenobarbital)&lt;br&gt;- Estrogen will decrease lamotrigine by 40-50%; avoid use with oral contraceptive pills (OCPs)</td>
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<tr>
<td><strong>Ethosuximide</strong> (Zarontin)</td>
<td>Syrup: 250 mg/5mL, Capsule: 250 mg</td>
<td>- N/V/D&lt;br&gt;- GI upset&lt;br&gt;- Hiccups&lt;br&gt;- Headaches&lt;br&gt;- Sedation</td>
<td>Laboratory monitoring:&lt;br&gt;- Baseline CBC with diff and LFTs, repeat in 6 weeks and periodically thereafter&lt;br&gt;Drug level monitoring:&lt;br&gt;- To assist with titration and/or toxicity if needed&lt;br&gt;- Therapeutic range 40-100 mcg/mL&lt;br&gt;Drug Interactions:&lt;br&gt;- May increase or decrease serum concentrations of other anticonvulsant medications.&lt;br&gt;- <strong>Take with food or milk</strong> to minimize GI upset</td>
</tr>
<tr>
<td><strong>Valproic acid</strong> (Depakene)</td>
<td>Softgel: 250 mg, Syrup: 250 mg/5mL</td>
<td>- GI upset <em>(esp. liquid)</em>&lt;br&gt;- Alopecia&lt;br&gt;- N/V/D&lt;br&gt;- Sedation&lt;br&gt;- Unsteadiness&lt;br&gt;- Tremor&lt;br&gt;- Thrombocytopenia&lt;br&gt;- Drowsiness&lt;br&gt;- Weight gain</td>
<td>Black Boxed warnings:&lt;br&gt;- Hepatotoxicity&lt;br&gt;- Pancreatitis&lt;br&gt;- Teratogenicity&lt;br&gt;Drug level monitoring:&lt;br&gt;- Baseline CBC with diff and LFTs, repeat in 6 weeks and periodically thereafter&lt;br&gt;- Pregnancy test in patients of childbearing potential prior to initiation&lt;br&gt;- To assist with titration and/or toxicity if needed</td>
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Sprinkle cap: 125 mg
Tablet DR: 125, 250, 500 mg

Nonformulary for Kaiser:
Tablet ER 24hr: 250, 500 mg

- Therapeutic range 50-100 mcg/mL
- Drug interactions
  - Many through inhibition by valproic acid
  - Recommend drug interaction screening

Sprinkle Capsules given by:
- swallowed whole or
- emptying contents of capsule on small amount (teaspoonful) of soft food such as applesauce or pudding
- The drug/food mixture should be swallowed immediately (avoid chewing) and not stored for future use
- Sprinkle capsules are likely to clog g/j-tubes and alternative valproic acid products should be considered

If GI side effects, encourage patient to take with food or slow titration to effective dose or switch to sprinkles (if taking liquid)

### General Pediatric Dosing for anti-seizure medications
*Monotherapy Dosing Only, unless otherwise noted*

<table>
<thead>
<tr>
<th>Generic (Brand) Formulary Dosage Forms</th>
<th>Approved Seizure Types</th>
<th>Approved Ages</th>
<th>Dosing Recommendations</th>
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<tbody>
<tr>
<td><strong>Levetiracetam (Keppra)</strong></td>
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<tr>
<td>Solution: 100 mg/mL</td>
<td>Partial Seizure</td>
<td>≥ 1 month</td>
<td>Initial: 15 mg/kg/day in 2 divided doses x 1 week, then 30 mg/kg/day ▪ Increase daily dose by 20-25% every week based on clinical response and tolerability</td>
</tr>
<tr>
<td>Tablet IR: 250, 500mg</td>
<td>Tonic Clonic</td>
<td></td>
<td>Target dose: 30-60 mg/kg/day</td>
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<tr>
<td>Note: CHCO does not carry the ER formulation on formulary</td>
<td>Myoclonic</td>
<td></td>
<td>Maximum dose: 60 mg/kg/day in 2 divided doses or 1500 mg BID</td>
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<tr>
<td>Oral solution if ≤ 20 kg; oral solution or IR tablet if &gt; 20kg</td>
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<td></td>
<td>NOTE: doses &gt;3000 mg/day have been used in trials, however, there is no evidence of increased benefit</td>
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<tr>
<td>ER only approved for use in ≥ 12 yo</td>
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| **Oxcarbazepine (Trileptal)**         |                        |               |                        |
| Suspension: 300 mg/5mL                 | Partial Seizure        | ≥ 2 years     | Initial: 8-10 mg/kg/day in 2 divided doses ▪ If < 20kg, initial 16-20 mg/kg/day ▪ Increase by 5 mg/kg/day every 3 days based on clinical response and tolerability |
| Tablet IR: 150, 300, 600 mg            |                        |               | Target dose: 30-45 mg/kg/day in 2 divided doses |
| 75mg tablets available by compound     |                        |               | Maximum dose: 60 mg/kg/day (although more than 50 mg/kg/day not often used); 2400 mg/day commonly considered maximum dose |
### Lamotrigine (Lamictal)

Chewable/Dispersible tablet: 5, 25 mg 6.25mg and 12.5mg chewables available by compound

**Tablet:** 6.25, 12.5, 25, 100, 200 mg

**Lower doses MUST be used with Valproic Acid/Divalproex**

If patient on enzyme inducers (such as carbamazepine, oxcarbazepine, phenytoin, phenobarbital) refer to package insert for adjusted dosing recommendations

Doses are rounded DOWN to nearest whole tablet during titration

*Link to Micromedex for dose adjustment on next page

#### Partial Seizure

**Lennox-Gastaut Tonic Clonic ≥ 2 years**

**MONOTHERAPY**

All doses rounded DOWN to nearest whole tablet

**Weeks 1-2:** 0.3 mg/kg/dose once a day OR 0.15 mg/kg/dose twice a day (rounded down to the nearest whole tablet). Max dose: 25mg/day (175 mg/week)

**Weeks 3-4:** 0.3 mg/kg/dose twice a day (rounded down to the nearest whole tablet). Max dose: 50mg/day (350 mg/week).

**Weeks 5 and on:** Increase dose every 2 weeks by 0.3 mg/kg/dose twice a day (rounded down to the nearest whole tablet)

**Target dose:** 2.25 to 3.75 mg/kg/dose twice a day

**Max dose:** 150 mg/kg/dose twice a day (2100 mg/week)

- If patient < 30kg, may need to increase dose by up to 50% based on clinical response

#### COMBINATION with Valproic Acid/Divalproex

All doses rounded DOWN to nearest whole tablet

**Weeks 1-2:** 0.15 mg/kg/dose once a day OR 0.075 mg/kg/dose twice a day (rounded down to the nearest whole tablet). Use 2 mg every other day for patients weighing >6.7kg and <14kg. Max dose: 25 mg/dose every other day (100 mg/week)

**Weeks 3-4:** 0.3 mg/kg/dose once a day OR 0.15 mg/kg/dose twice a day (rounded down to the nearest whole tablet). Max dose: 25 mg/day (175 mg/week).

**Weeks 5 and on:** Increase dose every 2 weeks by 0.3 mg/kg/dose once a day OR 0.15 mg/kg/dose twice a day (rounded down to the nearest whole tablet).

**Target dose:** 1 to 5 mg/kg/dose every day or 0.5 to 2.5 mg/kg/dose twice a day

**Max dose:** 200mg/dose once a day or 100 mg/dose twice a day (1400 mg/week)

- If patient < 30kg, may need to increase dose by up to 50% based on clinical response

### Ethosuximide (Zarontin)

**Syrup:** 250 mg/5mL  
**Capsule:** 250 mg

**Doses exceeding 1.5 g/day should only be done under strict supervision

#### Absence ≥ 6 years

**Initial:** 250 -500 mg PO daily

- Increase daily dose by 250 mg every 4-7 days based on clinical response, serum levels, and tolerability

**Target dose:** 20 mg/kg/day

- If clinical response not achieved, serum levels can be checked to see if they are within accepted therapeutic range (40-100 mcg/mL)
Valproic acid (Depakene)
Softgel: 250 mg
Syrup: 250 mg/5mL

Divalproex (Depakote)
Sprinkle cap: 125 mg
DR cap: 125, 250, 500 mg
ER tab: 250mg, 500mg

1:1 conversion from valproic acid to
divalproex formulations (except 24hr ER

Note: ER is intended for once daily
dosing while DR can be given more
frequently.
Conversion to Depakote ER from a
stable dose of Depakote may require
an increase in the total daily dose
between 8% and 20% to maintain
similar serum concentrations.

Divide doses greater than 250 mg

Initial: 10-15 mg/kg/day
- Increase by 5-10 mg/kg/day at 1 week intervals
  based on clinical response, serum levels, and
tolerability
- If clinical response not achieved, serum levels can
  be checked to see if they are within accepted
  therapeutic range (50-100 mcg/mL)

Max dose: 60 mg/kg/day

*Link for dose adjustment information for lamotrigine: Click Here

#### Acute Treatment Options

**AT HOME ADMINISTERED MEDICATIONS**
- Recommended for single seizure lasting more than 5 minutes and/or more than 6 seizures in an hour

<table>
<thead>
<tr>
<th>Generic (Brand) Formulation</th>
<th>Approved Ages</th>
<th>Dosing Recommendations</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diazepam (Diastat Rectal, Diastat AcuDial)</strong></td>
<td>2 years to 5 years</td>
<td>0.5 mg/kg rectally x 1 Maximum total dose: 20 mg</td>
<td>▪ Drowsiness  ▪ Dizziness  ▪ Unsteadiness  ▪ Respiratory depression (in overdose or with other CNS depressants)</td>
</tr>
<tr>
<td></td>
<td>6 years to 11 years</td>
<td>0.3 mg/kg rectally x 1 Maximum total dose: 20 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>≥ 12 years</td>
<td>0.2 mg/kg rectally x 1 Maximum total dose: 20 mg</td>
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</tr>
<tr>
<td></td>
<td>2.5 mg kit</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 mg kit (delivers 5, 7.5, and 10 mg doses)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20 mg kit (delivers 12.5, 15, 17.5, and 20 mg doses)</td>
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<td></td>
</tr>
</tbody>
</table>

When calculating dose, round UPWARD to next available dose

Common guidelines for use include:
a single seizure more than 5 minutes and more
than 6 seizures in an hour, with case-by-case
exceptions.

We typically recommend calling 911 the first time
it is used.
<table>
<thead>
<tr>
<th>Generic (Brand) Formulation</th>
<th>Approved Ages</th>
<th>Dosing Recommendations</th>
<th>Side Effects and caution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam (Versed)</td>
<td>Non-FDA Approved</td>
<td>High risk medication Do NOT prescribe without neurology consult/input</td>
<td>Consult/phone neurology referral for initiation of this medication. At Children’s we do not provide the prescription until caregivers have had hands-on training from our nurses regarding use.</td>
</tr>
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<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Nasal burning/irritation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Local irritation (sneezing, dry mouth, coughing, tears)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Drowsiness</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>▪ Respiratory depression (in overdose or with other CNS depressants)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Midazolam (Versed) IV formulation. Caution- high risk for pharmacy errors such as use of oral syrup (incorrect) rather than IV formulation. There are a variety of vial sizes and concentrations- so excellent communication about dosing is needed.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Schools without RNs cannot manage doses that require partial vial doses.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Intranasal infuser device (atomizer) and needle-free systems for withdrawing can be hard to obtain.</td>
</tr>
</tbody>
</table>

### INDICATIONS FOR CONSULTATION WITH A NEUROLOGIST

Referral to Neurology should happen at any point in which the practitioner feels the patient is beyond their comfort level or scope of practice. In particular, consider referral for:

1. New onset seizures under 3 years of age
2. Unclear etiology
3. Multiple neurologic diagnoses
4. Suspected infantile spasms
5. Type of seizure is unclear
6. Seizures are refractory to medication
7. Complicated medication management
8. Considering the use of intranasal midazolam – consultation with neurologist is required
9. You may reach a Children’s Hospital neurologist for phone consultation 24/7.
10. For urgent consultations- use one call 720-777-3999 or for non-urgent use 720-777-6895 ext.2 for providers.
PARENT | CAREGIVER EDUCATION

Basic seizure safety information

- Click here for an Epilepsy Foundation resource

Work with the family to develop a written seizure action plan

- Description of seizure type(s)
- Action plan- multiple tiers including what should be treated as an emergency
- Rescue medication instructions

For a seizure action plan resource click on the following link:


For more information on Home Therapy for Seizures: Using Intranasal Midazolam Therapy, click the link for English or Spanish.

Community Resources

- AAP Center on Epilepsy
- Epilepsy Foundation of America. (This site is sometimes adult focused so not all information pertains to children.)
- Epilepsy Foundation of Colorado
- Wyoming Epilepsy Association
- Family Voices. In Colorado Family Voices services are limited but include navigators in large facilities like Children’s Colorado. In Wyoming click here.
- Parent to Parent helps link families to other families with similar issues.
- Grupo Vida is Spanish friendly family support.
- County Public Health RN- public health RNs can assist with case management. Anyone can initiate a request for case management with an HCP nurse. Colorado: Contact via the family’s county health department Wyoming
- Local School RN can assist with seizure safety at school

FREQUENTLY ASKED QUESTIONS (FAQS)

Q. When is an EEG needed for a first-time unprovoked convulsive seizure?
A. A sleep-deprived wake and sleep EEG is recommended for all first-time unprovoked seizures.

Q. When is an EEG needed for staring spells?
A. An EEG is helpful if you have a strong suspicion for absence epilepsy to confirm the diagnosis. Hyperventilation in the office is also a useful way to provoke an absence seizure such that treatment can be started without/before an EEG.

An extended outpatient EEG (EEG lasting 4 to 8 hours) is helpful if staring events are happening numerous times per day to capture an event. Those EEGs should be done with someone who knows the patient well, such as a parent or caretaker, interacting with the patient throughout the EEG to identify staring spells.
A routine sleep-deprived wake and sleep EEG is helpful for sporadic staring spells more suggestive of partial onset seizures, but a normal EEG does not rule out a seizure and an abnormal EEG does not necessarily confirm seizures. Providers should feel free to call neurology “doc of the day” to discuss use of EEG in this setting. One Call 720-777-3999 urgent or 720-777-6895 ext. 2 for non-urgent.

An EEG is not needed for staring spells which can be interrupted by a nudge, unless they are so brief that they cannot be assessed behaviorally.

Q. When is head imaging needed for a first-time unprovoked seizure?

A. Head imaging should be considered when there is a known preceding injury, focal/asymmetric motor symptoms during or after a seizure, or when the neurological exam as focal findings.

Head imaging is not urgent unless there is a close temporal relationship between an injury and new onset focal exam abnormalities, or concern for ongoing infectious/post infectious process.

Tip: unless you are considering an infection or other inflammatory process, non-contrast brain MRI is most often appropriate. When ordering, it is important to comment that the study is for seizure assessment or to choose a seizure protocol, if available, to assure that the correct views are obtained.

Q. When should medication be started after a first-time seizure?

A. Rescue medications such as rectal diazepam (Diastat) or intranasal midazolam can be considered for patients who have had seizures lasting more than a few minutes or for those patients in remote areas. Please note midazolam does not have FDA labeling for seizures.

Daily medication typically is not started after a first-time seizure unless you have strong reason to believe there are ongoing seizures, such as absence or myoclonic seizures. For example, if the patient has a generalized convulsive seizure and you are able to elicit an absence seizure in the office.

Q. What can I tell a patient and family about the likelihood of a repeat seizure?

A. For all comers, the risk of recurrence after a first-time unprovoked seizure, in untreated individuals is around 40-50% within 2 years. Those at the greatest risk of recurrence have either an abnormal EEG or an identifiable neurological condition or symptoms consistent with a neurological disorder (“symptomatic”). The great majority of people who are seen for a first-time unprovoked seizure, and placed on treatment, attain a one to two year remission within 4 or 5 years of the initial event.

Identifying a seizure trigger, such as lack of sleep or intoxication, can be helpful in counseling families to reduce risk of recurrence.

Q. What are useful resources for families whose child has had a first-time seizure?

A. All caregivers should be instructed in basic first aid for seizures and choking at the time of their first presentation for seizures. http://www.epilepsy.com/firstaid

The Epilepsy Foundation https://www.epilepsy.com/ and international league against epilepsy https://www.ilae.org/ have patient centered information and instructional videos on a variety of topics. (Please note the opinions expressed by those groups are not necessarily those of Children’s Hospital Colorado).

Children’s Hospital Colorado will assist families with literature searches as well: http://www.childrenscolorado.org/wellness-safety/health-library

Q. If the child has recurrent seizures, how do I select the appropriate medication?
A. Treatment choice is typically based on seizure type. In most cases there is little data providing head-to-head comparison of efficacy between medications for a specific syndrome. Usually there are first and second line medications that are considered.

Children's Hospital Colorado neurology department has a neurologist on call, the "doc of the day," to assist with advice regarding patient care. For urgent calls, it is best to call ‘One Call’ at 720-777-3999. For non-urgent calls, please call the neurology office at 720-777-6985 ext. 2.

The epilepsy Foundation https://www.epilepsy.com/ and international league against epilepsy https://www.ilae.org/ have resources for professionals. However, please know the opinions expressed by those groups are not necessarily those of Children’s Hospital Colorado.

Tip: If the seizure type is unclear, having families make a video of the events can be helpful.

Q. Can children who have had a seizure participate in sports?

A. Yes.

- Contact sports are not precluded; there is no evidence they induce seizures.
- **Safe with appropriate supervision:**
  - Swimming, water sports, harnessed rock climbing, horseback riding, and gymnastics
- Not safe:
  - Free climbing, sky-diving, hang-gliding, and scuba diving
- Helmets are necessary for anything with wheels.
  - Tip: Ask kids what color their helmet is to be sure they really have one

Q. Can children who have had a seizure drive?

A. Laws about driving vary from state to state.

Colorado has no set seizure-free period or requirement for medical providers to report their patients. The medical provider should instruct patients to report their seizures at the time of licensing. A common recommendation is to allow 6 months with no seizures and no changes in medication before driving.

Tip: driving information can be found at:
http://www.epilepsy.com/driving-laws
References


Clinical pathways are intended for informational purposes only. They are current at the date of publication and are reviewed on a regular basis to align with the best available evidence. Some information and links may not be available to external viewers. External viewers are encouraged to consult other available sources if needed to confirm and supplement the content presented in the clinical pathways. Clinical pathways are not intended to take the place of a physician’s or other health care provider’s advice, and is not intended to diagnose, treat, cure or prevent any disease or other medical condition. The information should not be used in place of a visit, call, consultation or advice of a physician or other health care provider. Furthermore, the information is provided for use solely at your own risk. CHCO accepts no liability for the content, or for the consequences of any actions taken on the basis of the information provided. The information provided to you and the actions taken thereof are provided on an “as is” basis without any warranty of any kind, express or implied, from CHCO. CHCO declares no affiliation, sponsorship, nor any partnerships with any listed organization, or its respective directors, officers, employees, agents, contractors, affiliates, and representatives.

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### APPROVED BY

Clinical Care Guideline and Measures Review Committee – developed prior to inception of committee  
Pharmacy & Therapeutics Committee – June 11, 2015

<table>
<thead>
<tr>
<th>MANUAL/DEPARTMENT</th>
<th>Clinical Care Guidelines/Quality</th>
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<tr>
<td>ORIGINATION DATE</td>
<td>September 25, 2015</td>
</tr>
<tr>
<td>LAST DATE OF REVIEW OR REVISION</td>
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</tr>
</tbody>
</table>

**APPROVED BY**  
Chief Quality and Patient Safety Officer  
Dan Hyman, MD, MMM

### REVIEW/REVISION SCHEDULE

Scheduled for full review on September 25, 2019.
Discrimination is Against the Law. Children’s Hospital Colorado complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Children’s Hospital Colorado does not exclude people or treat them differently because of race, color, national origin, age, disability, or sex.

Children’s Hospital Colorado provides free aids and services to people with disabilities to communicate effectively with us, such as: Qualified sign language interpreters, written information in other formats (large print, audio, accessible electronic formats, other formats). Children’s Hospital Colorado provides free language services to people whose primary language is not English, such as: Qualified interpreters, information written in other languages.

If you need these services, contact the Medical Interpreters Department at 720-777-9800.

If you believe that Children’s Hospital Colorado has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability, or sex, you can file a grievance with: Corporate Compliance Officer, 13123 E 10th Avenue, B450, Aurora, Colorado 80045, Phone: 720.777.1234, Fax: 720.777.7257, corporate.compliance@childrenscolorado.org. You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, the Corporate Compliance Officer is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at ocr.hhs.gov/ocr/office/complaints.htm, or by mail or phone at: U.S. Department of Health and Human Services 200 Independence Avenue, SW Room 509F, HHH Building Washington, D.C. 20201 1-800-368-1010, 800-537-7587 (TDD) Complaint forms are available at www.hhs.gov/ocr/office/file/index.html.