CLINICAL PRACTICE GUIDELINE

Epilepsy in Infants 1 - 36 Months

Evidence-based recommendations for pharmacologic, dietary & surgical management | Infantile spasms excluded — see separate AAN/CNS guidelines

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STEP 1 | ALL NEW-ONSET SEIZURES
Diagnostic Evaluation & Antiseizure Medications

EEG
Evaluate EEG background, classify seizure type, and identify epilepsy syndrome if appropriate.

Brain MRI
Identify structural lesions including malformations of cortical development.

Genetic Testing
Guide etiology-specific therapy; identify genetic etiologies.

GOAL OF EARLY WORKUP
Define seizure type, syndrome, and etiology to direct personalized, evidence-based treatment and enable timely referral decisions.

FIRST-LINE TREATMENT

Generalized/Unknown
- Levetiracetam [I-A-1; I-A-4]
- Lacosamide [I-A-6]
- Topiramate [I-A-5]

Focal Epilepsy
- Carbamazepine [I-A-5]
- Lacosamide [I-A-6]
- Levetiracetam [I-A-1; I-A-4]
- Oxcarbazepine [I-A-3]
- Topiramate [I-A-5]

Persistent Seizures
*With certain genetic etiologies, targeted therapies may be available.

Referral to Pediatric Epilepsy Center

SECOND-LINE TREATMENT

Generalized/Unknown
- Lacosamide
- Lamotrigine
- Levetiracetam
- Topiramate

Focal Epilepsy
- Carbamazepine
- Lacosamide
- Lamotrigine
- Levetiracetam
- Oxcarbazepine
- Topiramate

Persistent Seizures
*With certain genetic etiologies, targeted therapies may be available.

Meets Criteria for Drug-Resistant Epilepsy

IMPORTANT MEDICATION CAUTIONS

Lamotrigine: caution for Stevens-Johnson syndrome and long titration period.
Oxcarbazepine & Carbamazepine: contraindicated in Dravet syndrome and some generalized epilepsies.
Phenobarbital: concern for neurotoxicity and adverse • cognitive effects.
Topiramate: increased risk of metabolic acidosis and nephrolithiasis, especially with ketogenic diet.
Valproate: risk of hepatotoxicity in children <2 years, especially with POLG or mitochondrial • disorders.

Medications listed alphabetically, not in order of efficacy. All recommendations are Conditional with Very Low Certainty of Evidence except I-A-4 and I-B-2 (Conditional with Low CoE). Not evaluated by this guideline: clobazam, cannabidiol, zonisamide, phenobarbital, phenytoin, fenfluramine. Felbamate and gabapentin not used often. Zonisamide lacks FDA approval in this age range.

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STEP 2
REFERRAL TRIGGERS
Consider Referral to Pediatric Epilepsy Center

Structural Brain Lesion
Any lesion on MRI — presurgical candidacy assessment warranted.

Gene-Specific Dietary Indication
GLUT1 deficiency · PDH deficiency — refer before ASM failure; dietary therapy is first- line.

Seizures Persist After 1 ASM
Do not await a second trial before referring — early specialist involvement improves outcomes.

STEP 3
DRUG-RESISTANT EPILEPSY
Surgical, Dietary & Pharmacologic Therapy

DRUG-RESISTANT EPILEPSY (DRE)
- Failure of ≥ 2 appropriate ASMs at adequate doses & duration
- Initiate presurgical evaluation (video-EEG, advanced MRI)
- Concurrent dietary therapy evaluation
- Ongoing individualized reassessment

All three pathways considered on a case-by-case basis — patients may be candidates for more than one simultaneously.

SURGICAL CANDIDATE

Hemispheric Procedures
Hemispherotomy or functional hemispherectomy for refractory unilateral hemispheric pathology.

- Hemimegaloencephaly
- Sturge-Weber syndrome
- Rasmussen syndrome
- Perinatal stroke
- Hemispheric cortical dysplasia

Focal Resections & Disconnections
For drug-resistant focal or lesional epilepsy with defined epileptogenic zone.

- Intralobar resection
- Posterior disconnection
- Multilobar resection

case-by-case ⟷

CONTINUE/TRIAL PHARMACOLOGIC THERAPY

GENERALIZED/ UNKNOWN	FOCAL EPILEPSY
• Brivaracetam [I-B-3]	• Brivaracetam
• Lamotrigine [I-B-5]	• Carbamazepine
• Lacosamide	• Lacosamide
• Levetiracetam	• Lamotrigine [I-B-3]
• Rufinamide [I-B-4]	• Levetiracetam
• Topiramate [I-B-2]	• Oxcarbazepine
• Valproate* [I-B-1]	• Topiramate [I-B-2]

***Valproate: use with caution with unknown etiology or in the absence of other treatment.**

case-by-case ⟷ **DIETARY THERAPY** ⟷ *case-by-case*

Classic Ketogenic Diet (4:1)
preferred for infants <24 months — higher efficacy and precise nutritional control during rapid growth. Requires trained dietitian.

First-line (before (ASM failure)
- GLUT1 deficiency
- PDH deficiency

SURGICAL PRINCIPLE
Early surgical intervention in infancy takes advantage of neuroplasticity and is associated with better neurodevelopmental outcomes. Dietary therapy or additional ASMs may serve as a bridge while surgical planning proceeds.

SPECIAL EPILEPSY SYNDROMES

LENNOX-GASTAUT SYNDROME:
Consider clobazam, rufinamide, valproate, Epidiolex.
DRAVET SYNDROME:
Consider clobazam, stiripentol, Epidiolex (follow published protocol). Avoid sodium channel-blocking ASMs — may worsen seizures and overall outcomes.

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