



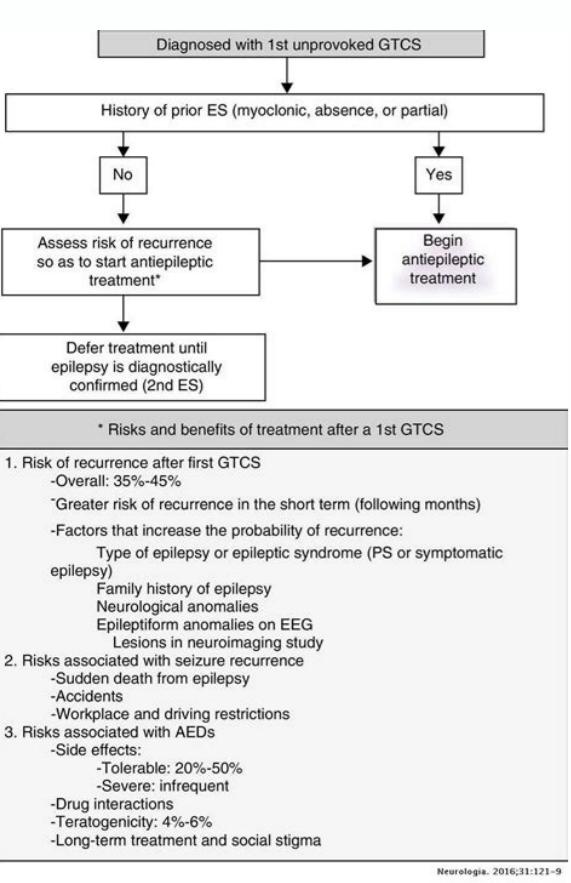
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Refractory epilepsy guidelines



Version 2016/2014

Table 3. Course of Therapy for Patients With Refractory Status Epilepticus (RSE)

Hospital Stay, d	ICU Stay, d	Ventilatory Support, d	MAC Hours of Isoflurane (d)	RSE Prior to Isoflurane, d	Other AEDs Tried During RSE
1 55	30	27	33.8 (2)	3	LZP, diazepam, MOI, PHT, PB, TS, PRO, VPA, LMT
2 19	12	14	43.0 (3)	4	LZP, diazepam, MOI, PRO, CSE, VPA, GBP, TFM
3 49	27	18	151.4 (6)	1	LZP, diazepam, diazepam, MOI, PRO, PHT, PB, TS, PRO, CSE, VPA
4 84	58	56	278.2 (1)*	Isoflurane 7.6	LZP, diazepam, diazepam, MOI, PRO, CSE, VPA, GBP, TFM
5 67	67	57	11.8 (19)	103	LZP, diazepam, MOI, PHT, PB, proline, PIB, TS, PRO, CSE, VPA
6 9	9	9	248.2 (8)	2	LZP, MOI, PHT, PB, CSE, VPA, LMT, fentanyl citrate
7 18	17	17	444.3 (13)	2	LZP, diazepam, MOI, PHT, PRO, CSE

Abbreviations: AED, antiepileptic drug; LZP, carbamazepine; GBP, gabapentin; IGI, intensive care unit; LMT, lamotrigine; LZP, lorazepam; MAC, minimum steroid concentration; MOI, midazolam; PB, phenobarbital; PIB, phenylethanolamine N-methyltransferase; PRO, propofol; TFM, topiramate; TS, thioctic acid; VPA, valproic acid.

*Data for MAC hours (7 days) of diazepam and 30 MAC hours (7 days) of isoflurane.



EPI.....

- Epilepsy - prevalence ~ 5/1000
- Incidence ~ 50/100,000/year.
- Assuming that 20% of patients with active epilepsy would be resistant to AED treatment
- One bn population of India,
- There would be about one mn people with medically refractory epilepsy.

Surgical treatment of medically refractory epilepsy

CURRENT SCIENCE, VOL. 102, NO. 4, 27 MARCH 2012

AAN Guideline Treatments For Refractory Epilepsy

USE OF AEDs IN MANAGEMENT OF REFRACTORY PARTIAL EPILEPSY

AED	As adjunctive therapy in adults	As adjunctive therapy in children	As monotherapy
Gabapentin	It is appropriate to use gabapentin as add-on therapy in patients with refractory epilepsy (Level A*).	Gabapentin may be used as adjunctive treatment of children with refractory partial seizures (Level A).	There is insufficient evidence to recommend use of gabapentin as monotherapy for refractory partial epilepsy (Level U).
Lamotrigine	It is appropriate to use lamotrigine as add-on therapy in patients with refractory epilepsy (Level A).	Lamotrigine may be used as adjunctive treatment of children with refractory partial seizures (Level A).	Lamotrigine can be used as monotherapy in patients with refractory partial epilepsy (Level B, downgraded due to dropout).
Topiramate	It is appropriate to use topiramate as add-on therapy in patients with refractory epilepsy (Level A).	Topiramate may be used as adjunctive treatment of children with refractory partial seizures (Level A).	Topiramate can be used as monotherapy in patients with refractory partial epilepsy (Level A).
Tiagabine	It is appropriate to use tiagabine as add-on therapy in patients with refractory epilepsy (Level A).		There is insufficient evidence to recommend use of tiagabine as monotherapy for refractory partial epilepsy (Level U).
Oxcarbazepine	It is appropriate to use oxcarbazepine as add-on therapy in patients with refractory epilepsy (Level A).	Oxcarbazepine may be used as adjunctive treatment of children with refractory partial seizures (Level A).	Oxcarbazepine can be used as monotherapy in patients with refractory partial epilepsy (Level A).
Levetiracetam	It is appropriate to use levetiracetam as add-on therapy in patients with refractory epilepsy (Level A).		There is insufficient evidence to recommend use of levetiracetam as monotherapy for refractory partial epilepsy (Level U).
Zonisamide	It is appropriate to use zonisamide as add-on therapy in patients with refractory epilepsy (Level A).		There is insufficient evidence to recommend use of zonisamide as monotherapy for refractory partial epilepsy (Level U).

Note: Felbamate was assessed in a prior guideline. See "Practice Advisory: The use of Felbamate in the treatment of patients with intractable epilepsy" Neurology 1999;52:1540-1545



USE OF AEDs IN REFRACTORY PRIMARY GENERALIZED EPILEPSY AND LENNOX GASTAUT SYNDROME

AED	Refactory Primary Generalized Epilepsy	Lennox Gastaut Syndrome
Gabapentin	There is insufficient evidence to recommend gabapentin for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U).	
Lamotrigine	There is insufficient evidence to recommend lamotrigine for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U).	Lamotrigine may be used to treat drop attacks associated with the Lennox-Gastaut syndrome in adults and children (Level A).
Topiramate	Topiramate may be used for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level A).	Topiramate may be used to treat drop attacks associated with the Lennox-Gastaut syndrome in adults and children (Level A).
Tiagabine	There is insufficient evidence to recommend tiagabine for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U).	
Oxcarbazepine	There is insufficient evidence to recommend oxcarbazepine for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U).	
Levetiracetam	There is insufficient evidence to recommend levetiracetam for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U).	
Zonisamide	There is insufficient evidence to recommend zonisamide for the treatment of refractory generalized tonic-clonic seizures in adults and children (Level U).	



Refractory epilepsy treatment guidelines. Ketogenic diet guidelines for infants with refractory epilepsy. Nice guidelines refractory epilepsy.

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Lancet Neurol 8:1019-1030. ♦ Article PubMed Central Google Scholar Page 2 Skip to main content From: Recommendations for the treatment of epilepsy in adult and pediatric patients in Belgium: 2020 update Product name Reimbursed and non-reimbursed indicationsb Pharmacokinetic interactionsc Caution in patients withd Brivaracetam R: focal-onset, add-on after failure \geq 3 AEDs, age \geq 4 y NR: focal-onset, add-on, age \geq 4 y p.o. + i.v \geq 1/10: dizziness, somnolence, behavioral changes (children) Selected: suicidal thoughts 0 Liver impairment, pregnancy (data lacking) Carbamazepine R: focal-onset, generalized-onset [GTCS], mono + add-on, any age p.o. \geq 1/10: dizziness, ataxia, somnolence, fatigue, nausea, vomiting, allergic dermatitis, urticaria, leukopenia, elevated y-GT (usually not clinically relevant) Selected: serious skin reactions/hypersensitivity (SJS, TEN, DRESS), blood dyscrasia, osteoporosis, osteomalacia, behavioral changes (suicidal thoughts), liver dysfunction, AV block + + + Older age, history of heart, liver or kidney disease, history of drug-induced hematological reactions or oxcarbazepine/phenytoin-induced hypersensitivity, elevated intra-ocular pressure, mixed seizures, pregnancy (teratogen) Contra-indications: AV block, history of bone marrow depression or hepatic porphyria, combination with MAO inhibitors Ethosuximide R: generalized-onset [absence, atonic, myoclonic], mono + add-on, age \geq 3 y p.o. \geq 1/10: none Selected: abdominal discomfort, serious skin reactions/hypersensitivity (SJS, DRESS), SLE, blood dyscrasia, suicidal thoughts, liver and kidney dysfunction, psychosis 0 Liver and kidney disease, mixed seizures, pregnancy (teratogen) Felbamate R: Lennox-Gastaut (if refractory to all relevant AEDs), add-on, age \geq 4 y p.o. \geq 1/10: none Selected: serious skin reactions/hypersensitivity (SJS, anaphylaxis), severe blood dyscrasia (incl.[aplastic] anemia: 30% fatal), suicidal thoughts + + + Pregnancy (data lacking) Contra-indications: history of blood dyscrasia, liver disease Gabapentin R: focal-onset, add-on, age \geq 6 y NR: focal-onset, mono, age \geq 12 y p.o. \geq 1/10: dizziness, ataxia, somnolence, fatigue, fever, viral infection Selected: weight gain, serious skin reactions/hypersensitivity (DRESS, anaphylaxis), suicidal thoughts, acute pancreatitis, respiratory depression 0 Use of opioids or other CNS depressants, underlying respiratory condition, older age, renal failure, neurological disease, history of drug abuse, mixed seizures, pregnancy (teratogen) Lacosamide R: focal-onset, add-on after failure \geq 3 AEDs, age \geq 4 y NR: focal-onset, mono + add-on, age \geq 4 y p.o. + i.v \geq 1/10: dizziness, headache, nausea, diplopia Selected: prolonged PR interval, AV block, suicidal thoughts 0 Underlying arrhythmic conditions, treatment with compounds affecting cardiac conduction, older age, pregnancy (data lacking) Contra-indications: 2nd or 3rd degree AV block Lamotrigine R: focal-onset, generalized-onset [GTCS], mono, age \geq 12 y, add-on, age \geq 2 y p.o. \geq 1/10: headache, rash Selected: serious skin reactions/hypersensitivity (SJS, TEN, DRESS), hemophagocytic lymphohistiocytosis, osteoporosis, suicidal thoughts, arrhythmogenic ST-T abnormality, Brugada ECG, insomnia, hallucinations + History of rash or allergy to other AEDs, bipolar and other psychiatric disorders, kidney failure, Brugada syndrome, myoclonic seizures Levetiracetam R: focal-onset, mono, age \geq 16 y, add-on, age \geq 1 m R: myoclonic in JME, add-on, age \geq 12 y p.o. + i.v \geq 1/10: somnolence, headache Selected: acute kidney injury, blood dyscrasia, suicidal thoughts, behavioral changes 0 Kidney or severe liver dysfunction Oxcarbazepine R: focal-onset, mono + add-on, age \geq 6 y p.o. \geq 1/10: dizziness, somnolence, fatigue, headache, nausea, diplopia Selected: severe acute hypersensitivity (SJS, TEN, anaphylaxis), hyponatremia, cardiac conduction defects, liver dysfunction, hypothyroidy, blood dyscrasia, osteoporosis, suicidal thoughts + Heart, liver or kidney disease, history of carbamazepine-induced hypersensitivity, treatment with sodium-lowering drugs Perampanel R: focal-onset, add-on after failure \geq 3 AEDs, age \geq 12 y NR: focal-onset, generalized-onset [GTCS] in patients with IGE, add-on, age \geq 12 y p.o. \geq 1/10: dizziness, somnolence Selected: serious skin reactions/hypersensitivity (DRESS), behavioral changes, suicidal thoughts + History of drug abuse, severe liver or kidney dysfunction, pregnancy (data lacking) Phenobarbital R: focal-onset, generalized-onset (except absence), mono + add-on, any age R: absence, add-on, any age p.o. + i.v Dizziness, ataxia, somnolence, nausea, visual impairment, nystagmus, diplopiae Selected: serious skin reactions/hypersensitivity (SJS, TEN, DRESS), blood dyscrasia, osteoporosis, osteomalacia, kidney disease, hepatic encephalopathy, addiction, behavioral/cognitive changes, suicidal thoughts, connective tissue disorders + + + Older age, alcoholism, kidney, liver and lung disease, depression, history of drug abuse, pregnancy (teratogen) Contraindications: hypersensitivity to barbiturates, porphyria, (severe) respiratory insufficiency, severe liver or kidney dysfunction Phenytoin R: focal-onset, generalized-onset [GTCS], second-line mono + add-on, any age Never for absence p.o. \geq 1/10: gingival hyperplasia or hypertrophy, somnolence, ataxia, fatigue, diplopia, nystagmus, dysarthriae Selected: serious skin reactions/hypersensitivity (SJS, TEN, DRESS), SLE, hepatotoxicity, lymphadenopathy, osteoporosis, osteomalacia, megaloblastic anemia, blood dyscrasia, absences, myoclonic seizures, suicidal thoughts, cerebellar atrophy, peripheral polyneuropathy, AV block + + + Liver and kidney disease, mixed seizures, pregnancy (teratogen) Contraindications: blood dyscrasia, sinus bradycardia, sinoatrial block, 2nd and 3rd degree AV block, heart failure, Adams-Stokes syndrome, history of hypersensitivity to aromatic anticonvulsants, acute intermittent porphyria Pregabalin R: focal-onset, add-on, age \geq 18 y p.o. \geq 1/10: dizziness, somnolence, headache Selected: hypersensitivity (angio-edema), blurred vision, kidney failure, congestive heart failure, suicidal thoughts, constipation, addiction, encephalopathy 0 Older age, diabetes, heart disease, kidney dysfunction, history of drug abuse Primidone R: focal-onset, generalized-onset [e.g., GTCS, myoclonic, atonic], mono + add-on, any age R: absence, add-on, any age p.o. Dizziness, ataxia, somnolence, nausea, visual impairment, nystagmuse Selected: serious skin reactions/hypersensitivity (SJS, TEN), addiction, suicidal thoughts, osteoporosis, osteomalacia, megaloblastic anemia + + + Older age, children, liver, kidney or respiratory impairment, history of drug abuse, mixed seizures, pregnancy (teratogen) Contraindications: acute intermittent porphyria, hypersensitivity to phenobarbital Rufinamide R: Lennox-Gastaut (if clinical and EEG-based diagnosis and failure \geq 2 AEDs incl. Neurology 91:82-90. ♦ Article PubMed Google Scholar 17.Scottish Intercollegiate Guidelines Network (2003) SIGN 70: Diagnosis and management of epilepsy in adults. ♦ Article PubMed Google Scholar 42.Zhu LN, Chen D, Xu D, Tan G, Wang HJ, Liu L (2017) Newer antiepileptic drugs compared to levetiracetam as adjunctive treatments for uncontrolled focal epilepsy: an indirect comparison. 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Accessed 19 June 202011.European Medicines Agency Brivact: Authorisation details. ♦ PubMed Google Scholar 92.Talati R, Scholle JM, Phung OP, Baker EL, Baker WL, Ashaye A, Kluger J, Coleman CI, White CM (2012) Efficacy and safety of innovator versus generic drugs in patients with epilepsy: a systematic review. valproate and topiramate/lamotrigine), add-on, age \geq 4 y NR: Lennox-Gastaut, add-on, age \geq 1 year p.o. \geq 1/10: dizziness, somnolence, fatigue, headache, nausea, vomiting Selected: serious skin reactions/hypersensitivity (SJS, DRESS), induction of seizures/status epilepticus, reduced QT interval, suicidal thoughts + Liver dysfunction, increased risk of short QT interval, pregnancy (data lacking) Stiripentol R: Dravet, add-on with valproate and clobazam if insufficiently controlled by valproate and clobazam, children p.o. \geq 1/10: ataxia, somnolence, hypotonia, dystonia, insomnia, anorexia, reduced appetite, weight loss Selected: neutropenia + + Liver or kidney dysfunction, pregnancy (data lacking) Contraindications: history of delirium Tiagabine R: focal-onset, add-on, age \geq 12 y p.o. \geq 1/10: dizziness, tremor, somnolence, fatigue, depression, nervousness, concentration problems, nausea Selected: induction of seizures/status epilepticus, visual impairment, ecchymosis, behavioral changes, suicidal thoughts 0 History of behavioral disorders, pregnancy (data lacking) Contraindications: severe liver dysfunction Topiramate R: focal-onset, generalized-onset [GTCS], mono, age \geq 6 y, add-on, age \geq 2 y R: Lennox-Gastaut, add-on, age \geq 2 y p.o. \geq 1/10: dizziness, somnolence, fatigue, paresthesia, depression, nausea, diarrhea, weight loss Selected: oligohydrosis, hyperthermia, kidney stones, acute myopia with secondary angle closure glaucoma, visual impairment, metabolic acidosis, hyperammonemia (with/without encephalopathy), cognitive deterioration, suicidal thoughts + Liver or kidney dysfunction, increased risk of kidney stones or metabolic acidosis, history of eye disorders, pregnancy (fetal growth, teratogen) Valproate R: focal-onset, generalized-onset [GTCS, absence, atonic, myoclonic], mono + add-on, any age p.o. + i.v \geq 1/10: tremor, nausea, vomiting, abdominal pain, hyperammonemia Selected: weight gain, hepatotoxicity, pancreatitis, mitochondrial disease (exacerbation), suicidal thoughts, polycystic ovaries, hyperammonemic and non hyperammonemic encephalopathy, thrombocytopenia, osteoporosis + + Hemorrhagic diathesis, AIDS, diabetes, CPTII deficiency Contraindication: acute/chronic hepatitis, (family) history of hepatitis or pancreas impairment, hepatic porphyria, clotting disorders, mitochondrial disease, urea cycle disorders, women of childbearing potential, pregnancy (teratogen, neurodevelopment) Vigabatrin R: focal-onset, last-choice add-on, any age R: West, mono, children p.o. \geq 1/10: somnolence, fatigue, (irreversible) visual field defects, arthralgia Selected: encephalopathic symptoms, movement disorders, psychiatric problems, suicidal thoughts 0 History of visual field defects or behavioral problems/depression/psychosis, older age, kidney impairment, myoclonic and absence seizures, pregnancy (data lacking) add-on on therapy, AED antiepileptic drug, AIDS acquired immune deficiency syndrome, ATC Anatomical Therapeutic Chemical (Classification System), AV atrioventricular, CNS central nervous system, CPTII carnitine palmitoyltransferase II, DRESS drug reaction with eosinophilia and systemic symptoms, ECG electrocardiogram, EEG electroencephalogram, focal-onset refers to focal-onset seizures with or without focal-to-bilateral tonic-clonic seizures, y-GT gamma-glutamyl transferase, GTCS generalized-onset tonic-clonic seizures, IGE idiopathic generalized epilepsy, i.v. intravenous, JME juvenile myoclonic epilepsy, m months of age, MAO monoamine oxidase, NR non-reimbursed indication, p.o. per os, R reimbursed indication, SJS Stevens-Johnson syndrome, SLE systemic lupus erythematosus, TEN toxic epidermal necrolysis, y years of age aInformation retrieved from each AED's summary of product characteristics (SmPC) and [25] bSide effects taken from each AED's SmPC: " \geq 1/10" are those listed as occurring at a frequency of 1/10 or higher in clinical trials or observational studies; "selected" are those listed in Sect. 4.4 "Special warnings and precautions for use", as well as a small number listed in Sect. 4.8 "Side effects" cInformation based on SmPCs and author consensus; the risk of pharmacokinetic interactions is graded from 0 (no or minimal risk) to + + (high risk) dTaken from each AED's SmPC, Sect. 4.4 "Special warnings and precautions for use" and Sect. 4.3 "Contraindications". . 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