



NICE Bites

Epilepsy

NICE CG137; 2012

This guideline provides recommendations on the diagnosis, treatment and management of children, young people and adults with epilepsy.

Definition of terms

AED	antiepileptic drug
IUD	intrauterine device
POP	progestogen-only pill
COC	combined oral contraceptive
SUDEP	sudden unexpected death in epilepsy

Diagnosis

- ◆ All patients with a recent onset suspected seizure should be seen by a specialist within two weeks for diagnosis.

Investigations – see full guideline

Classification

- ◆ Determine seizure type(s), epilepsy syndrome, aetiology and co-morbidity to identify the most appropriate treatment.
- ◆ Classify epileptic seizures and epilepsy syndrome using a multi-axial diagnostic scheme.

Treatment and management

- ◆ Treatment with an AED is generally recommended after:
 - a second epileptic seizure and,
 - a diagnosis of epilepsy has been confirmed by a specialist.
- ◆ In children and young people, AED treatment should be started by a specialist, and in adults on the recommendation of a specialist.
- ◆ Give all patients a comprehensive care plan that is agreed between the patient, their family and/or carers and primary and secondary care providers.
- ◆ Involve the patient, their family and/or carers in all decisions about their care, considering race, culture and any specific needs.

Pharmacological treatment

Also see Prescribing section and Tables 1 and 2 (pages 3 and 4)

- ◆ Choose an AED based on the presenting epilepsy syndrome (Table 2).
- ◆ If the epilepsy syndrome is not clear, base the decision on seizure type (Table 1).
- ◆ Individualise AED treatment by considering:
 - concomitant medication and co-morbidities,
 - patient's lifestyle and preferences.
- ◆ Review the diagnosis of epilepsy if seizures continue despite an optimal dose of a first-line AED.

Monotherapy

- ◆ Treatment with a single AED is preferred.
- ◆ If treatment with the initial AED is unsuccessful: give a different AED (either an alternative first-line or a second-line drug):
 - increase to the maximum effective or tolerated dose and then slowly taper off the first AED,
 - if the second AED is unhelpful, taper either the first or second drug, depending on efficacy, side effects and how well the drugs are tolerated before starting another drug.
- ◆ Caution is required when switching AEDs.

Combination therapy

- ◆ Only consider combination therapy (adjunctive or 'add-on') if monotherapy with AED/s has not resulted in seizure freedom.
- ◆ If trials of combination therapy do not improve seizure control:
 - revert to the regimen that was previously most accepted by the patient.

Other interventions

- ◆ The following interventions may be used as adjunctive treatment in some circumstances in adults, children and young people – see full guideline for details:
 - psychological interventions,
 - vagus nerve stimulation.
- ◆ Children and young people whose seizures are unresponsive to AEDs may be referred to a tertiary paediatric specialist for consideration of a ketogenic diet.

Review

- ◆ Give adults, children and young people with epilepsy a regular structured review. This can be carried out by a:
 - GP or specialist in adults,
 - specialist in children and young people.
- ◆ The maximum interval between reviews should be one year.

Continuing, withdrawing or stopping therapy

- ◆ Discuss risks and benefits of continuing or withdrawing treatment in individuals who have been seizure free for at least two years. The decision to continue or withdraw medication should be made between the patient, family and/or carers and specialist – see full guideline.
- ◆ Withdrawal of AEDs should be managed by a specialist.
- ◆ Withdraw one AED at a time, over at least 2 to 3 months.
- ◆ Withdraw benzodiazepines and barbiturates over ≥ 6 months to prevent withdrawal symptoms and/or seizure recurrence.
- ◆ Advise patients that if seizures recur during withdrawal to reverse the last dose reduction and seek medical advice.

Referral for complex or refractory epilepsy

- ◆ All children, young people and adults should have access to a tertiary service via their specialist when needed.
- ◆ Consider referral if one or more of the following criteria are present:
 - epilepsy not controlled with AEDs within two years,
 - management unsuccessful after two AEDs,
 - children age < 2 years,
 - unacceptable adverse effects of AEDs,
 - unilateral structural lesion,
 - psychological and/or psychiatric co-morbidity,
 - diagnostic doubt about seizure type or syndrome.

Monitoring

- ◆ **Do NOT** routinely carry out regular blood test monitoring.
- ◆ Indications for AED levels include: detection of non-adherence, suspected toxicity, adjustment of phenytoin dose, management of drug interactions.

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Special Groups

Women and girls with epilepsy

Counselling

- ◆ Give information and counselling about contraception, conception, pregnancy, breastfeeding and the menopause as appropriate.
- ◆ Discuss the risks of AEDs causing malformations and possible neurodevelopmental impairments in an unborn child. Assess the risks and benefits of individual drugs.
- ◆ Specifically discuss the increased risk to the unborn child with continued use of sodium valproate particularly at high doses (>800mg/day) and polytherapy.

Contraception

- ◆ In women/girls of childbearing potential:
 - > discuss the risks and benefits of different contraceptive methods including hormone-releasing IUDs,
 - > discuss interactions between AEDs and oral contraceptives and assess the risks and benefits of individual drugs.
- ◆ In women taking **enzyme-inducing AEDs**:
 - > POPs and progestogen implants are **NOT** recommended,
 - > if choosing a COC, check BNF and SPC for dosage recommendations,
 - > discuss using additional barrier methods if taking oral contraception or having depot progestogen injections,
 - > if emergency contraception is required check BNF and SPC for dosage recommendations.
- ◆ In women taking **lamotrigine**:
 - > use of any oestrogen-based contraceptive can significantly reduce lamotrigine levels and cause loss of seizure control. Adjust dose of lamotrigine when starting or stopping these contraceptives.

Pregnancy

- ◆ Aim for seizure freedom before conception and during pregnancy.
- ◆ Consider the risk of adverse effects of AEDs. Use the lowest possible dose and avoid polytherapy if possible.
- ◆ Give all women/girls on AEDs folic acid 5mg per day before becoming pregnant.
- ◆ Discuss the:
 - > possibility of status epilepticus and SUDEP with a woman/girl who plans to stop AEDs,
 - > relative benefits and risks of adjusting medication. If appropriate contact a specialist,
 - > risks associated with epilepsy in pregnancy – see full guideline.
- ◆ Encourage the woman/girl to notify the **UK Epilepsy and Pregnancy Register**.
- ◆ Offer a high resolution ultrasound scan at 18 to 20 weeks to anyone taking AEDs during pregnancy. Earlier scanning may allow major malformations to be detected sooner.
- ◆ Give 1mg of vitamin K parenterally at delivery to all children born to mothers taking enzyme-inducing AEDs.

Breastfeeding

- ◆ Breastfeeding while taking AEDs is generally safe and should be encouraged.
- ◆ Consult the BNF and SPC for individual drugs when prescribing AEDs during breastfeeding.

People with learning disabilities, young people, older people, and those from black and minority ethnic groups – see full guideline

Prolonged/repeated seizures

Treatment in the community

- ◆ For children, young people and adults who have prolonged (≥ 5minutes) or repeated (≥ 3 in one hour) convulsive seizures:
 - > give immediate emergency care,
 - > secure the airway and assess respiratory and cardiac function.

First-line - buccal midazolam#

Second-line - rectal diazepam (if preferred or if buccal midazolam not available)

Give IV lorazepam if IV access is already established and resuscitation facilities are available.

- ◆ Treatment should be administered by trained:
 - > clinical personnel, or
 - > family members and/or carers if specified by an individually agreed protocol drawn up with a specialist.
- ◆ Call an ambulance if:
 - > the seizure continues 5 minutes after emergency medication has been given,
 - > this is the first episode requiring emergency treatment or the person has a history of frequent episodes of serial seizures, or has convulsive status epilepticus,
 - > there are concerns/difficulties monitoring the person's airway, breathing, circulation or vital signs.

Treatment in hospital

Convulsive status epilepticus

- ◆ For children, young people and adults with ongoing generalised tonic-clonic seizures who are in hospital, immediately:**
 - > secure airway,
 - > give high concentration oxygen,
 - > assess cardiac and respiratory function,
 - > check blood glucose levels,
 - > secure IV access in a large vein.

First-line; IV lorazepam

Second-line; IV diazepam, **OR** buccal midazolam# if unable to secure immediate IV access.**

- ◆ Give a maximum of two doses of first-line treatment.
- ◆ If seizures continue, administer IV phenobarbital or phenytoin.**

#Buccolam® is currently the only product with a UK marketing authorisation. It is licensed for use in children from 3 months to <18 years.*

Refractory convulsive status epilepticus

- ◆ **Adults;** give IV midazolam, propofol or thiopental sodium.
- ◆ **Children;** give IV midazolam or thiopental sodium.
- ◆ Adequate monitoring, including blood levels of AEDs, and critical life systems support are required.**
- ◆ As the treatment pathway progresses, seek the expertise of an anaesthetist/intensivist.
- ◆ Consult the tertiary service if either the whole protocol or intensive care is required.
- ◆ Regular AEDs should be continued at optimal doses and the reasons for status epilepticus should be investigated.

* See Summary of Product Characteristics (SPC) for full prescribing information.

**See suggested protocols in full guideline.

Visit the **NICE Pathway: epilepsy**



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Please read this section in conjunction with pages 1 and 2.

Prescribing

- ◆ Different preparations of some AEDs may vary in bioavailability or pharmacokinetic profiles.
- ◆ Consistent supply of the same brand of AED is recommended, unless the prescriber and/or patient/carer consider this **not** to be a concern.
- ◆ All AEDs are associated with a small risk of suicidal thoughts and behaviour. This may be seen as early as one week after starting treatment.
- ◆ Some AEDs may worsen seizures and should not be used in certain seizure types/epilepsy syndrome - see full guideline.
- ◆ See section on **Women and girls with epilepsy** (page 2) for advice on use of AEDs before and during pregnancy.

Sodium valproate*

- ◆ Be aware of the teratogenic risk of sodium valproate particularly at high doses (>800mg/day) and polytherapy.

Carbamazepine*

- ◆ Prescribe controlled-release preparations.
- ◆ Stevens-Johnson syndrome can occur rarely. §

Vigabatrin*

- ◆ Assess the risk-benefit ratio because of the risk of an irreversible effect on visual fields.

Topiramate*

- ◆ Has a less favourable adverse effect profile than levetiracetam and sodium valproate.

§ **Editorial note** - The risk of carbamazepine-induced Stevens-Johnson syndrome is strongly associated with presence of the HLA-B*1502 allele in individuals of Han /Hong Kong Chinese, or Thai origin. Screen these individuals for HLA-B*1502 and **do NOT** start carbamazepine in those who test positive unless the benefits clearly outweigh the risks.

Related guidance: [NICE TA232; Retigabine for the adjunctive treatment of partial onset seizures in epilepsy.](#)

* See Summary of Product Characteristics for full prescribing information.

Table 1: Antiepileptic drug options by seizure type

Treatment should be based on epilepsy syndrome – see Table 2.
If the syndrome is not clear then base the decision on seizure type.

		Seizure type				
		Primary generalised tonic-clonic	Tonic or atonic	Absence	Myoclonic	Focal
Anti-epileptic drug	Carbamazepine*	3rd line				1st line / adjunct
	Clobazam*	adjunct U				adjunct U
	Ethosuximide*			1st line / adjunct		
	Gabapentin*					adjunct U
	Lamotrigine*	2nd line / adjunct	adjunct U	2nd line U / adjunct U		1st line / adjunct
	α Levetiracetam*	adjunct			2nd line U / adjunct	2nd line / adjunct
	Oxcarbazepine*	3rd line U				2nd line / adjunct
	Sodium valproate	1st line / adjunct	1st line	1st line / adjunct	1st line / adjunct	2nd line / adjunct
	Topiramate*	adjunct			2nd line U / adjunct U	adjunct

See full guideline for:

- ◆ further treatment options which may be prescribed on referral to tertiary care,
- ◆ drugs to be avoided in each seizure type.

Key

1st line = first-line treatment
2nd line = second-line treatment
3rd line = third-line treatment
adjunct = adjunctive treatment

U At the time of publication this drug did not have marketing authorisation for this indication and/or population. Obtain and document informed consent. See [Licensing indications](#) in full guideline.

α **Editorial note** – Levetiracetam was not cost-effective compared to other AEDs in June 2011; estimated cost of 1500mg daily dose £2.74. It is now off-patent and will be cost-effective if acquisition costs fall to at least 50% of June 2011 prices as listed in the NHS Drug tariff.

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Table 2: Antiepileptic drug options by epilepsy syndrome

		Epilepsy syndrome									
		Childhood absence, juvenile absence or other absence syndromes	Juvenile myoclonic	Generalised tonic-clonic seizures only	Idiopathic generalised epilepsy	Infantile spasms NOT due to tuberous sclerosis R	Infantile spasms due to tuberous sclerosis R	Benign epilepsy with centrotemporal spikes or Panayiotopoulos syndrome R	Late-onset childhood occipital (Gastaut type)	Dravet syndrome R	Lennox-Gastaut syndrome R
Anti-epileptic drug	Carbamazepine*			2nd line				1st line U / adjunct U	1st line U / adjunct U		
	Clobazam*			adjunct U				adjunct U	adjunct U	adjunct U	
	Ethosuximide*	1st line / adjunct									
	Gabapentin*							adjunct U	adjunct U		
	Lamotrigine*	2nd line U / adjunct U	2nd line U / adjunct U	1st line / adjunct	2nd line U / adjunct U			1st line U / adjunct U	1st line U / adjunct U		adjunct
	Levetiracetam*		2nd line U / adjunct	adjunct	adjunct U			2nd line U / adjunct U	2nd line U / adjunct U		
	Oxcarbazepine*			2nd line U				2nd line U / adjunct U	2nd line U / adjunct U		
	Prednisolone*					1st line	2nd line				
	Sodium valproate*	1st line / adjunct	1st line / adjunct	1st line / adjunct	1st line / adjunct			2nd line / adjunct	2nd line / adjunct	1st line	1st line
	Stiripentol*									adjunct	
	Tetracosactide*					1st line U	2nd line U				
	Topiramate*		2nd line U / adjunct U	adjunct	3rd line U / adjunct U			adjunct U	adjunct U	1st line U	
Vigabatrin*					1st line	1st line					

See full guideline for:

- ◆ further treatment options which may be prescribed on referral to tertiary care,
- ◆ drugs to be avoided in each epilepsy syndrome.

Key

1st line = first-line treatment
2nd line = second-line treatment

3rd line = third-line treatment
adjunct = adjunctive treatment

R Refer to a tertiary paediatric epilepsy specialist. This also applies to Landau-Kleffner syndrome, myoclonic-astatic epilepsy and continuous spike and wave during sleep.

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*This bulletin summarises key prescribing points from NICE guidance. Please refer to the full guidance at www.nice.org.uk for further detail.
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