PHC Chapter 15: Central nervous system conditions

15.1 STROKE

I61.0-6/I61.8-9/I63.0-6/I63.8-9/I64

DESCRIPTION

Stroke consists of rapidly developing clinical signs of focal (at times global) disturbance of cerebral function, lasting >24 hours or leading to death. Most strokes are ischaemic (embolism or thrombosis) whilst others may be caused by cerebral haemorrhage. A transient ischaemic attack (TIA) is defined as stroke symptoms and signs that resolve within 24 hours.

The diagnosis of stroke depends on the presentation of sudden onset of neurological loss, including:

» Weakness, numbness or paralysis of the face or limb/s.
» Sudden onset of blurred or decreased vision in one or both eyes; or double vision.
» Difficulty speaking or understanding.
» Dizziness, loss of balance or any unexplained fall or unsteady gait.
» Headache (severe, abrupt).

GENERAL MEASURES

Acute management

» Assess airway, breathing, circulation and disability.
» Measure blood glucose and treat hypoglycaemia if present. See Section 21.2.6: Hypoglycaemia and hypoglycaemic coma.
» BP is often elevated in acute stroke. Do not treat elevated BP at PHC but refer patient urgently.
» Patients should be given nil by mouth until swallowing is formally assessed.

Long term management

» Optimise treatment for existing medical conditions such as hypertension, diabetes mellitus, dyslipidaemia and cardiac conditions.
» Increase regular physical activity: aim for 30 minutes 5 times a week.
» Advise patient regarding appropriate weight loss, if weight exceeds ideal weight.
» Advise patient regarding smoking cessation.
» Refer for rehabilitative therapy including physiotherapy, occupational therapy and / or speech therapy if indicated.
» Initiate a palliative care approach if the patient's condition is deteriorating / in case of a massive stroke (see Chapter 22: Medicines used in palliative care).

LoE:IIb[1]

MEDICINE TREATMENT

Acute treatment

- Aspirin, oral, 300 mg, as a pre-referral dose. *LoE:Ia*[2]

Note: Do not give aspirin if the patient:

» is unconscious;
» cannot swallow;
» is on long-term anticoagulation therapy;

» has signs of a subarachnoid bleed: i.e. neck stiffness, headache;
» or will be transferred and treated with a thrombolytic within 3 hours. *LoE:Ia*[3]

Secondary prevention for adults (i.e. continuation of aftercare treatment initiated at higher level of care).

Antiplatelet therapy

All patients, if not contraindicated (e.g. haemorrhagic stroke, peptic ulcer, patients on anticoagulation therapy, etc.):

- Aspirin, oral, 150 mg daily. *LoE:Ia*[4]

Lipid-lowering therapy

See Section 4.1: Prevention of ischaemic heart disease and atherosclerosis.

Hypertensive therapy

For blood pressure management, see Section 4.7: Hypertension.

Diabetes mellitus and dietary management information

See Chapter 9: Endocrine conditions.

REFERRAL

Urgent

» Refer all acute stroke cases for further management (preferably within 3 hours).

15.2 DEMENTIA

A52.3/B23.8 + (F02.8)/E03.2-3/E03.8-9/E52/F03

DESCRIPTION

Progressive loss of cognitive function, usually of insidious onset. Initial presentation may be with mild personality or memory changes, before more pronounced deficits become evident.

Common reversible causes of dementia include:

» Metabolic:
  - Hypothyroidism.
  - Vitamin B12 deficiency.
  - Pellagra.
» Medications and drugs:
  - Long-term alcohol abuse.
  - Many medications have CNS side effects.
» Infections:
  - Neurosyphilis.
  - HIV dementia.
» Surgical:
  - Normal pressure hydrocephalus.
» Severe depression (pseudo-dementia).

GENERAL MEASURES

All patients must be seen by a doctor to confirm the diagnosis.
People with dementia are vulnerable to delirium and worsening confusion.
Manage conditions that may worsen symptoms, including:

» Electrolyte disturbances and dehydration.
» Infections, usually originating from the respiratory or urinary tract.
» Medication toxicity.
» For confirmed diagnosis of mild to moderate dementia, the following supportive measure may be taken:
  - Refer patients to occupational therapy, if available, for assessment of functioning and advice to the family on adaptive measures.
  - Disclose the diagnosis to family members/ primary care giver. *LoE:IIb*[5]
  - Explain that the condition is evolving, and future planning is necessary.
  - Advise driving cessation for the patient, if relevant.
  - Discuss home safety risks – e.g. potential for patient to leave stove on while cooking or wander if unattended.
  - Ensure that the patient has a caregiver that can supervise medication taking when the patient is unable to do so themselves.
  - Monitor functional problems and manage as they arise e.g. urinary incontinence.
  - Monitor nutritional status and intervene or refer if necessary.
  - Provide ongoing medical care.
» Initiate a palliative care approach as the patient's condition deteriorates. (See Chapter 22: Medicines Used in Palliative Care.)

REFERRAL

» Adults < 60 years of age, adolescents, and children, where common reversible causes of dementia could not be identified.
» When behavioural and/or psychological symptoms pose a risk to patient or carer.

15.3 PARKISONISM

G20/G21.0-4/G21.8-9/G22

DESCRIPTION

Parkinsonism is a syndrome that affects the nervous system and the parts of the body controlled by the nerves. It may be characterised by tremor, rigidity, stiffness, slow movements and postural disturbances. It may be primary, i.e. Parkinson's disease, or secondary, i.e. drug-induced, or due to uncommon disorders that may initially resemble Parkinson's disease.
Patients and caregivers may report:

» A tremor, or rhythmic shaking, which usually begins in a limb, often the hand or fingers.
» Slowed movement (bradykinesia), for example steps may become shorter as they walk and it may be difficult to get out of a chair.

» Decreased ability to perform unconscious movements, including blinking, smiling or swinging their arms while walking.
» Speech changes such as slurring or hesitation in speaking.
» Difficulty in writing.

The objective of treatment is to:
» minimise disabling symptoms;
» prevent complications and avoid serious drug-induced side effects.

GENERAL MEASURES
All patients demonstrating signs and symptoms of parkinsonism should be referred to a medical practitioner for assessment and treatment.

REFERRAL
» Patients suffering from motor difficulties should be referred for general supportive therapy and advice about lifestyle modification, and multidisciplinary rehabilitation to optimise their functioning. *LoE:IIIb*[6]

15.4 EPILEPTIC SEIZURES
G40.6-7; G41.0-2; G41.8-9; R56.8

DESCRIPTION
An epileptic seizure is a change in movement, attention or level of awareness that is sustained or repetitive and occurs because of abnormal and excessive neuronal discharge within the brain.

LoE:IVb[7]

Epileptic seizures should be differentiated from:
» Collapse, e.g. syncope, anoxic seizures, transient ischaemic attack, cardiac arrhythmias;
» Movement disorders, e.g., paroxysmal dyskinesias, tic disorders;
» Mental health conditions, e.g., functional/dissociative seizures (also called psychogenic non-epileptic seizures), rage reactions, panic attacks, daydreaming/ inattention;
» Sleep-related conditions, e.g., parasomnias, narcolepsy;
» Migraine associated disorders, e.g., migraine with visual aura.

See https://www.epilepsydiagnosis.org/epilepsy-imitators.html for a full list of conditions which may look like an epileptic seizure.

LoE:IVb[8]

Not all persons who have an epileptic seizure have epilepsy.
Specific criteria must be met to diagnose epilepsy (see Section 15.7: Epilepsy).

DIAGNOSIS

Epileptic seizures are diagnosed clinically, through eye-witness accounts, videos, careful observation by the healthcare professional, and a history from the patient of the symptoms, signs and behaviours experienced prior to and during the seizure. Epileptic seizures are classified by the International League Against Epilepsy (ILAE) into three types: focal, generalised, and unknown (see Figure 1). The evolution of the seizure (how it starts and progresses clinically) directs investigations to determine the cause of the seizure and related management.

LoE:IVb[9]

SEIZURE TYPES

Focal seizures:

The epileptic activity arises from a specific focus, or networks limited to one hemisphere of the brain.

Focal seizures may present with motor signs (e.g., rhythmic jerking of one limb; automatisms such as lip-smacking) or with non-motor signs (e.g., olfactory, tactile, or visual hallucinations, or intense emotions such as fear). This depends on the site of origin, which may be the frontal lobe, temporal lobe, parietal lobe or occipital lobe. A focal brain lesion should always be excluded in new focal seizures.

Focal seizures are classified according to the degree of impaired consciousness and whether there is progression to a tonic-clonic seizure. Consciousness is evaluated by assessing the levels of awareness (of themselves and their surroundings) and responsiveness (to other people or stimuli) of the person during the seizure. Any impairment in consciousness means that the person's safety and the safety of others must be protected during the seizure.

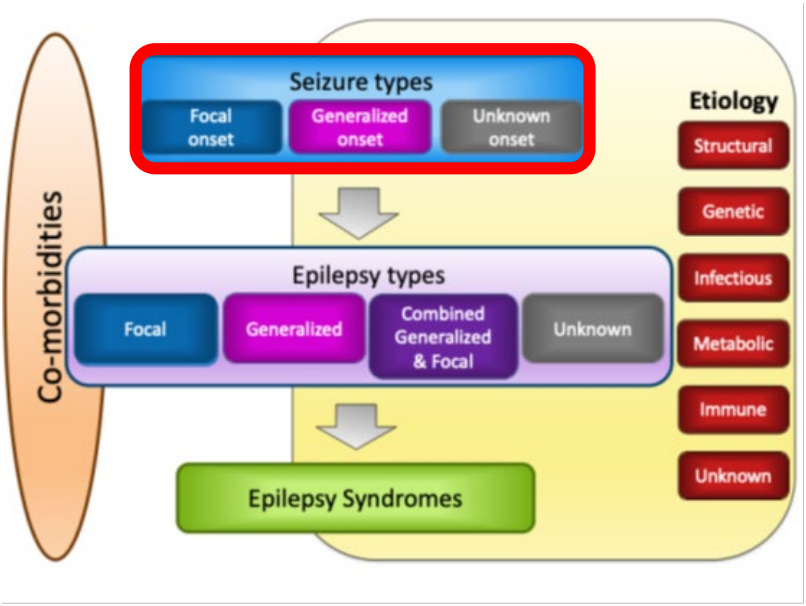


Figure 1. International League Against Epilepsy classification of seizure types *(Taken From: Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L. ILAE classification of epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017, 58 (4): 512-521).*

LoE:IVb[10]

» **Focal preserved consciousness seizures** (previously termed 'simple partial seizures'): the person is fully aware of themselves and their surroundings and fully responsive to others throughout the seizure.
» **Focal impaired consciousness seizures:** (previously termed 'complex partial seizures'), the person has impaired awareness or responsiveness at any time during the seizure.
» **Focal unknown state of consciousness seizures:** used when the state of consciousness is not known (e.g. unclear information).
» **Focal-to-bilateral tonic-clonic seizure:** the epileptic seizure progresses to both brain hemispheres. Bilateral tonic-clonic seizures are differentiated from generalised tonic-clonic seizures by a history of preceding focal signs (either sensory or motor) occurring before complete loss of consciousness and the development of tonic-clonic movements. The terms 'aura' or 'warning signs' may be used by people for the focal signs of the seizure.

Generalised seizures

The epileptic activity arises within and rapidly spreads to involve networks in both hemispheres of the brain. Generalised seizures are almost always associated with impaired or loss of consciousness.

Generalised seizures are classified as:

» **Generalised motor seizures**, which include:
  – **Generalised tonic-clonic seizures**, with loss of consciousness and bilateral tonic-clonic limb movements.
  – **Generalised seizures other than tonic-clonic**, including seizures with varying degrees of impaired consciousness and bilateral *tonic* movements (stiffening, sometimes with vibratory movements) of limbs or eyes, bilateral *atonic* movements (sudden loss of muscle tone) of head, trunk or limbs, bilateral jerks (brief shock-like muscle contractions), as in *myoclonic* seizures.

» **Absence seizures** (previously termed 'petit-mal seizures'), which usually occur in association with an epilepsy syndrome (see Section 15.7: Epilepsy). Absence seizures may be:
  – **'typical'** with abrupt loss of consciousness lasting 5-30 seconds and clonic movements of face and/or automatisms, or
  – **'atypical'** with a less abrupt onset of impaired consciousness, longer seizure duration and loss of muscle tone of head, trunk and limbs. Atypical absence seizures are rare and can be challenging to differentiate from focal sensory seizures.

LoE:IVb[11]

Unknown:
The category of 'unknown onset' is used when there is not enough information, or the clinical presentation is too unclear, to distinguish between focal or generalised seizures.
For more detail and educational videos on seizure types, see https://www.epilepsydiagnosis.org/seizure/seizure-classification-groupoverview.html

15.5 STATUS EPILEPTICUS

G41.0-2; G41.8-9

DESCRIPTION

In status epilepticus, the seizures do not stop, or they occur repeatedly in close succession with impaired consciousness between seizures. Status epilepticus may be 'convulsive' (associated with prominent motor symptoms) or 'non-convulsive' (i.e., without prominent motor symptoms).

Convulsive status epilepticus:
Convulsive status epilepticus is defined as ≥ 5 minutes of either:
» a continuous generalised or bilateral tonic-clonic seizure, or
» two or more discrete generalised, or bilateral tonic-clonic seizures with incomplete recovery of consciousness between the seizures.

Convulsive status epilepticus is a **medical emergency**. There are two critical time points:

» Time point 1: **5 minutes** from the onset of the initial epileptic seizure (i.e., at the point of diagnosis). Immediate treatment is needed to prevent ongoing epileptic seizure activity.
» Time point 2: **30 minutes** of epileptic seizure activity, timed from the onset of the seizure. After 30 minutes of seizure activity, irreversible brain damage related to hypoxia, acidosis, depletion of local energy stores, cerebral oedema and structural damage, is likely to occur.

Complications of convulsive status epilepticus include:

» hyperpyrexia
» respiratory depression
» cerebral oedema
» blood pressure disturbances
» inappropriate antidiuretic hormone (ADH) secretion
» hypoxic ischaemic damage to brain, myocardium and muscles.
» disturbances of blood glucose
» renal failure
» acidosis

Non-convulsive status epilepticus:
Non-convulsive status epilepticus refers to abnormally prolonged or rapidly recurring epileptic seizures with impaired consciousness but no major motor symptoms (e.g., focal seizures with autonomic, sensory or perceptual manifestations or absence seizures). The presentation is often subtle, and the seizures may not be recognised. Diagnosis is confirmed on EEG. Treat as for convulsive status epilepticus below; see Sections 15.5.1: Epileptic seizures and status epilepticus in children <13 years and 15.5.2: Epileptic seizures and status epilepticus in adolescents (13 – 18 years) and adults. Ensure that underlying causes are identified and managed.

Causes of epileptic seizures and status epilepticus
With every epileptic seizure, the underlying cause of the seizure must be determined and treated, including in people with epilepsy.
Important causes of epileptic seizures that must be considered include:

» Infectious conditions e.g., meningitis or encephalitis.
» Encephalopathy e.g., hypertensive encephalopathy or cerebral hypoxia
» Metabolic conditions e.g., hypoglycaemia, hypo- or hypernatraemia, hypocalcaemia.
» Brain lesions e.g., brain tumours, stroke and post-stroke sequelae, trauma and post-traumatic sequelae.
» Substance withdrawal e.g., alcohol or benzodiazepines.
» Substance intoxication e.g., cocaine or amphetamines.
» Poisoning or toxin ingestion (accidental or intentional as in an overdose) e.g. isoniazid.
» Other neurological (e.g., cerebral palsy) or neurodegenerative (e.g., Alzheimer's dementia) conditions.

» Epilepsies e.g., breakthrough seizures, treatment non-adherence, recent changes to antiseizure medicine (ASM), antiseizure medication toxicity.

15.5.1 EPILEPTIC SEIZURES AND STATUS EPILEPTICUS IN CHILDREN < 13 YEARS OF AGE

DESCRIPTION

Central nervous system infections are a common cause of epileptic seizures in children < 13 years of age in South Africa. The most common seizures in children are febrile seizures (see Section 15.6: Febrile seizures) but the history, examination and investigations must aim at excluding the following conditions:

Perinatal conditions	Infections	Poisoning
» congenital infection » hypoxic-ischaemic damage » trauma » cerebral haemorrhage or thrombosis	» meningitis » encephalitis » brain abscess » neurocysticercosis	» medicine toxicity, e.g., isoniazid, antihistamines, antiseizure medicines » substance abuse, e.g., solvents, amphetamines » environmental and other toxins e.g., pesticides (organophosphates), essential oils » substance withdrawal, e.g. benzodiazepines.
Metabolic abnormalities	**Systemic disorders**	**Primary cerebral causes**
» hypoglycaemia » hypocalcaemia » hypomagnesaemia » hyponatraemia » hypernatraemia » inborn errors of metabolism	» vasculitis » hypertensive encephalopathy » uraemia (renal failure) » hyperammonaemia (liver failure)	» cerebral malformation » genetic/familial (syndromic) » tumour » idiopathic/ unknown

Special considerations by age group

Neonates:

Neonatal seizures are usually provoked, most commonly by hypoxic ischaemic encephalopathy (HIE). They rarely lead to a subsequent diagnosis of epilepsy. For management, refer to Section 19.6.2: Seizures, Neonatal.

Infants and children up to 2 years of age:

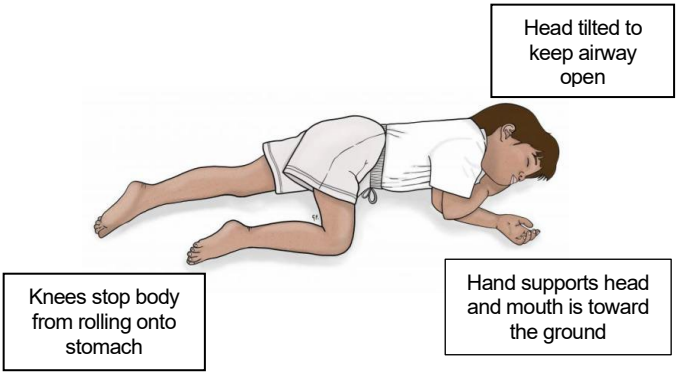
» The most frequent cause of epileptic seizures that present in infancy are febrile seizures (see Section 15.6: Febrile seizures).

- Infants under 6 months of age cannot manifest generalised tonic-clonic seizures.
- Most provoked seizures presenting in this age group appear to be focal even when a generalised brain pathology is present.
- Infants and children under 2 years may not have typical signs of meningitis, i.e. neck stiffness or Kernig sign. Meningitis should be excluded in all children with a fever and seizure.
- Infants and children are at risk of metabolic derangement which may be from common triggers (e.g., dehydration) or rare causes (e.g., inborn errors of metabolism).
- Neuroimaging is often very useful, especially to exclude structural aetiologies (e.g., intracranial bleeds).

Children 2 to 12 years of age:
Older children are often able to present with clearer descriptions of seizure onset, i.e. a focal onset seizure is more likely to be specifically driven by an underlying focal cause (potentially a structural pathology):
- Ask for focality – point to the side of movement or change.
- Change in behaviour before convulsive seizure evident.
- Altered consciousness.
- Type of seizure is related to the underlying aetiology.

GENERAL MEASURES

On arrival/ while fitting:
- Ensure the environment is safe. Remove all sharp objects and hot liquids.
- Place the child in a recovery position to prevent aspiration of secretions or vomitus, on the floor if necessary.
- Do not place anything (spoon or spatula, etc.) in the patient's mouth.
- Ensure the airway is not obstructed.



Adapted from https://www.kidshealth.org.nz/emergencies/emergencies-cpr

LoE:IVb[12]

- » Administer oxygen via face mask or nasal cannula to maintain $SaO_2 \geq 95\%$.
- » Notify the medical doctor on duty to conduct a medical examination, supervise care and prescribe required medicines. If there is no doctor on site, discuss the patient with a medical doctor telephonically.
- » Obtain eyewitness account of when the seizure started and associated impaired consciousness: **If seizure duration is ≥ 5 minutes, commence urgent medicine treatment for convulsive status epilepticus** (refer to table below on medicine management and supportive care of status epilepticus in children < 13 years).
- » Examine for fever, dehydration, meningism, hypoglycaemia, evidence of toxin or poison ingestion, head, neck or other trauma, obvious focal neurology and other possible causes of the seizure.
- » Establish vascular (IV or IO) access, if possible. See Paediatric Hospital Level STGs and EML Chapter 1: Emergencies and Trauma, Section 1.1.10 Intra-Osseous Infusion in Emergencies.
- » Once threat of falling no longer present, move to bed (with cot sides up), if needed.
- » Monitor vital signs every 15 minutes.
- » Keep nil per mouth.
- » Ensure the family/caregiver/escort is attended to; social worker or auxiliary staff member should obtain all contact details and provide counselling as needed.

MEDICINE TREATMENT

The aim is to control the seizure within 30 minutes of its onset, prevent complications of status epilepticus with supportive care, and identify and

correct underlying causes. Follow standard resuscitation protocols, such as the ABCDE approach.

Schedule 5 antiseizure medicines (i.e., benzodiazepines and phenobarbital) must be prescribed by a medical doctor. If there is no doctor on site, a nurse may administer the medicine in accordance with a telephonic prescription provided by a medical doctor. The medical doctor must provide a written, signed prescription within 72 hours of the telephonic prescription.

Table 1: MEDICINE MANAGEMENT AND SUPPORTIVE CARE OF STATUS EPILEPTICUS IN CHILDREN < 13 YEARS OF AGE

PHASE	MEDICINE MANAGEMENT	SUPPORTIVE CARE
EARLY STATUS EPILEPTICUS **5-10 minutes after seizure onset**	**LEVEL 1 INTERVENTION:** (benzodiazepines, up to 2 doses). If vascular access is available: • Midazolam, IV, 0.2 mg/kg over 60 secs, (max 10mg/dose) (Doctor prescribed). **OR** *LoE:IVba*[13] • Diazepam, IV, 0.25mg/kg IV over 60 secs (max 10mg/dose) (Doctor prescribed). *LoE:IIVb*[14] If vascular access is not available: • Midazolam, IM 0.2 mg/kg, **OR** buccal* 0.5 mg/kg (Doctor prescribed). *LoE:IIIa*[15] **OR** • Diazepam, rectal**, 0.5 mg/kg (max 10mg/dose) (Doctor prescribed). *LoE:IIIa*[16] Expect a response within 1–5 minutes. **If the seizure does not resolve within 5 minutes after first dose, give a repeat dose of benzodiazepine.** **CAUTION** Benzodiazepines can cause respiratory depression. Monitor oxygen saturation and respiratory rate. If respiratory depression occurs, assist ventilation with bag-valve mask (1 breath every 3–5 seconds) and refer urgently/transfer to a high care setting.	» Aim for seizure control within 30 minutes of onset. » Provide supplemental oxygen, maintain $SaO_2 \geq 95\%$. » Monitor cerebral perfusion pressure (CPP), heart rate, oxygen saturation. » Check glucose. If low, correct and start maintenance IV fluid with dextrose 5% in sodium chloride 0.9%. Do not overhydrate. » Blood gas analysis for electrolytes. Correct as required. Other biochemical disorders: Correct abnormalities, if present, e.g. glucose, calcium and sodium. Take blood for electrolytes, LFTs, FBC. If patient is a known epileptic, check therapeutic levels of ASMs. If meningitis cannot be excluded, give: • Ceftriaxone, W IM or IV, 100 mg/kg/dose stat
ESTABLISHED STATUS **10-30 minutes after seizure onset**	**LEVEL 2 INTERVENTION:** If no vascular access: • Phenobarbital, IM 20mg/kg (Doctor prescribed) ○ Slow IM Injection.	» Consult with higher level care, refer urgently. » Prepare for intubation and ventilation.

PHASE	MEDICINE MANAGEMENT	SUPPORTIVE CARE
	OR if no IM formulation available: • Levetiracetam oral, crushed and given by nasogastric tube, 60 mg/kg as a single dose (maximum dose: 4500 mg). (Doctor prescribed, administered by a nurse with approval by a doctor) **OR** *LoE:IIIb*[17] • Phenobarbital, oral, crushed and given by nasogastric tube, 20 mg/kg as a single dose. (Doctor prescribed) Note: if no response to phenobarbital IM or oral after 5–20 minutes, levetiracetam oral may be given via NG tube, but avoid repeating oral phenobarbital as it may take over an hour to achieve therapeutic concentrations and repeat doses increases the risk of respiratory depression. **Refer to higher level of care**	
» Watch for complications of the prolonged seizure. » Check all possible underlining conditions. » Watch for adverse effects of administered ASM.		

Prescribing notes:

* Midazolam, buccal , 0.5 mg/kg/dose. See dosing table: Chapter 23. (Doctor prescribed, administered by a nurse with approval by a doctor)
  - Use midazolam for injection 5 mg in 1 mL undiluted.
  - Draw up the required volume in a 5 mL syringe.
  - Remove needle then administer midazolam into the buccal cavity (between gum and cheeks).
  - Note: Buccal midazolam should not be used in infants < 6 months of age.

LoE:IIIa[18]

**Diazepam, rectal, 0.5 mg/kg/dose as a single dose. See dosing table: Chapter 23. (Doctor prescribed, administered by a nurse with approval by a doctor)
  - Use diazepam for injection 10 mg in 2 mL undiluted.
  - Draw up the required volume in a 2 mL syringe.
  - Remove needle then connect syringe to an NGT and gently insert into the rectum (or insert the whole barrel of the lubricated syringe if no NGT available) and inject the contents.
  - Remove NGT / syringe and hold buttocks together to minimise leakage.

After The Seizure

Post-ictal phase

» Keep nil per mouth and haemodynamically stable until child has regained consciousness.
» Determine the seizure type (focal or generalised) and cause of the seizure. Further investigations are driven by clinical signs and seizure onset, e.g.:
  – History of toxin exposure.
  – Evidence of neuro-infection.
  – History of trauma.
  – Focal onset (e.g., a warning experience prior to generalised tonic-clonic movements) and/or focal neurology warrants neuroimaging.
» If meningitis cannot be excluded, commence antibiotic therapy within one hour of arrival. See Section 15.8.1: Acute meningitis.

Pre-discharge

» Consider whether the criteria for a diagnosis of epilepsy are met (see Section 15.7: Epilepsy). Initiate appropriate ASM for type of epilepsy and develop an emergency care plan for recurrent seizures.
» If not epilepsy, start weaning any ASMs.
» Counsel the caregiver on the current state of the child, the reason for the seizure, management given and likely sequelae of the seizure. Offer only as much information as the caregiver can receive at that time.
» Set up a follow up appointment to re-evaluate the diagnosis, educational and social needs, and to reinforce educational counselling about the child's condition.

Active follow-up

» Ensure underlying medical conditions are appropriately managed.
» Reduce and stop any residual ASMs if not epilepsy.
» Assess neurodevelopmental conditions, educational and social needs. Refer as necessary.
» If epilepsy is the cause of the seizure, check seizure control and if emergency care plan is understood.

Referral

» All children with status epilepticus.
» All children < 2 years.
» Children over ≥ 2 years, except for those with simple febrile seizures (see Section 15.6: Febrile seizures).
» Follow up social worker or rehabilitation services required.

15.5.2. EPILEPTIC SEIZURES AND STATUS EPILEPTICUS IN ADOLESCENTS (13 – 18 YEARS) AND ADULTS

Additional causes of epileptic seizures to consider in adolescents and adults are categorised below:

Pregnancy related	Infections	Substances & poisoning
» eclampsia (see Adult Hospital STGs and EML, Section 6.4.2: Eclampsia) » electrolyte abnormalities (e.g. in hyperemesis gravidarum) » stroke » reduced blood levels of antiseizure medication	» meningitis » encephalitis » brain abscess » neurocysticercosis	» substance abuse (e.g. cocaine, amphetamines) » withdrawal syndromes (e.g., benzodiazepine, alcohol) » medicine toxicity and overdose (e.g., antiseizure medications, antidepressants, antipsychotics, isoniazid) » environmental toxins (e.g. pesticides)
Metabolic conditions	**Systemic disorders**	**Primary cerebral causes**
» hypoglycaemia » hypocalcaemia » hypomagnesaemia » hyponatraemia » hypernatraemia	» vasculitis » hypertensive encephalopathy » uraemia (renal failure) » hyperammonaemia (liver failure)	» tumour » trauma » neurodegenerative conditions » idiopathic/unknown

Special considerations

Adolescents and young adults:

» High risk for substance intoxication or withdrawal, and for traumatic brain injuries.
» Mental health conditions are common, and may present as 'epilepsy imitators' (see differentials of epileptic seizures above and https://www.epilepsydiagnosis.org/epilepsy-imitators.html).
» Idiopathic generalised epilepsies (including epilepsy with generalised tonic-clonic seizures, juvenile myoclonic epilepsy, juvenile absence epilepsy) may first present in this age group.
» High risk for poor adherence to ASMs and breakthrough seizures.
» Often require intensive individual and family counselling and support, with appropriate involvement of social welfare and education sectors.

Girls and women in child-bearing age group:

» Exclude pregnancy and pregnancy related complications.
» ASM concentrations may become sub-therapeutic in pregnant women with epilepsy, causing breakthrough seizures. An increase in ASM dose may be required during pregnancy (reduce dose after delivery). Where possible monitor.

CAUTION

Children born to women taking valproate are at significant risk of birth defects (11%) and persistent developmental disorders (40%).
Valproate is contra-indicated and should be avoided in pregnancy and in adolescents and women of child-bearing potential.

LoE:IIIb[19]

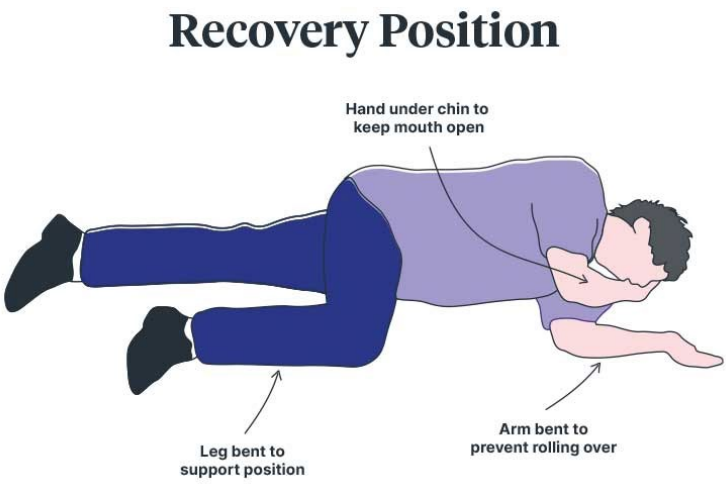
People > 65 years of age:

» Common reversible conditions include metabolic abnormalities, medications, alcohol withdrawal.
» The risk of developing epilepsy increases with age. Epilepsy in this age group is commonly caused by stroke, brain tumours and dementias. Continued ASM may be advisable after a single seizure in these patients.

GENERAL MEASURES

On arrival/ while fitting:

» Ensure the environment is safe. Remove all sharp objects and hot liquids.
» Place the patient in a lateral position to prevent aspiration of secretions or vomitus, on the floor if necessary.
» Do not place anything (spoon or spatula, etc.) in the patient's mouth.
» Notify the medical doctor on duty to conduct a medical examination, supervise care and prescribe required medicines. If there is no doctor on site, discuss the patient with a medical doctor telephonically.



Taken from Ausmed: Adult Basic Life Support

LoE:IVb[20]

» Obtain an eyewitness account of the seizure onset and any associated impaired consciousness. **If seizure duration is ≥ 5 minutes, commence urgent medicine treatment for convulsive status epilepticus** (refer to table below on medicine management and supportive care of status epilepticus in adolescents and adults).
» Ensure the airway is not obstructed and administer oxygen via face mask or nasal cannula to maintain SaO_2 ≥ 95%.
» Intubation should be performed if airway, ventilation, or oxygenation cannot be maintained, or if seizure is prolonged.
» Examine for fever; dehydration; meningism; hypoglycaemia; evidence of toxin or poison ingestion; head, neck or other trauma; obvious focal neurology; and other possible causes of the seizure.
» Secure intravenous access.
» Monitor vital signs every 15 minutes.
» Keep nil per mouth.
» Ensure the family/caregiver/escort is attended to. Social worker or auxiliary staff member should obtain all contact details and provide counselling as needed.

Convulsive status epilepticus:
If the seizure does not resolve within 5 minutes of onset, commence urgent medicine treatment.

MEDICINE TREATMENT

The aim is to control the seizure within 30 minutes of its onset, prevent complications of status epilepticus with supportive care, and identify and correct underlying causes. Follow standard resuscitation protocols, such as the ABCDE approach.

Schedule 5 antiseizure medicines (i.e., benzodiazepines and phenobarbital) must be prescribed by a medical doctor. If there is no doctor on site, a nurse may administer the medicine in accordance with a telephonic prescription provided by a medical doctor. The medical doctor must provide a written, signed prescription within 72 hours of the telephonic prescription.

Table 2: MEDICINE MANAGEMENT AND SUPPORTIVE CARE OF STATUS EPILEPTICUS IN ADOLESCENTS AND ADULTS

PHASE	MANAGEMENT	SUPPORTIVE CARE
EARLY STATUS EPILEPTICUS (5 – 10 minutes)	**LEVEL 1 INTERVENTION:** (Benzodiazepines; See Caution below). If IV access is available: • Midazolam, IV, 10mg (Doctor prescribed, administered by a nurse with approval by a doctor). *LoE:IIb*[21] • **OR** • Diazepam, IV, 10mg administered over at least 5 minutes (not faster than 2mg/min) (Doctor prescribed, administered by a nurse with approval by a doctor). *LoE:IIb*[22] • . If IV access is not available: • Midazolam, 10 mg, IM or buccal, using the parenteral formulation, while continuing to establish IV access (Doctor prescribed, administered by a nurse with approval by a doctor). **OR** If no midazolam available: • Diazepam, rectal, 0.2–0.5 mg/kg as a single dose (maximum 20 mg/dose) (Doctor prescribed). *LoE:IVb*[23] If the seizure does not resolve 5 minutes after first dose of benzodiazepine, repeat the dose of benzodiazepine. If seizure aborts after 1 or 2 doses of benzodiazepines, but patient is at high risk of recurrent seizures (e.g., known with epilepsy and defaulted treatment), recommence with antiseizure medicine or start new ASM if indicated (see Section 15.7: Epilepsy).	» Stabilize and support airway breathing and circulation. » Identify and treat the underlying cause of seizures such as: – Hypoglycaemia. – Electrolyte derangements (e.g. calcium, sodium, potassium, magnesium and urea). – Poisoning. – Intoxication/overdoses (e.g. isoniazid, theophylline, tricyclic antidepressants, cocaine, methamphetamine). – Withdrawal syndromes (e.g. alcohol, benzodiazepines). » If patient is known with epilepsy and on treatment, take blood for measurement of antiseizure medicine levels.
ESTABLISHED STATUS EPILEPTICUS	**LEVEL 2 INTERVENTION:** (Antiseizure medicine)	» Prepare for intubation/ventilation.

(10 – 30 minutes)	• Levetiracetam oral crushed and given by nasogastric tube, 60 mg/kg as a single dose (Maximum dose: 4500 mg). (Doctor prescribed, administered by a nurse with approval by a doctor). *LoE:IIb*[24] **Refer all patients.**	» Arrange referral to higher level of care.
CAUTION: Benzodiazepines can cause respiratory depression. Monitor closely for respiratory depression. If this occurs, assist ventilation with bag-valve mask (1 breath every 3–5 seconds) and refer urgently/transfer to a high-care setting.		

After The Seizure

Post Ictal Phase:

» Keep nil per mouth and haemodynamically stable until patient has regained consciousness and is aware of themself and their surroundings.
» If there is agitation or disturbed behaviour, consider post-ictal delirium and manage as for delirium – see Section 21.2.4: Delirium.
» Clarify the cause of the seizure and manage appropriately. Further investigations (e.g. lumber puncture and neuroimaging) are driven by clinical signs and seizure onset (e.g. focal onset).
  » If meningitis is suspected, commence antibiotic therapy urgently.
  » Counsel the patient and their family regarding the cause of the seizure, management given and likely sequelae of the seizure. Offer only as much information as the family or patient is able to receive at that time.
  » If reversible causes of the epileptic seizure have been addressed, wean and stop ASMs. Consider whether the person meets the criteria for a diagnosis of epilepsy that requires ongoing ASMs (see Section 15.7: Epilepsy).
» On discharge, set up a follow-up appointment to reinforce the counselling messages.

Active follow up:

» Wean any residual ASMs, unless ongoing maintenance treatment is indicated, or epilepsy has been diagnosed.

Referral

» All patients with status epilepticus must be referred to hospital for continued acute management and evaluation of the cause.
» New focal seizures for neuroimaging.
» Suspected meningitis.

Follow up social worker or rehabilitation services required.

15.6 FEBRILE SEIZURES

R56.0

DESCRIPTION

Febrile seizures occur between the ages of 6 months and 6 years of age in association with a significant fever (>38.5°C) in the absence of an intracranial infection and typically associated with viral upper respiratory tract infections. These are the most common type of seizures in children of this age. *LoE:IVb*[25]

However, the diagnosis requires the exclusion of other causes of seizures.
Febrile convulsions can be simple or complex.

Simple febrile seizures (SFS):
» are generalised,
» occur once per illness,
» are less than 15 minutes (typically 1–2 minutes),
» are not associated with any neurological deficit,
» are self-limiting,
» consist of only one seizure during the febrile illness which needs no specific treatment, and
» may be associated with a family history of simple febrile seizures.

Complex febrile seizures have *one or more* of the following characteristics:
» Seizure duration of 15 minutes or more;
OR
» are recurrent within the same febrile illness;
AND/OR
» have a focal onset.
AND/OR
» are associated with post-ictal, focal neurological abnormalities.

Children with febrile seizures have a good prognosis, and very rarely develop epilepsy. The overall risk for recurrence of simple febrile seizures is 30–40%. Factors which increase the risk for recurrent febrile seizures include:
» seizure disorder in a first-degree relative,
» onset before 12 months of age,
» initial complex seizures.

DIAGNOSTIC CRITERIA

Clinical

» Investigate for intracranial, extracranial, and biochemical causes of fever or seizure.
» Signs of meningism are unreliable in children under 18 months of age.
» If raised intracranial pressure or meningitis cannot be excluded, the diagnosis of febrile seizures cannot be made. Treat children empirically for meningitis if suspected.

Investigations

Lumbar puncture
» Lumbar puncture is indicated in:
  – All children with clinical features of meningitis.
» Lumbar puncture may be indicated in:
  – Children where meningitis cannot be excluded, e.g. under 18 months of age or those who have received antibiotics prior to the event.
» In children ≥ 18 months of age, where a focus of extracranial infection is present and intracranial infection such as meningitis has been excluded clinically, no further investigation is required.

Neuroimaging

» Children with complex febrile seizures and/or persistent lethargy may require neuroimaging, followed by a lumbar puncture if raised intracranial pressure can reliably be excluded based on clinical assessment. (See Paediatric Hospital Level STGs and EML, Section 13.2: Lumbar Puncture).

» Based on clinical findings, investigate complex febrile seizures for possible underlying conditions such as meningitis, focal brain lesions and epilepsy.
Note: An EEG is of no value in simple febrile seizures but may be considered in recurrent complex febrile seizures.

GENERAL AND SUPPORTIVE MEASURES

» Reassure parents and caregivers.
» Educate parents and caregivers regarding the first aid management of seizures.
» Counsel against tepid sponging and fans as this increases the core temperature.
» Counsel that recurrent febrile seizures occur in 30-40% of patients.
» Look for a cause of the fever.
» **Always exclude meningitis** (see Section 15.8: Meningitis).

MEDICINE TREATMENT

For fever related symptoms (temperature > 38.5°C):

- Paracetamol, oral, 15 mg/kg/dose 6 hourly.
  - Note: Paracetamol has no effect on seizure prevention.

If convulsing for > 5 minutes:
See Section 15.5: Status epilepticus (convulsive).

Continuous antiseizure medication prophylactic therapy

» Routine daily antiseizure medication prophylaxis is not recommended for patients with simple febrile seizures.
» For children with recurrent complex febrile seizures, discuss the treatment options with a specialist.

REFERRAL

» All febrile seizures, except if:
  – Previous episode of simple febrile seizures has been investigated,
  AND
  – the child regains full consciousness and function immediately after the seizure,
  AND
  - meningitis has been excluded (see Section 15.8: Meningitis).

» Complex convulsions:
  - All patients with recurrent complex febrile seizures without an obvious cause of the seizure and/or not responding to initial management should be discussed with a specialist.
  - Developmental delay/regression.

15.7 EPILEPSY
G40.0-9

DESCRIPTION
Epilepsy is a disease of the brain defined by any of the following conditions:
» At least two unprovoked (or reflex) seizures occurring >24 hours apart,
» One unprovoked (or reflex) seizure if there is a high risk (60% or more) of having recurrent seizures within the next 10 years (i.e., if the person is vulnerable to having another unprovoked seizure, e.g., because of structural damage such as from a stroke),
» Diagnosis of an epilepsy syndrome.

Note:
» The initial diagnosis of epilepsy must be made by a medical doctor.
» An "unprovoked" epileptic seizure is a seizure which does not have evidence of an identifiable temporary or reversible factor acting on a healthy brain (e.g., hypoglycaemia, alcohol withdrawal, concussion).
» A "reflex" epileptic seizure is a seizure which occurs in response to a stimulus such as flashing lights. Such epileptic seizures indicate the person's brain is predisposed to having seizures and therefore warrant a diagnosis of epilepsy.
» Epilepsy may be diagnosed after a single unprovoked seizure in people with an increased risk of recurrence for example in people with previous conditions such as TB meningitis, neurocysticercosis, stroke, brain tumour or traumatic brain injury. Note that the single unprovoked seizure is not caused by the immediate insult to the brain but occurs spontaneously (i.e., is unprovoked) because of the long-term sequelae of the initial insult. The damaged brain is thus at high risk of a recurrent unprovoked epileptic seizure.
» Epileptic syndromes confer a diagnosis of epilepsy, even if the risk of recurrent epileptic seizures is low for a particular individual.
» Epilepsy is considered to be resolved and no longer needing maintenance treatment in individuals who either:
  - had an age-dependent epilepsy syndrome, but are now past the applicable age, **OR**
  - have remained seizure-free for the last 10 years and weaned off ASM for at least the last 5 years.

» Epilepsy is associated with many psychological, social and legal problems, and cultural misperceptions which should be explored and addressed at the time of diagnosis and throughout the course of the illness.

Epilepsy types

As shown in Figure 2, epilepsies are classified by the International League Against Epilepsy (ILAE) according to:

» Type of seizures experienced, e.g.: focal, generalised, combined generalised and focal, or unknown.

AND

» Aetiology, which may be:
  – Structural (e.g., cerebral or vascular malformations, stroke, traumatic brain injury, brain tumours).
  – Genetic (the epilepsy is a direct result of chromosomal or gene abnormalities, e.g., Down syndrome, Fragile X syndrome, Dravet syndrome).
  – Infectious (e.g., post-infectious sequelae of TB meningitis).
  – Metabolic (e.g., inborn errors of metabolism).
  – Immune (rare conditions involving neuroreceptor antibodies).
  – Unknown.

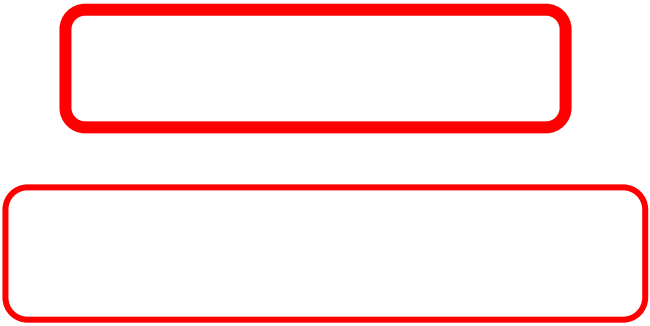


Figure 2. International League Against Epilepsy classification of seizure types *(Source: Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L. ILAE classification of epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017, 58 (4): 512-521).*

LoE:IVb[26]

Focal epilepsy

Characterised by unprovoked focal seizures, which may or may not evolve to bilateral tonic-clonic seizures. The diagnosis is made clinically and requires a detailed description of how the seizure started. In people presenting with generalised tonic-clonic seizures, it is important to ask about any warning symptoms or 'aura' experienced by the person before losing consciousness. Typical interictal and/or ictal EEG findings may be present, and neuroimaging may reveal a focal brain lesion, supporting the diagnosis, but may also be normal.

Generalised epilepsy
Characterised by unprovoked generalized seizures, including tonic-clonic, tonic, myoclonic, and absence seizures. Typical interictal and/or ictal EEG findings may be present.

Combined generalised and focal epilepsy
Diagnosed in people with more than one type of seizure, e.g., unprovoked focal seizures and unprovoked generalised seizures. This may occur in people with Dravet syndrome or Lennox-Gastaut syndrome.

Unknown epilepsy
This classification is used when it is not possible to determine whether the epilepsy is focal, generalised, or combined generalised and focal epilepsy from the available history, clinical, and investigative findings.

For seizure types, see Section 15.4: Epileptic seizures.
For more information and educational videos on epilepsy types, see https://www.epilepsydiagnosis.org/epilepsy/epilepsy-classification-groupoverview.html.

Investigations:
- Neuroimaging (a CT Brain or MRI if available) should be conducted:
  - in new focal onset seizures to exclude a focal brain lesion,
  - if the epilepsy features change in an individual (i.e., new symptoms appear, noting that most people will experience the same march of symptoms with each seizure),
  - if epileptic seizures recur despite adherence to treatment and the diagnosis is unclear.
- EEG is indicated for recurrent or syndromic seizures where a diagnosis cannot be made on clinical grounds alone. Delay an EEG for at least one week after the convulsive episode.
- EEG is not indicated for simple febrile seizures.
- If the seizure presentation is atypical, a 12-lead ECG should be considered to identify prolonged QT interval syndromes. Syncope with exercise, syncope in response to loud noise, fright, or extreme emotional stress, syncope whilst supine, a family history of sudden

death in a young person e.g., <40 years old, or sensorineural deafness are associated with some types of long QT syndrome.

15.7.1 EPILEPSY IN CHILDREN <13 YEARS OF AGE

A child may be diagnosed with focal, generalised, combined generalised and focal, or unknown epilepsy types.

Special considerations

Seizures in neonates

Seizures in the neonatal period seldom confer a diagnosis of epilepsy. For management of seizures, See Paediatric Hospital Level STGs and EML Chapter 19: Prematurity And Neonatal Conditions, Section 19.6.2: Seizures, Neonatal.

Underlying conditions and co-morbidities

The sequelae of neurocysticercosis and TB meningitis are a common cause of childhood epilepsy in South Africa. See Paediatric Hospital Level STGs and EML Chapter 13: The Nervous System, Section 13.7: Neurocysticercosis and Chapter 10: Tuberculosis, Section 10.4: Meningitis, Tuberculosis in Children.

Common co-morbidities with epilepsy which need to be managed in conjunction with treatment of the epilepsy include:

» Neurodevelopmental disorders, e.g., autism spectrum disorder, intellectual disability, attention deficit hyperactivity disorder, specific learning disorders.
» Behavioural and psychiatric disorders, e.g., anxiety disorder, depression, oppositional defiant disorder, conduct disorder, sleep disorders.
» Cognitive and academic difficulties.
» Developmental delays, particularly with epilepsies that have their onset in early childhood.

Infantile epileptic spasms (see syndromes below)

Infantile epileptic spasms (previously called infantile spasms) are a type of seizure that typically occur in infants between 3 and 12 months of age. They involve brief, repetitive stiffening of the body (for 1-2 seconds), typically recurring in clusters, and usually happen when the infant is waking up or falling asleep.

These spasms are often associated with a severe epilepsy syndrome called West syndrome or Infantile Epileptic Spasms Syndrome, which includes:

» Epileptic spasms.
» Developmental delay or regression.
» A specific abnormal EEG pattern called hypsarrhythmia.

Infantile spasms are a **medical emergency.** Early diagnosis and treatment are crucial to prevent long-term developmental problems. Discuss with a specialist and refer immediately.

Children on ART

Drug interactions between ASM and ARVs can arise from several mechanisms, including liver metabolism (increased or decreased) and competition for protein binding. There is a lack of strong evidence to guide clinicians at present.

The following points are important to remember when treating epilepsy in patients on ART:

» Carbamazepine, phenobarbital and phenytoin induce hepatic enzymes, which may lead to sub-therapeutic ARV plasma concentrations, especially of INSTIs, NNRTIs and PIs.
» If clinically indicated, monitor ASM levels in patients taking concurrent ART and ASM therapy.
» Consider lamotrigine, levetiracetam or valproate, and avoid prescribing carbamazepine, phenytoin or phenobarbital.

Girls likely to need treatment when of child-bearing potential/ after 10 years of age

» The potential for child-bearing must be considered in all girls requiring treatment for epilepsy.
» Choose the ASM with the least potential for harm in pregnancy (see Figure 3).
» Valproate should not be used if the child is likely to need epilepsy treatment as they grow older / develop child-bearing potential, unless other ASMs are not effective or intolerable. Annual acknowledgment of risk must be obtained if valproate is used.
» Girls over the age of 10 years should be counselled regarding sexual activity and contraception needs.
» Refer any girls who may be vulnerable to sexual abuse to a social worker.

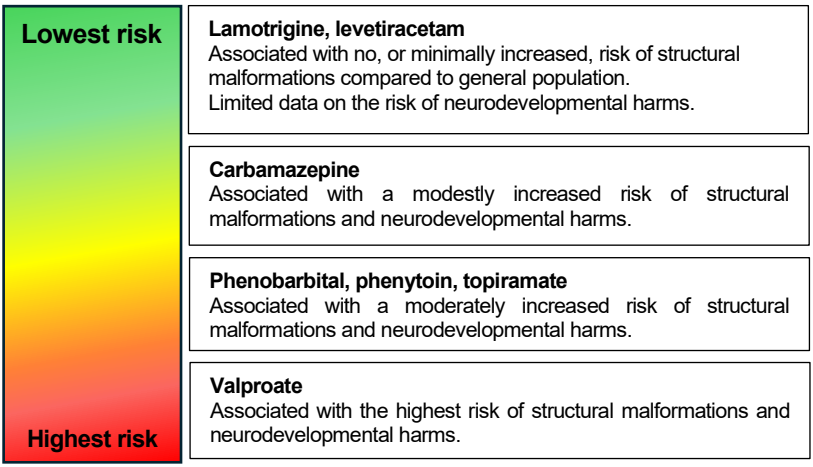


Figure 3. Risk of congenital structural malformations and neurodevelopment harms associated with various antiseizures medicines.
Increasing risk refers to increasing number of pregnancies or children affected. (Adapted from Pennell PB. *Neurotherapeutics*. 2016 and Medicines & Healthcare products Regulatory Agency safety leaflet).

LoE:IVb[27]

GENERAL AND SUPPORTIVE MEASURES

» Offer ongoing counselling to the patient and caregiver about epilepsy, its associated complications and comorbidities e.g. learning difficulties, ADHD, anxiety, and aggression.
» Encourage participation in activities of daily living and ensure that the patient is not precluded from school and lifestyle activities, unless valid safety concerns are evident.

MEDICINE TREATMENT

The goal of medicine treatment is to prevent recurrent seizures and optimise quality of life, balanced against potential adverse effects of ASM. Being seizure-free may not be achievable with all children and may require individualised treatment goals, e.g., in severe to profound intellectual disability with intractable seizures that do not interfere with the care of that child, cautious escalation of treatment should be done with consideration of potential adverse effects.

In settings of apparent drug-resistant epilepsy, revisit the diagnosis, check adherence, consider if the prescribed ASM and dose are correct, and refer to a specialist if treatment goals are not achieved.

Note: Treatment initiation must be conducted by a medical doctor at the time of diagnosis. Continued prescription of ASMs may only be performed by health

care professionals other than medical doctors once seizure control has been achieved and the patient is stable on maintenance therapy. Cross-titration of ASMs should be managed by a medical doctor, as should assessment for treatment discontinuation.

Acute therapy

Manage acute seizure and status epilepticus as per seizures/status epilepticus, see Sections 15.4: Epileptic Seizures, and 15.5: Status epilepticus.

Maintenance therapy

Principles of management

» Monotherapy is preferred.
» Combination therapy, if necessary, should be specialist initiated in the form of add-on management.
» As a general rule, start with low doses according to the lower dose per kilogram for the child and titrate upwards slowly until seizures are controlled. This is often at the low-to-mid-therapeutic dose range.
» If seizures continue, titrate to high therapeutic doses, monitoring for unacceptable adverse effects.
» If the patient experiences unacceptable adverse effects, consult a doctor about cross-titrating to another ASM. Verify that the ASM is being given correctly and that the epilepsy type has been correctly identified.
» ASMs can interact with other drugs, affecting their effectiveness and safety. These interactions mainly occur through changes in drug metabolism (enzyme induction or inhibition) and protein binding.
» Monitoring of therapeutic ASM levels is only indicated when there is concern about toxicity or adherence. It is not recommended when titrating to establish the appropriate dose.

Continuation and cross-titration of treatment

» Cross-titration may be required when changing from one ASM to another if there is poor control or adverse effects. Add on the new medication, up-titrate to a therapeutic dose; when seizures are controlled, slowly reduce and stop the initial medication (doses should only be changed at 2 weekly intervals).

In most children, it is appropriate to continue effective ASM therapy as they grow older as indicated by the type of epilepsy. Exceptions are:

» **Valproate in girls approaching puberty and of child-bearing potential**.
Valproate should be deprescribed by cross-titration onto another suitable ASM in girls at approximately 10 years of age. **Lamotrigine and levetiracetam are the safest ASMs in pregnancy** and therefore the first choice in girls and women of child-bearing potential. As carbamazepine and topiramate are both teratogenic, they should be avoided.

» **Phenobarbital** may be initiated in infants under 6 months of age or for children with severe or profound intellectual disability, for whom the adverse effects will not interfere with their care or activities of daily living. In children who are controlled on phenobarbital, cross-titration onto another suitable ASM should be undertaken by 2 years of age.

Discontinuation of treatment may be considered in patients who have remained seizure-free for at least 2 years. A careful risk-benefit assessment for treatment discontinuation should be conducted by a medical practitioner**.** Medicines must be weaned off gradually over several months if necessary. If the patient is on two or more ASMs, one medicine should be stopped at a time, each with a slow tapering of the dose.

Table 3: Epilepsy treatment in children 1 month to ≤ 12 years

Epilepsy type		Population	1st line	2nd line	Comments
Focal	With or without evolution to bilateral tonic-clonic seizures *LoE:IIIb*[28]	All	Lamotrigine	Carbamazepine **OR** Levetiracetam	Avoid carbamazepine in children on ART due to drug-drug interactions. Avoid carbamazepine in girls who are likely to require treatment when/ if of child-bearing potential.
Generalised epilepsy	Tonic-clonic, atonic, clonic, or tonic seizures	» Boys » Girls unlikely to need treatment after 10 years of age or develop child-bearing potential	Lamotrigine (low risk*) **OR** Levetiracetam (high-risk*)	Levetiracetam or lamotrigine (whichever not used as first line) **OR** Valproate	Valproate should not be used unless lamotrigine and levetiracetam are poorly tolerated or ineffective. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
		Girls likely to need treatment after 10 years of age	Lamotrigine (low risk*) **OR** Levetiracetam (high-risk*)	Levetiracetam or lamotrigine (whichever not used as first line) **OR** Consider combination therapy with lamotrigine and levetiracetam	Valproate should not be used unless lamotrigine or levetiracetam, alone or in combination, are ineffective or poorly tolerated. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
	Absence	» Boys » Girls unlikely to need treatment after 10 years age of age or to develop child-bearing potential	Valproate	Lamotrigine	Girls aged 10 years or older that are on valproate should be cross-titrated to lamotrigine. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).

Epilepsy type	Population	1st line	2nd line	Comments
Absence (Continued)	Girls likely to continue treatment after 10 years of age	Lamotrigine	Levetiracetam	**If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
Myoclonic *Confirm diagnosis and discuss management with a specialist in all cases*	» Boys » Girls unlikely to need treatment after 10 years of age or to develop child-bearing potential	Valproate	Levetiracetam	Seizures may be aggravated by phenytoin or carbamazepine. Lamotrigine may be effective but may also exacerbate myoclonic seizures. Girls aged 10 years or older should be cross titrated to levetiracetam or lamotrigine. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
	Girls likely to continue treatment after age of 10 years	Levetiracetam	Lamotrigine	These seizures may be aggravated by phenytoin or carbamazepine. Lamotrigine may be effective but may also exacerbate myoclonic seizures. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
Combined generalised and focal epilepsy OR Unknown/unclassified Discuss clinical presentation and management with a specialist in all cases.				

Epilepsy type	Population	1st line	2nd line	Comments
NOTE: » All anti-seizure medicines are doctor initiated, except valproate which is doctor prescribed when used in girls and women of childbearing potential. » Lamotrigine is the preferred first line treatment for all adult patients, including women of child-bearing potential, pregnant women, and people on ART. » Lamotrigine requires slow dose up-titration and may not be suitable in people at high-risk of seizures. » **If valproate is used in girls, an acknowledgment of risk form must be obtained annually, even if not of child-bearing potential. Girls aged 10 years and older should receive effective family planning, as indicated, and consider a long-acting form of contraception.** https://www.sahpra.org.za/wp-content/uploads/2025/05/GLF-CEM-PV-S01_v2-Valproate-Annual-Risk-Acknowledgement-Form-ARF.pdf *Assess level of risk (high vs low) based on clinical judgement and discuss with a specialist if unsure. In general, high-risk patients are those with frequent seizures, a previous history of hospitalization for seizures, or previous history of status epilepticus. Low-risk patients are those with infrequent seizures, no previous hospitalization for seizures, and no history of status epilepticus.				*LoE:IVb*[29]

- Lamotrigine, oral (Doctor initiated)
  Monotherapy:
  - Starting daily dose: 0.2 mg/kg/dose.
  - Increase slowly at 2 weekly intervals to 1–5 mg/kg/dose 12–24 hourly.
  - Rapid escalation is associated with adverse effects (e.g., skin rash).

  Cross-titration to lamotrigine:
  Start as add-on therapy, titrate up to a usual maintenance dose, then gradually wean the first medicine in small increments every 1–2 weeks. Note: Lamotrigine levels will increase as carbamazepine doses are reduced but will decrease as valproate doses are reduced. Therefore, lamotrigine dose may need to be increased as valproate is weaned off.

Table 4: Dosing regimens when lamotrigine is used as add-on therapy:

	Week 1 and 2	Week 3 and 4	Maintenance dose
Add on therapy where regimen **does not include valproate** or other inducers/inhibitors of lamotrigine glucuronidation	0.3 mg/kg in one or two divided doses.	0.6 mg/kg in one or two divided doses.	0.6 mg/kg increments every 1–2 weeks to achieve a maintenance dose of 1–10 mg/kg (once a day or two divided doses) to a maximum of 200 mg/day.
Add-on therapy where **regimen includes ASMs that induce lamotrigine glucuronidation** *(e.g. phenytoin, carbamazepine, phenobarbital, etc.)*	0.6 mg/kg in two divided doses.	1.2 mg/kg in two divided doses.	1.2 mg/kg increments every 1–2 weeks to achieve a maintenance dose of 5–15 mg/kg (once a day or two divided doses) to a maximum of 400 mg/day.
Add-on therapy where **regimen includes valproate** *(regardless of other concomitant medication)*	0.15 mg/kg daily.	0.3 mg/kg daily.	0.3 mg/kg increments every 1–2 weeks to achieve a maintenance dose of 1–5 mg/kg (once a day or two divided doses) to a maximum of 200 mg/day.

LoE:IVb[30]

CAUTION - LAMOTRIGINE
Lamotrigine may cause Stevens-Johnson Syndrome.

- Levetiracetam, oral, (Doctor initiated)
  - Infants 1 to < 6 months:
    - Initial dose: 7 mg/kg/dose twice daily.
    - Increase dosage every 2 weeks by 7 mg/kg/dose twice daily based on response and tolerability to the recommended dose of 21 mg/kg/dose twice daily.
  - Infants ≥ 6 months and children < 4 years:
    - Initial dose: 10 mg/kg/dose twice daily.
    - Increase dosage every 2 weeks by 10 mg/kg/dose twice daily based on response and tolerability to the recommended dose of 25 mg/kg/dose twice daily.
  - Children ≥ 4 years to 12 years:
    - Initial dose: 10 mg/kg/dose twice daily.
    - Increase dosage every 2 weeks by 10 mg/kg/dose twice daily based on response and tolerability to the recommended dose of 30 mg/kg/dose twice daily.

  Cross-titration to levetiracetam
  Start as add-on therapy and increase every 2 weeks to the recommended dose. Once at the recommended dose and seizures are controlled, gradually wean the previous ASM every 2 weeks until stopped.

- Carbamazepine, oral, 5 mg/kg/day (starting dose), 8–12 hourly. (Doctor initiated)
  - Increase slowly by 2 mg/kg/day at 2 weekly intervals.
  - Usual maintenance total daily dose: 10–20 mg/kg/day.
  - Maximum total daily dose: 20 mg/kg/day.
  - Dosage intervals: syrup 8 hourly, tablets 12 hourly.
  - Exacerbates myoclonic seizures and absence seizures.

- Valproate, oral, 5 mg/kg/dose (starting dose), 8–12 hourly.
  (Doctor prescribed if used in girls and women of childbearing potential; doctor initiated for other patients)
  - Increase by 5 mg/kg weekly to 15–20 mg/kg/day, given 8–12 hourly over 4 weeks.
  - Usual maintenance dose: 20–30 mg/kg/day.
  - Maximum total daily dose: 40 mg/kg/day.
  - Exclude liver dysfunction prior to initiating therapy (at least ALT), in children under 2 years or if clinical suspicion of liver dysfunction or metabolic disease.
  - Consider hepatotoxicity if clinical signs such as nausea, vomiting, malaise, jaundice or abdominal pain develop.

- Phenobarbital, oral, 3–5 mg/kg/dose as single dose at night.
  (Doctor prescribed if phenobarbital dose is 90 mg or more, e.g. 18 kg / 5 year old child; doctor initiated for other patients)
  - May be used in children under six months of age.
  - Not recommended as maintenance therapy for children older than 2 years due to undesirable side-effects such as sedation, behaviour disturbances, hyperkinesia and dependence, except in situations where there is poor adherence to other drugs.
  - Exacerbates absence seizures.

REFERRAL

» Suspected but undiagnosed secondary cause for seizures (e.g., structural, metabolic, infectious, genetic causes).
» All myoclonic seizures and infantile epileptic spasms at presentation.
» Mixed seizure types in one patient.
» Focal seizures requiring neuroimaging (MRI preferred).
» Neuroregression (loss of previously acquired milestones or skills).
» Seizure-free patients on therapy for ≥ 5 years to assess whether treatment discontinuation is appropriate.

Information that should accompany each referral case.

» Number and frequency of seizures per month (or year).
» Date and time of most recent seizures.
» Detailed description of the seizures, including:
  – aura or warning sign ;
  – what happens during the seizure? (give a step-by-step account);
  – is the person conscious during the seizure?
  – how long do the seizures last on average?
  – what does the patient experience after the seizure e.g., weakness, loss of speech?
  – how long does this experience last?
» Is there a family history of seizures?
» What is the initial date of diagnosis?
» Is there evidence of alcohol use?
» Are there any comorbid conditions, e.g., diabetes, HIV and what medication is used?
» What is the name and dosage of the ASM used to date?
» Does the person return regularly for repeat of medication?

15.7.1.1 EPILEPSY SYNDROMES

G40.3-5

See Paediatric Hospital Level STGs and EML Chapter 13: the Nervous System, Section 13.4.1.1: Epilepsy Syndromes.

15.7.2 EPILEPSY IN ADOLESCENTS AND ADULTS
G40.0-9

DESCRIPTION
See Section 15.7: Epilepsy.

Diagnostic criteria
» The diagnosis of epilepsy is usually made clinically and must be made by a medical doctor
» Take an adequate history and get an accurate witness description of the seizures to define the type of epilepsy.
» Juvenile myoclonic epilepsy and absence seizures specifically should be considered and identified, as some first line medicines may be less efficacious or may even worsen seizure frequency or severity.
» Patients with new onset epilepsy should have a CT scan (this is essential in immunocompromised patients), & other investigations as clinically indicated.

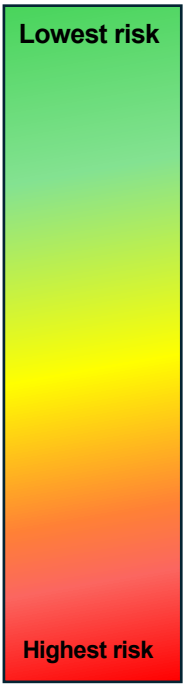
Special considerations
Women and girls of child-bearing potential and pregnancy
» Antiseizure medicines during pregnancy can cause structural or physical malformations and neurodevelopmental harms that may impact learning and education.
» The risk of antiseizure medicine to the unborn child needs to be balanced against the risk of uncontrolled seizures to both the mother and unborn child.
» The risk associated with each antiseizure medicine during pregnancy differs (see Figure 4).
» Women and girls of child-bearing potential with epilepsy should be counselled regarding contraception and the need to plan pregnancy.
  – NOTE: There are important drug-drug interactions between hormonal contraceptives (except DMPA) and several anticonvulsant medicines (e.g. carbamazepine, phenobarbital, phenytoin).
  – Progestin-only injectable contraceptives or IUCDs are the preferred contraceptive methods for women of child-bearing potential on ASM medication. See Chapter 7: Family planning.

It is crucial to treat epilepsy during pregnancy to prevent epileptic seizures, which pose significant risks to both the mother and the fetus/infant.

» In pregnant women, women of child-bearing potential (i.e. women < 55 years), and young girls who are likely to need to continue treatment into their child-bearing years, should initiate treatment with a lower risk antiseizure medication.

  - Lamotrigine and levetiracetam are safer antiseizure medicines to use.
  - Large amounts of data consistently show no increased risk of major congenital malformations associated with the use of lamotrigine or levetiracetam at usual doses.
  - Since lamotrigine requires slow dose titration, initiation of lamotrigine is best suited to low-risk patients.
  - Levetiracetam may be used if there is a poor response or adverse effects to lamotrigine, or in high-risk patients.
  - Seizure risk is based on clinical judgement (discuss with a specialist if unsure). In general, high-risk patients are those with frequent seizures, a previous history of hospitalisation for seizures, or previous history of status epilepticus. Low-risk patients are those with infrequent seizures, no previous hospitalisation for seizures, and no history of status epilepticus.
- Valproate **must not** be used in pregnant women, women of child-bearing potential and young girls who are likely to need continued treatment into their child-bearing years.
  - In women who take valproate while pregnant, around 1 in 9 babies (11%) will have a major birth defect and about 3–4 children in every 10 may have neurodevelopmental problems and these disorders can be seriously debilitating and permanent (e.g. delayed learning to walk and talk, lower intelligence, poor speech and language skills, memory problems, autism or autism spectrum disorders, attention deficit hyperactivity disorder).
  - In situations where valproate is deemed the only option in a female patient after all other treatment options have been ruled out, health professionals (prescribers and dispensers) are required to:
    - Regularly review treatment.
    - Provide counselling on the risks of valproate use in pregnancy.
    - Ensure that the woman has completed and signed an acknowledgment of risk form annually: https://www.sahpra.org.za/wp-content/uploads/2025/05/GLF-CEM-PV-S01_v2-Valproate-Annual-Risk-Acknowledgement-Form-ARF.pdf
    - Provide supplemental folic acid, oral, 5 mg daily.
- Women and girls with epilepsy who discover they are pregnant should not abruptly stop their ASM due to the risk of seizures.
  - Women and girls who become pregnant while on valproate should be transitioned off valproate and onto levetiracetam as early as possible during pregnancy to decrease the risk of neurodevelopmental harms, provided their seizures are not refractory to other antiseizure medications.
- During pregnancy, women may experience an increased number of seizures.
  - This may be due to sleep deprivation, increased emotional stress and changes in antiseizure medicine concentrations.

- Antiseizure medication concentrations may decrease during pregnancy due to decreased absorption from nausea and vomiting, increased volume of distribution and increased clearance of antiseizure medicines.
- There is increased hepatic metabolism of lamotrigine and increased renal clearance of levetiracetam in pregnancy, which returns to normal post-partum. Increase the dose if necessary, according to clinical response.



Lamotrigine, levetiracetam

Compared to the general population, lamotrigine and levetiracetam are associated with no increased risk or only a minimally increased risk of structural malformations. There is limited data on the risk of neurodevelopmental harms associated with levetiracetam and lamotrigine.

Carbamazepine

Carbamazepine is associated with a modestly increased risk of structural malformations and neurodevelopmental harms.

Phenobarbital, phenytoin, topiramate

Phenobarbital, phenytoin and topiramate are associated with a moderately increased risk of structural malformations and neurodevelopmental harms.

Valproate

Valproate is associated with the highest risk of structural malformations and neurodevelopmental harms.

Figure 4. Risk of congenital structural malformations and neurodevelopment harms associated with various antiseizures medicines. Increasing risk refers to increasing number of pregnancies or children affected. Adapted from Pennell PB. *Neurotherapeutics*. 2016 and Medicines & Healthcare products Regulatory Agency safety leaflet. *LoE:IVb*[31]

CAUTION – ASM and pregnancy

Children born to women taking valproate are at significant risk of birth defects (11%) and persistent developmental disorders (40%).
Valproate is contra-indicated and should be avoided in pregnancy and women or adolescents of child-bearing potential. *LoE:IIIb*[32]

Children and adolescents transitioning to adult care

» Children and adolescents whose seizures are controlled on levetiracetam should be continued on levetiracetam in adulthood.

Adults on ART

» Lamotrigine is the preferred ASM in people on ART because of fewer medicine interactions.
» Phenytoin, phenobarbital and carbamazepine are enzyme inducing ASM. Due to potential drug interactions with ARVs, switch these medicines to lamotrigine.
» Where concurrent use of dolutegravir and carbamazepine, phenytoin, or phenobarbital is unavoidable, double dolutegravir dose to 50 mg 12-hourly.
» The metabolism of lamotrigine is induced by lopinavir/ritonavir and atazanavir/ritonavir. The dose of lamotrigine may need to be increased if patients are switched to/initiated on lopinavir/ritonavir or atazanavir/ritonavir.

GENERAL AND SUPPORTIVE MEASURES

» Patients should record dates and, if possible, times of seizures in a seizure diary. Review seizure diary at each consultation for assessment of therapy.
» Patients with epilepsy should be issued a disease identification bracelet, necklace or card.
» Patients with uncontrolled seizures should avoid driving, swimming, working at heights and operating machinery until they have been seizure free for one year. Refer to an occupational therapist for rehabilitation and a workplace assessment. The patient should sign in the medical notes that they have received workplace and lifestyle advice.
» Provide counselling and advice on:
  – the adverse effect of alcohol on seizures,
  – sleep hygiene,
  – the effect of missing a dose of medication,
  – discontinuing the medication without advice of a doctor.

MEDICINE TREATMENT

Note: Treatment initiation must be conducted by a medical doctor at the time of diagnosis. Continued prescription of ASMs may only be performed by health care professionals other than medical doctors once seizure control has been achieved and the patient is stable on maintenance therapy. Cross-titration of ASMs should be managed by a medical doctor, as should assessment for treatment discontinuation.

Acute treatment
Manage acute seizure and status epilepticus as per seizures/status epilepticus, see Sections 15.4: Epileptic Seizures, and 15.5: Status epilepticus.

Maintenance Treatment
» Refer to the table below for guidance around the choice of medicine by seizure type.
» HIV status, child-bearing potential and pregnancy are important determinants of medicine choice.
» The antiseizure treatment strategy should also be individualised based on use of other medicines, comorbidities, as well as response to medication, and adverse effects.
» The goal of medicine treatment is to prevent recurrent seizures and optimise quality of life.
» As a rule, a single ASM (monotherapy) is best. Progressively increase the dose of the ASM until the seizures are controlled or clinically important side effects occur.
» Recommended drug doses are general guides and will be effective in most patients. However, some patients may need much higher or lower doses. Doses should be increased at 2-weekly intervals only.
» If the initial ASM fails to achieve satisfactory control (no seizures) at optimal dosages, or causes unacceptable adverse effects, then a trial of a second ASM medicine may be commenced.
» Initiate second medicine, titrate to therapeutic dose, then gradually reduce and stop the first ASM over 6–8 weeks or longer if necessary. (See notes below for individual medicines).
» Failure of second-line monotherapy, after exclusion of alcohol use/misuse and poor adherence, may require add on therapy. Add on therapy may be initiated by a medical practitioner in consultation with a specialist. If necessary, initiate add on treatment and follow-up clinically in one to two weeks while awaiting specialist advice or appointment.
» Therapeutic drug monitoring is not necessary in stable patients, but should be performed in the following situations:
  – To confirm ASM toxicity in a symptomatic patient,
  – In patients with poor seizure control,
  – To confirm suspected poor adherence despite self-reported good adherence.
» Phenytoin is not recommended in the table below; however, it may be continued in adults whose seizures are well-controlled on phenytoin. Therapeutic drug monitoring should be conducted in patients receiving higher than usual doses of phenytoin.
» Long term use of phenytoin and carbamazepine are associated with potential risks. Continued use of these ASM requires careful

consideration of the balance between benefits and risks in individual patients.

MEDICINE INTERACTIONS *LoE:IVb*[33]

Phenytoin, phenobarbital and carbamazepine are potent enzyme inducing agents and should be used with caution with other medicines metabolised by the liver, especially warfarin, antiretrovirals, progestin subdermal implants and oral contraceptives

Discontinuation of treatment may be considered in patients who have remained seizure-free for at least 2 years. A careful risk-benefit assessment for treatment discontinuation should be conducted by a medical practitioner**.** Medicines must be weaned off gradually over several months if necessary. If the patient is on two or more ASMs, one medicine should be stopped at a time, each with a slow tapering of the dose.

Table 5: Epilepsy treatment in adolescents and adults

Epilepsy type		Population	1st line	2nd line	Comments
Focal epilepsy	With and without evolution to bilateral tonic-clonic seizures	Adolescent boys, men and women not able to have children	Lamotrigine	Carbamazepine OR Levetiracetam	Avoid carbamazepine in people with HIV on ART due to drug-drug interactions
		Pregnant women and women of child-bearing potential	Lamotrigine	Levetiracetam	Avoid carbamazepine in people with HIV on ART due to drug-drug interactions
Generalised epilepsy	Tonic-clonic, atonic, clonic or tonic seizures	Adolescent boys, men and women not able to have children.	Lamotrigine (low-risk)* **OR** Levetiracetam (high-risk)*	Lamotrigine or levetiracetam (whichever not used as first line) **OR** Valproate	Valproate should not be used unless lamotrigine and levetiracetam are poorly tolerated or ineffective. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
		Pregnant women and women of child-bearing potential	Lamotrigine (low risk)* **OR** Levetiracetam (high-risk)*	Levetiracetam or lamotrigine (whichever not used as first line) **OR** Consider combination therapy with lamotrigine and levetiracetam	Valproate should not be used unless lamotrigine or levetiracetam alone or in combination are ineffective or poorly tolerated. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
	Myoclonic *Confirm diagnosis and discuss*	Adolescent boys, men and women	Valproate	Lamotrigine	These seizures may be aggravated by phenytoin or carbamazepine.

Epilepsy type	Population	1st line	2nd line	Comments
management with a specialist Myoclonic (continued)	not able to have children			Lamotrigine may be effective but may also exacerbate myoclonic seizures. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).
	Pregnant women and women of child-bearing potential	Lamotrigine	Levetiracetam	These seizures may be aggravated by phenytoin or carbamazepine. Lamotrigine may be effective but may also exacerbate myoclonic seizures.
Absence *e.g. Juvenile absence epilepsy or persistent childhood absence epilepsy*	Adolescent boys, men and women not able to have children	Valproate	Lamotrigine	These seizures may be aggravated by phenytoin or carbamazepine. If valproate used in girls aged 10 years or older - see note below on acknowledgement of risk form.
	Pregnant women and women of child-bearing potential	Lamotrigine	Levetiracetam	These seizures may be aggravated by phenytoin or carbamazepine. Valproate should not be used unless lamotrigine or levetiracetam, alone or in combination, are ineffective or poorly tolerated. **If valproate is used** in girls aged 10 years or older, it should be doctor prescribed, along with an "**Acknowledgement of risk form"** and family planning (see note below).

Epilepsy type	Population	1st line	2nd line	Comments
Combined generalised and focal epilepsy OR Unknown/unclassified Discuss clinical presentation and management with a specialist in all cases.				
NOTE: » All anti-seizure medicines are doctor initiated, except valproate which is doctor prescribed when used in girls and women of childbearing potential Lamotrigine is the preferred first line treatment for all adult patients, including women of child-bearing potential, pregnant women, and people living with HIV. » Lamotrigine requires slow dose up-titration and may not be suitable in people at high-risk of seizures. *High-risk patients are those with frequent seizures, a previous history of hospitalization for seizures, or previous history of status epilepticus. Low-risk patients are those with infrequent seizures, no previous hospitalization for seizures, and no history of status epilepticus. » **If valproate is used in girls, an acknowledgment of risk form must be obtained annually, even if not of child-bearing potential. Girls aged 10 years and older should receive effective family planning as indicated and consider a long-acting form of contraception**: *LoE:IVb*[34] https://www.sahpra.org.za/wp-content/uploads/2025/05/GLF-CEM-PV-S01_v2-Valproate-Annual-Risk-Acknowledgement-Form-ARF.pdf. *Assess level of risk (high vs low) based on clinical judgement and discuss with a specialist if unsure. In general, high-risk patients are those with frequent seizures, a previous history of hospitalization for seizures, or previous history of status epilepticus. Low-risk patients are those with infrequent seizures, no previous hospitalization for seizures, and no history of status epilepticus.				

MEDICINE TREATMENT

- Lamotrigine, oral (Doctor initiated).

Table 6: Dosing table for lamotrigine as monotherapy or add-on therapy
Dose-titrate as per table below:

	Week 1 and 2	Week 3 and 4	Maintenance dose
Monotherapy	25 mg daily	50 mg daily	100–200 mg (once a day or two divided doses). To achieve maintenance, doses may be increased by 50–100 mg every 1–2 weeks.
Add on therapy where **regimen does not include** valproate or other inducers/inhibitors of lamotrigine glucuronidation	25 mg daily	50 mg daily	100–200 mg (once a day or two divided doses). To achieve maintenance, doses may be increased by 50–100 mg every 1–2 weeks.
Add-on therapy where **regimen includes ASMs that induce glucuronidation** *(e.g. phenytoin, carbamazepine, phenobarbital, etc.)*	50 mg daily	100 mg in two divided doses	200–400 mg (two divided doses). To achieve maintenance, doses may be increased by 100 mg every 1–2 weeks.
Add-on therapy where **regimen contains valproate** *(regardless of other concomitant medication)*	25 mg on alternate days	25 mg daily	100–200 mg (once a day or two divided doses). To achieve maintenance, doses may be increased by 25–50 mg every 1–2 weeks.

Note:

» If therapy is interrupted for more than a week, restart the titration protocol.
» Metabolism of lamotrigine is induced by lopinavir/ritonavir and atazanavir/ritonavir. The dose of lamotrigine may need to be increased when people with HIV are switched to or initiate lopinavir/ritonavir or atazanavir/ritonavir.
» Metabolism of lamotrigine is induced during pregnancy. The dose of lamotrigine may need to be increased during pregnancy. Where possible monitor plasma concentrations and adjust as necessary. Discuss with a specialist as the dose may have to be increased depending on background risk of seizures.

LoE:IVb[35]

Cross-titration to lamotrigine:
Start as add-on therapy, titrate up to a usual maintenance dose, then gradually wean the first medicine in small increments every 1–2 weeks.

Note: Lamotrigine levels will increase as carbamazepine doses are reduced but will decrease as valproate doses are reduced. Therefore, lamotrigine dose may need to be increased as valproate is weaned off.

CAUTION - LAMOTRIGINE
Lamotrigine may cause Stevens-Johnson Syndrome.

LoE:IVb[36]

- Carbamazepine, oral: (Doctor initiated)
  - Start with 100 mg 12 hourly.
  - Increase by 100–200 mg/day at weekly intervals according to seizure control and adverse events.
  - Usual maximal dose: 600 mg 12 hourly. *LoE:IIIb*[37]

- Levetiracetam, oral: (Doctor initiated)
  - Initially, 250 mg 12 hourly, increasing to a therapeutic dose of 500 mg 12 hourly.
  - Dose can be adjusted upwards in increments of 500 mg 12 hourly every 2 to 4 weeks to a maximum of 1500 mg 12 hourly (3000 mg per day).

  Note: levetiracetam may occasionally cause adverse neuropsychiatric effects. Risk factors include being of female sex, having a history of depression or anxiety, and/or recreational substance use.

  LoE:IVb[38]

- Valproate, oral:
  (Doctor prescribed if used in girls older than 10 years or women of childbearing potential, otherwise doctor initiated).
  - Usual starting dose: 200–300 mg 12 hourly.
  - Increase, as required, every 3 days to 2 weeks (depending on the seizure frequency) to a maximum dose of 1200 mg 12 hourly.

- Phenytoin, oral, 4.5–5 mg/kg (lean body mass) daily, at night. (Doctor initiated).
  - Only consider continuing phenytoin in patients already well controlled on phenytoin, and in whom phenytoin is well tolerated.
  - Usual starting and maintenance dose in adults: 300 mg once daily.
  - If epilepsy is not controlled on 300mg daily, treatment should be changed to the appropriate ASM for the epilepsy type as in Table 5.

  LoE:IVb

Poorly controlled epilepsy

» Ensure diagnosis of epilepsy and seizure type is confirmed, and imitators of epileptic seizures excluded.

» Ask the patient, and if possible, a family member or primary care giver, about the following, as these factors can influence decisions regarding medicine therapy:
  – Has the patient been adherent in taking the medication regularly for at least 2 weeks or more before the seizure? Ask about medicine dosage and frequency.
  – If non-adherence has been established, ask for reasons contributing to non-adherence and offer guidance.
  – Has the patient recently used some other medicine and/or herbal remedy (i.e. look for drug interactions, substance use or traditional medicine use).
  – Is there a chance that alcohol is involved?
  – If ≥ 1 of the above are present, address the problem/s but leave ASM unchanged (unless dose adjustment is necessary because of a drug interaction). Reassess the patient within 2 weeks.

REFERRAL

» All patients with new onset epilepsy for further investigations such as neuroimaging.
» Patients with seizures other than generalised tonic-clonic seizures, including absence seizures.
» Patients with an increase in seizure frequency despite attempts to address adherence issues.
» Patients with a change in seizure type.
» Patients who have been seizure free on ASM for 2 years or more, to review medications and to consider cessation of treatment.
» Development of new neurological signs and symptoms.
» Adverse medicine reactions or suspected toxicity in children.
» If uncontrolled on monotherapy, and patient has been shown to be adherent, referral for initiation of a second agent can be made to a medical officer at primary care level and does not require hospital / specialist referral.

Information that should accompany each referral case:

» Number and frequency of seizures per month (or year).
» Date and time of most recent seizures.
» Detailed description of the seizures, including:
  – Presence of an aura or warning signs;
  – what happens during the seizure? (give a step-by-step account)
  – is the person conscious during the seizure?
  – how long do the seizures last on average?
  – what does the patient experience after the seizure?
  – how long does this experience last?
» Is there a family history of seizures?
» What is the initial date of diagnosis?

» Is there evidence of alcohol use?
» Is there another medical condition, e.g. diabetes, HIV and what medication is used?
» What is the name and dosage of the ASM used to date?
» Does the person return regularly for repeat of medication?

15.8 MENINGITIS

15.8.1 ACUTE MENINGITIS

A39.0+(G01*)/G00.0-3/G00.8-9/G01/G02.0-1/G02.8/G03.0/G03.8-9

DESCRIPTION

Infection of the membranes of the brain.
Clinical signs and symptoms include:

» headache
» neck stiffness
» vomiting
» fever
» impaired level of consciousness
» photophobia
» bulging fontanelle in infants

Note:

» During the early phase of TB meningitis, malaise, low-grade fever, headache and personality change rather than the above-mentioned symptoms may be present.
» Duration of treatment for TB meningitis is 9 months.

Neck stiffness is rare in young children, especially in neonates, and may be absent in adults, especially debilitated patients and the elderly.
Young children with fever, vomiting and convulsions or an impaired level of consciousness must be assumed to have meningitis. Signs may be even more subtle in newborns.

EMERGENCY MEASURES

» Stabilise before referral.
» Treat for shock, if present.
» If patient's level of consciousness is depressed:
  - maintain airway
  - give oxygen
» Ensure hydration.
» If convulsing, see Section 21.2.11: Seizures and status epilepticus.

MEDICINE TREATMENT

Initiate medicine treatment before transfer.
Children

- Ceftriaxone, IM/IV, 100 mg/kg/dose immediately as a single dose before referral. See dosing table: Chapter 23.
  - For IM administration, do not inject more than 1 g at one injection site.
  - Maximum pre-referral dose: 2 g IM/IV.
  - If referral is delayed, repeat dose after 12 hours.
  - Maximum daily dose of 4 g, given in divided doses 12 hourly.

LoE:IVb[39]

CAUTION: USE OF CEFTRIAXONE IN NEONATES AND CHILDREN

» If *SUSPECTING SERIOUS BACTERIAL INFECTION* in neonate, give ceftriaxone, even if jaundiced.
» Avoid giving calcium-containing IV fluids (e.g. Ringer Lactate) together with ceftriaxone:
  - If ≤ 28 days old, avoid calcium-containing IV fluids for 48 hours after ceftriaxone administered.
  - If > 28 days old, ceftriaxone and calcium-containing IV fluids may be given sequentially provided the giving set is flushed thoroughly with sodium chloride 0.9% before and after.
  - Preferably administer IV fluids without calcium contents.
» Always include the dose and route of administration of ceftriaxone in the referral letter.

- Paracetamol, oral, 10–15 mg/kg/dose 6 hourly when required. See dosing table: Chapter 23.

AND/OR

- NSAID, e.g.:
- Ibuprofen, oral, 5–10 mg/kg/dose 8 hourly with or after a meal. See dosing table: Chapter 23.

Adults

- Ceftriaxone, W IM, 2 g immediately before referral.
  - Do not inject more than 1 g at one injection site.
  - If referral is delayed, repeat dose after 12 hours.

LoE:IVb[40]

- Paracetamol, oral, 500 mg–1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

AND/OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg then 8 hourly with meals, if needed.

Severe pain:

- Tramadol, oral, 50–100 mg 4–6 hourly. (Doctor prescribed)
  - May be increased to a maximum daily dose of 400 mg.

During a listeria outbreak, ADD as a pre-referral dose:

A32.1/A32.7-9

Children

- Ampicillin, A IM/IV 75 mg/kg/dose immediately before referral.
  - If referral is delayed by 6 hours or more, administer second dose.

Weight kg	**Dose** mg	**Injection** 500 mg/mL (500 mg diluted in 0.9 mL water for injection (WFI))	**Age** months/years
>3.5–5.5 kg	300 mg	0.6 mL	>1–3 months
>5–7 kg	450 mg	0.9 mL	>3–6 months
>7–9 kg	600 mg	1.2 mL	>6–12 months
>9–11 kg	750 mg	1.5 mL	>12–18 months
>11–17.5 kg	1000 mg	2 mL	>18 months–5 years
>17.5–25 kg	1500 mg	3 mL	>5–7 years
>25–35 kg	2000 mg	4 mL	>7–11 years
>35 kg	3000 mg	6 mL	>11 years

Adults

- Ampicillin, A IM/IV, 3 g immediately before referral.
  - If referral is delayed by 6 hours or more, administer second dose.

Severe penicillin allergy:

Z88.0

Children

- Cotrimoxazole, A oral, immediately before referral. See dosing table: Chapter 23.
  - If referral delayed by 12 hours or more, administer second dose.

Adults

- Cotrimoxazole, A oral, 80/400 mg immediately before referral. *LoE:IVb*[41]
  - If referral delayed by 12 hours or more, administer second dose.

REFERRAL

All patients with meningitis, or suspected meningitis or suspected listeria meningitis.

15.8.2 MENINGOCOCCAL MENINGITIS, PROPHYLAXIS

Z20.8+Z29.2

In cases of meningococcal infection, the following close contacts should receive prophylaxis:

» household members,
» child-care centre contacts, and
» anyone directly exposed to the patient's oral secretions, e.g. kissing, mouth-to-mouth resuscitation, endotracheal intubation, or endotracheal tube management.

Chemoprophylaxis is only effective for the current exposure.

MEDICINE TREATMENT

Prophylaxis

Children < 6 years of age

- Ceftriaxone, (W) IM, 125 mg, as a single dose.

CAUTION: USE OF CEFTRIAXONE IN NEONATES AND CHILDREN

- If *SUSPECTING SERIOUS BACTERIAL INFECTION* in neonate, give ceftriaxone, even if jaundiced.
- Always include the dose and route of administration of ceftriaxone in the referral letter.

Children 6–12 years of age

- Ciprofloxacin, (W) oral, 250 mg, as a single dose.

Children > 12 years of age and adults

- Ciprofloxacin, (W) oral, 500 mg, as a single dose.

LoE:IIIb[42]

Pregnant women

- Ceftriaxone, (W) IM, 250 mg, as a single dose.

15.8.3 CRYPTOCOCCAL MENINGITIS

See Section 11.3.4: Cryptococcosis.

15.9 HEADACHE, MILD, NON-SPECIFIC

R51

DESCRIPTION

Headache can be benign or serious.

Headache can have serious underlying causes including:

- » encephalitis
- » meningitis
- » mastoiditis
- » benign intracranial hypertension
- » hypertensive emergencies
- » venous sinus thrombosis
- » stroke
- » brain tumour

Headache due to a serious disease will often be associated with neurological symptoms and signs including:

- » vomiting
- » fever
- » mood change
- » cranial nerve fall-out
- » convulsions
- » confusion
- » impaired consciousness
- » pupillary changes and difference in size
- » focal paralysis
- » visual disturbances
- » neck stiffness

Tension headache due to muscle spasm:

- » May be worse in the afternoon but often present all day.

» Is normally felt in the neck and the back of the head but may be felt over the entire head.
» Is often associated with dizziness and/or blurring of vision.
» Is often described as a tight band around the head or pressure on the top of the head.
» Does not progress through stages like a migraine (no nausea, no visual symptoms).

GENERAL MEASURES

» Teach relaxation techniques where appropriate.
» Reassurance, where applicable.
» Exclude analgesia overuse headache.

MEDICINE TREATMENT

Children

- Paracetamol, oral, 10–15 mg/kg/dose 6 hourly when required. See dosing tables: Chapter 23.

Adults

- Paracetamol, oral, 500 mg–1 g, 4–6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

REFERRAL

» Refer patients with suspected meningitis immediately after initial treatment. See Section 15.8: Meningitis.
» Headache in children lasting for 3 days.
» Recent headache of increasing severity.
» Headache with neurological manifestations.
» Analgesia overuse headache.
» Newly developed headache persisting for >1 week in an adult.
» Chronic recurrent headaches in an otherwise healthy patient: refer if no improvement after 1 month of treatment.
» Tension headache due to muscle spasm: refer if no improvement after 1 month of treatment.

15.10 NEUROPATHY

DESCRIPTION

Defective functioning of nerves, which may involve peripheral nerves (peripheral neuropathy) and/or cranial nerves.
Clinical features may be predominantly of a sensory, sensorimotor or motor nature.

15.10.1 POST-HERPES ZOSTER NEUROPATHY (POST HERPETIC NEURALGIA)

See Section 10.13: Shingles (Herpes zoster).

15.10.2 BELL'S PALSY

G51.0

DESCRIPTION

Unilateral paralysis of all the muscles of facial expression (the corner of the mouth drops, the forehead is unfurrowed, and the eyelid will not close).

Taste sensation may be lost unilaterally and hyperacusis (painful sensitivity to loud sounds) may be present.

Most patients recover within a few weeks or months.

GENERAL MEASURES

» HIV testing.
» Referral for facial muscle massage and exercises
» Eye patch for protection of the eye during sleep.

MEDICINE TREATMENT

Adults

LoE:IVb[43]

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 60 mg daily for 7 days started within 72 hours, preferably within 48 hours of onset (Doctor prescribed). *LoE:Ia*[44]

Children

- Corticosteroids (intermediate-acting) e.g.: *LoE:IVb*[45]
- Prednisone, oral, 2 mg/kg daily for 7 days within 3 days of onset (Doctor prescribed).

Weight (kg)	**Dose** (mg)	**Tablet** (5 mg)	**Age** (Months/years)
>17.5–25 kg	40 mg	8 tablets	>5–7 years
>25–40 kg	55 mg	11 tablets	>7–12 years

REFERRAL

» If diagnosis uncertain.
» All cases for physiotherapy, if available.
» Eye irritation requiring lubrication.

15.10.3 PERIPHERAL NEUROPATHY

E10.4/E11.4/G60.9/G62.0-1/G62.9

DESCRIPTION

Initially sensory symptoms consisting of tingling, prickling, burning in the balls of the feet or tips of the toes or in a general distribution over the soles. The symptoms are symmetrical and with progression spread proximally.

Later sensory loss over both feet and weakness of dorsiflexion of the toes may be present. Patients may experience difficulty in walking on their heels and foot drop becomes apparent.

Common causes include HIV, diabetes mellitus, isoniazid, antiretrovirals, vitamin B12 deficiency and alcohol.

GENERAL MEASURES

» HIV testing.
» Screen for diabetes mellitus, syphilis and vitamin B12 deficiency

» Avoid alcohol.
» A balanced diet to prevent nutritional deficiency.

MEDICINE TREATMENT

» Stop the offending medicine or give suitable substitute.
» Patients on isoniazid (TB treatment or prophylaxis): increase pyridoxine to 25–50 mg 8 hourly for 3 weeks, followed by 25–50 mg daily.
- Amitriptyline, oral, 25 mg at night (Doctor prescribed).
  - Titrate at two weekly intervals to a maximum of 75 mg at night.

REFERRAL

» All children.
» All patients to rehabilitation to improve postural control and gait as well as education for prevention of complications.
» Difficulty in walking or foot drop.
» Any limb weakness present.
» Unsteady/ataxic gait.
» Severe sensory loss. *LoE:IIIb*[46]

15.11 CEREBRAL PALSY

G80.0-4/G80.8-9

DESCRIPTION

Cerebral palsy (CP) is a neurodevelopmental disorder resulting from an injury to the developing brain.

The most common type of CP is hypertonia/spasticity (85%), followed by dyskinesia (7%), ataxia (4%), and hypotonia (3%). The distribution of motor impairment may be bilateral (as in diplegia, quadriplegia, or triplegia) or unilateral (as in hemiplegia).

The primary impairments associated with CP include reduced muscle strength, impaired sensation, abnormal muscle tone and reduced cardiorespiratory fitness, resulting in difficulties performing selfcare activities and mobility. Some children with CP experience hearing loss, which may affect posture and balance.

Poor communication from speech and language impairment may also occur.

GENERAL MEASURES

» Children with CP require regular screening of their general health and wellbeing e.g. for evidence of neglect or abuse, infections, constipation, and malnutrition.
» Refer to rehabilitation services to optimise function, training on assistive devices, assessment, and management of hearing and communication problems, as well as caregiver training and support.

LoE:IIIb[47]

15.12 SPINAL CORD INJURIES

DESCRIPTION

Multiple symptoms may manifest in these patients, requiring accompanying medications and rehabilitative therapy at different levels of care.

Patients with spinal cord injuries may initially be managed at hospital level before referral to primary care level for long-term management. After referral, patients should be assisted with access of items prescribed at hospital level to ensure continuity of care.

GENERAL MEASURES

LoE:IIb[48]

Refer patients with cervical spinal cord injury for multidisciplinary rehabilitation to optimise cardiorespiratory and functional (including mental health) performance.

MEDICINE TREATMENT

Neurogenic bowel dysfunction

For constipation, see Section 2.8: Constipation.

Neuropathic and nociceptive pain

See Section 20.3: Chronic non-cancer pain.

Depression

See Section 16.4.1: Depressive disorders.

Anxiety

See Section 16.3: Anxiety disorders.

Infections

See Chapter 10: Infections and related conditions.

Pressure sores

See Section 5.19: Pressure ulcers/sores.

REFERRAL

» All patients for initial multidisciplinary assessment and management.
» Patients who require treatment for chronic conditions not covered above, such as spasticity, neurogenic bladder, DVT (prophylaxis or treatment), and osteoporosis.

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SOUTH AFRICAN NATIONAL DEPARTMENT OF HEALTH
NEMLC SUMMARY REPORT ON UPDATES MADE TO THE THE STANDARD TREATMENT GUIDELINES AND ESSENTIAL MEDICINE LIST GUIDANCE PRODUCTS
PRIMARY HEALTH CARE
PHC Chapter 15: CENTRAL NERVOUS SYSTEM CONDITIONS

Document Version

Report Version	**Date**	**Detail**
V 1.0	*4 June 2026 and 30 July 2026*	• Prescriber Level - Antiseizure medicines (ASMs) and Schedule 5 medicines • Dose of Midazolam IV updated under the medicine management and supportive care of status epilepticus in children < 13 years of age • Guidance on management of combination therapy • Guidance regarding increasing the dose of lamotrigine in pregnancy • Neuropsychiatric adverse effects of levetiracetam • Guidance on management of patients not controlled on phenytoin • Cross-titration guidance for lamotrigine • Internal and external commentator queries and clinical editing queries • General guidance on discontinuation and periodic review of treatment

Specific guidance products (Tick relevant and specify chapter number)

No	Guidance Product	*Tick*	*Number*
1.	Primary Health Care Level STGs	✓	15.5 Status Epilepticus 15.7 Epilepsy 1.5 Acute Meningitis
2.	Adult Hospital Level STGs		
3.	Paediatric Hospital Level STGs		
4.	Tertiary and Quaternary EML		

Summary Tables

Medicine Amendments

Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG).

STG/SECTION	GUIDANCE PRODUCTS (Tick relevant)				MEDICINE / MANAGEMENT	ADDED / DELETED / AMENDED	TI* CONSIDERATIONS (if applicable)
	PHC STGs & EML	AH STG & EML	PaedH STG & EML	TQ EML			
Report Version v1.0							
15.5 Status Epilepticus **15.7 Epilepsy**	X				Antiseizure medicines	Clarification of prescriber level	Not applicable
15.5.1 Epileptic seizures and status epilepticus in children < 13 years of age	X		x		Midazolam, IV	Retained, dose updated	Not applicable
15.7 Epilepsy	X	X	X		Lamotrigine	Cross-titration guidance for lamotrigine added	Not applicable
15.8.1 Acute Meningitis	X				Tramadol	Prescriber level added	Not applicable

Report V1.0

15.5 STATUS EPILEPTICUS, 15.7 EPILEPSY

Anti-seizure medicine: *Prescriber level clarified.*

The epilepsy guidelines were updated in the 2020-2024 NEMLC review cycle with new updates for first- and second-line treatment for the different epilepsies at primary health care (PHC) level which has bearing on nurse prescribing at PHC level.

An external comment was received querying the prescriber level for levetiracetam at PHC level.

It was acknowledged that NEMLC has no mandate regarding prescriber level for nurses or clinical associates.

Nurses granted authorisation provided in terms of Section 56(6) of the Nursing Act 33, 2005, may prescribe medicines in accordance with the PHC STGs and EML and their scope of practice and the relevant Regulations. The STGs generally provide for all listed medicines to be prescribed by authorised nurse prescribers except where designated as “doctor prescribed” only or “doctor initiated”. Additionally, in some instances, a listed medicine may only be initiated by a nurse with the prior approval of a medical practitioner. The “doctor initiated” category

refers to an initial prescription prescribed by a doctor, which a nurse prescriber may repeat. However, the latter provision does not apply to Schedule 5 or 6 medicines. The PHC STGs were previously updated to include "Doctor prescribed" for all Schedule 5 and 6 medicines as PHC nurses with section 56(6) permits are limited to prescribing medicines up to Schedule 4 (GN.R. 2418 of 1984).

The prescriber level for all antiseizure medicines in the PHC epilepsy related STGs were reviewed and clarified.

The changes throughout the chapter are summarized as tabulated below:

Schedule 5 medicines	Schedule 5 antiseizure medicines for status epilepticus (i.e., benzodiazepines and phenobarbital) must be prescribed by a medical doctor. If there is no doctor on site, a nurse may administer the medicine in accordance with a telephonic prescription provided by a medical doctor. The medical doctor must provide a written, signed prescription within 72 hours of the telephonic prescription.
Epilepsy	The initial diagnosis of epilepsy must be made by a doctor. Only once seizure control has been achieved and the patient is stable on maintenance therapy should treatment be continued by a nurse. Doctors to take responsibility for the acknowledgment of risk form for use of valproate in girls and women of childbearing potential.
Status epilepticus	Notify the medical doctor on duty to conduct a medical examination, supervise care and prescribe required medicines. If there is no doctor on site, discuss the patient with a medical doctor telephonically. Schedule 5 antiseizure medicines for status epilepticus (i.e., benzodiazepines and phenobarbital) must be prescribed by a medical doctor. If there is no doctor on site, a nurse may administer the medicine in accordance with a telephonic prescription provided by a medical doctor. The medical doctor must provide a written, signed prescription within 72 hours of the telephonic prescription.

In summary the following decisions and updates were included in the chapter in response to additional internal and external queries on the STG:

- It is the responsibility of a doctor to diagnose epilepsy, initiate antiseizure medicines and ensure stabilization of the patient before a nurse can continue prescribing antiseizure medicines.
- The dose of Midazolam IV was updated[1][2] under the medicine management and supportive care of status epilepticus in children < 13 years of age.
- All antiseizure medicines are doctor initiated except when valproate is prescribed in girls and woman of childbearing potential (GWOCBP), then valproate is doctor prescribed. A note at the beginning of the epilepsy section now states: "The initial diagnosis of epilepsy must be made by a medical doctor. Continued prescription of ASM may only be performed by health care professionals other than medical doctors once seizure control has been achieved and the patient is stable on maintenance therapy. Cross-

[1] Midazolam IV: Drug Doses. Author, Frank Shann. Edition, 9. Publisher, Intensive Care Unit, Royal Children's Hospital, 1996. ISBN, 0646272047, 9780646272047.

[2] Midazolam IV: University of Cape Town, Faculty of Health Sciences, Division of Clinical Pharmacology. (2024). South African Medicines Formulary (SAMF). SAMF website. https://samf-app.com

titration of ASMs should be managed by a medical doctor", noting that clinical associates' scope of practice includes prescribing up to schedule 4, under the supervision of a doctor.

- Pregnant women on valproate should be switched to levetiracetam (not lamotrigine) to avoid the long titration period.
- The words "as indicated" added to "Girls aged 10 years and older should receive effective family planning" regarding valproate use in GWOCBP to avoid putting young girls who are not sexually active on family planning unnecessarily. The acknowledgement of risk form must still be completed in these girls.
- Regarding combination therapy, ideally a medical practitioner would first discuss with a specialist before initiating combination treatment e.g., as second line treatment in pregnant women and women of child-bearing potential as per the add-on recommendations in the STG. However, it was acknowledged that sometimes it is difficult to reach a specialist immediately. In this case wording was added to the STG to convey that the medical practitioner should add-on treatment and schedule a follow-up visit in 1 - 2 weeks, while awaiting specialist advice.
- There is currently no specific guidance provided on how to increase the dose of lamotrigine in pregnancy. No additional guidance is provided in the STGs, mainly because there is no standard approach.[3] It is acknowledged that this matter should be reviewed in a future iteration of the STG. The STG was updated to indicate that where possible one should monitor lamotrigine plasma concentrations and adjust as necessary. Discuss with a specialist as the dose may have to be increased depending on background risk of seizures.
- A note regarding potential neuropsychiatric adverse effects of levetiracetam was added to the STG[4].
- For patients on phenytoin management, frequent monitoring with doses above 300mg was removed (as 'frequent monitoring' is difficult to quantify or define), and the STG was updated to indicate that if epilepsy is not controlled on 300mg daily of phenytoin, treatment should be changed to the appropriate ASM for the epilepsy type as per the STG treatment algorithms provided.
- General guidance on discontinuation and periodic review of treatment was added to the STGs as follows:
    - Discontinuation of treatment may be considered in patients who have remained seizure-free for at least 2 years. A careful risk-benefit assessment for treatment discontinuation should be conducted by a medical practitioner. Medicines must be weaned off gradually over several months if necessary. If the patient is on two or more ASMs, one medicine should be stopped at a time, each with a slow tapering of the dose.

The Epilepsy and related STGs underwent detailed clinical editing with significant editorial updates. The adult and pediatric hospital level chapters to be aligned where appropriate.

[3] Kim, H. Y., Goo, Y., der Nederlanden, A. M., Bleasel, A., & Alffenaar, J.-W. (2024). Dose Monitoring of Lamotrigine Monotherapy in Pregnancy: Are Pregnant Women with Epilepsy Currently Optimally Managed? A Systematic Review. Therapeutic Drug Monitoring, 46(2), 181–194. https://doi.org/10.1097/FTD.0000000000001186

[4] Josephson CB, Engbers JDT, Jette N, et al. Prediction Tools for Psychiatric Adverse Effects After Levetiracetam Prescription. JAMA Neurol. 2019;76(4):440–446. http://www.ncbi.nlm.nih.gov/pubmed/9186252

Refer to the PHC CNS Conditions chapter for the detailed updates and changes to STGs regarding prescriber level: 15.4 EPILEPTIC SEIZURES, 15.5 STATUS EPILEPTICUS, 15.6 FEBRILE SEIZURES, 15.7 EPILEPSY

15.7 EPILEPSY

Cross-titration guidance for lamotrigine: *Added*

During review of the chapter additional guidance was added for epilepsy in children <13 Years of age and in adolescents and adults for cross-titration of lamotrigine (i.e., start as add-on therapy, titrate up to a usual maintenance dose, then gradually wean the first medicine in small increments every 1 - 2 weeks).

The following wording was added to the dosing tables for lamotrigine as monotherapy or add-on therapy

Start as add-on therapy, titrate up to a usual maintenance dose, then gradually wean the first medicine in small increments every 1 - 2 weeks. Note: Lamotrigine levels will increase as carbamazepine doses are reduced; lamotrigine levels will decrease as valproate doses are reduced (therefore, may need to increase lamotrigine dosing).

Hospital level chapters to be aligned.

15.8.1 ACUTE MENINGITIS

Tramadol (prescriber level): *Added*

As tramadol is a Schedule 5 medicine, the acute meningitis STG was updated stipulating “Dr Prescribed” for tramadol.