CHAPTER 14

NEUROLOGICAL DISORDERS

14.1 CEREBROVASCULAR DISEASE

14.1.1 STROKE

I61.0-6/I61.8-9/I63.0-6/I63.8-9/I64 + (G46.0-8*)

GENERAL MEASURES

Optimise hydration and nutrition; insert nasogastric tube if patient cannot swallow. Take precautions to ensure an open airway if patient is unconscious. Physiotherapy and good nursing care. Consider rehabilitation for suitable patients and refer if necessary.

Do an ECG to rule out an acute coronary event or atrial fibrillation as precipitants.

Do serology to exclude meningovascular syphilis (in patients <45 years old who do not have risk factors for stroke).

Check lipid profile in ischaemic strokes.

Ischaemic stroke in young adults (< 45 years of age) may be due to atherosclerosis, but also consider:

» Embolic: e.g. rheumatic heart disease, atrial fibrillation, cardiomyopathy, previous myocardial infarction, and, very rarely, patent foramen ovale: history, careful clinical cardiac examination, ECG/CXR, and echocardiography.
» Vessel wall disease: e.g. syphilis, HIV infection, collagen-vascular diseases, TB or bacterial meningitis, and extracranial arterial dissection. Investigate as guided by clinical presentation, but at least perform syphilis and HIV serology, urinalysis (haematuria and/or proteinuria), and ANF/RF. ANCA, and cerebral angiography or carotid Doppler may be indicated. Note that absence of a carotid bruit does not exclude significant carotid stenosis.
» Hypercoagulable states: e.g. antiphospholipid antibody syndrome, thrombotic thrombocytopenic purpura. Useful screening investigations are FBC and, in women, PTT/Anti-phospholipid Ab. Testing and management of thrombophilias should be done in consultation with an expert.

Initiate a palliative care approach if the patient's condition is deteriorating / in case of a massive stroke (See Chapter 24: Medicines Used in Palliative Care).

Ensure adequacy of swallowing ability by dietician or by asking the patient to swallow 10 mL of water.

MEDICINE TREATMENT

Hyper-acute management:

Symptom onset ≤ 3 hours:

» Do not give aspirin.
» Refer immediately to hospital that **can provide thrombolytic therapy:**

- Alteplase, IV, 0.9 mg/kg. Total dose should not exceed 90 mg.

- 10 % of total dose given as a bolus and the remainder continued as an infusion over an hour.

LoE:Ib[i]

Symptoms >3 hours:

LoE:Ia[ii]

- Aspirin, oral, 300 mg, immediately.

Followed by:

- Aspirin, oral, 150 mg daily.
  - If patient is unable to swallow, administer through a naso-gastric tube.

Do not administer aspirin if there are symptoms suggestive of a sub-arachnoid bleed, e.g. headache, stiff neck, etc.

AND

For DVT prophylaxis, see Section2.8: Venous thrombo-embolism.
Treat secondary pulmonary and urinary tract infections appropriately.

Secondary prevention:

Measures for secondary prevention may not be appropriate for patients with severe disability.

All patients with a thrombotic stroke, not on anticoagulation and irrespective of the LDL level:

- Aspirin, oral, 150 mg daily.

LoE:Ia[iii]

AND

- HMGCoA reductase inhibitors (statins), e.g.:
- Rosuvastatin, oral, 10 mg at night.

LoE:IIb[iv]

Patients on protease inhibitor:

- Atorvastatin, oral, 10 mg at night.

LoE:IIb[v]

Patients on amlodipine (and not on a protease inhibitor):

- Simvastatin, oral, 10 - 20 mg at night.

If patient complains of muscle pain:

LoE:IVb[vi]

Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management.

LoE:IVb[vii]

Anticoagulation:

In patients with cardioembolic strokes (e.g. secondary to atrial fibrillation) with no evidence of haemorrhage on CT scan, the optimal time to start anticoagulation therapy is likely to vary among individual patients; this can be from 7 to 14 days and up to 21 days and is dependent on the infarct size (> 1/3 of the hemisphere) and the patient's risk factors for recurrent events.

LoE:IIIb[viii]

Bridging anticoagulation with heparin, or earlier initiation of warfarin, is not recommended because, although it reduces ischaemic stroke recurrence, it increases symptomatic intracranial haemorrhage. LoE:IVb

Blood pressure management:
A transient increase in BP is common after an acute stroke. Lowering BP during the acute phase of stroke (within 6 hours of onset) may not improve morbidity.

Do not actively lower a systolic BP < 220 mm Hg or diastolic BP < 120 mm Hg in the first few days after stroke as this may be associated with an increased risk of death.

In patients presenting with stroke and BP > 220/120 mmHg, lower BP to about 180/110 mm Hg in the first 24 hours.

Antihypertensive medicines may be withheld until patients have suitable oral or enteral access. Cautious incremental reintroduction of treatment is advised to achieve long-term standard BP control. See Section: 3.6.3 Hypertensive crisis, hypertensive emergency.

If BP > 220/120 mm Hg: LoE:IIb[ix]
- Long-acting calcium channel blocker, e.g.:
- Amlodipine, oral, 5 mg daily.

OR
If adequate fluid intake can be ensured: LoE:IIb[x]
- Hydrochlorothiazide, oral, 12.5 mg daily. LoE:IVb

Note:
» There is some evidence of harm from BP reduction within 7 days of acute stroke; after 7 days cautious incremental re-introduction of treatment is advised to achieve long term standard BP control.
» Antihypertensive medicines should be stopped in acute stroke unless the BP is > 220/120 mm Hg (see above). LoE:IIb[xi]
» Reassess the need for re-initiation of patients' previous antihypertensive medication. See Section3.6: Hypertension. LoE:IIb[xii]

REFERRAL
Patients with aspirin intolerance
To a facility with a CT scan:
» Patients with atypical clinical presentation.
» Selected patients with suspected ischaemic stroke who may benefit from thrombolysis with tissue plasminogen activator if initiated within 3 hours of onset of symptoms.
» Patients with suspected posterior cerebral fossa haemorrhage who may require surgical decompression.

» If there is a history suggestive of subarachnoid haemorrhage or if there is neck stiffness.

14.1.2 TRANSIENT ISCHAEMIC ATTACK (TIA)

G45.0-4/G45.8-9

DESCRIPTION

A transient ischaemic attack is an episode of brain, spinal cord, or retinal ischaemia causing focal neurological dysfunction usually for less than one hour. Risk of subsequent stroke is highest in the week after a TIA. Consider hypoglycaemia, epilepsy, and migraine as alternative causes for the symptoms.

Feature	Points
Age ≥60 years	1
BP ≥ 140/90 mmHg	1
Clinical features:	
speech disturbance without weakness OR	1
unilateral weakness	2
Diabetes	1
Duration:	
10 to 59 minutes	1
≥ 1 hour	2

Table 14.1: The $ABCD^2$ scoring system

Reference: Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, Sidney S. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet. 2007 Jan 27;369(9558):283-92. doi: 10.1016/S0140-6736(07)60150-0. PMID: 17258668.

$ABCD^2$ score ≥ 4 is regarded as high risk and warrants urgent investigation and management as the risk of stroke within the next week is ≥ 4%.

MEDICINE TREATMENT

Cardioembolic disease:

- Warfarin, oral, 5 mg daily.
  - Measure INR after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to initiation dosing tables in Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to Maintenance dosing tables in the Appendix II).

LoE:IVb[xiii]

Other patients:

LoE:IIIb[xiv]

- Aspirin, oral, 150 mg daily.

Lipid control (all patients):

- HMGCoA reductase inhibitors (statins), e.g.:

LoE:IIb[xv]

- Simvastatin, oral, 40 mg at night.

Patients on protease inhibitor:

- Atorvastatin, oral, 10 mg at night. *LoE:IIb*[xvi]

Patients on amlodipine (and not on a protease inhibitor):

- Simvastatin, oral, 10- 20 mg at night. *LoE:IVb*[xvii]

If patient complains of muscle pain:
Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management. *LoE:IVb*[xviii]

Manage hypertension – see Section3.6: Hypertension.

14.1.3 SUBARACHNOID HAEMORRHAGE

I60.0-9

DESCRIPTION

Bleeding into the subarachnoid space, most commonly due to the rupture of a vascular aneurysm. Patients typically present with an acute onset of severe headache and may have additional neurological symptoms and signs. Diagnosis is confirmed preferably by neurological imaging and, when this is not available, by demonstrating CSF xanthochromia on lumbar puncture.

GENERAL MEASURES

Maintain normal hydration and electrolyte status.
Control blood pressure.

MEDICINE TREATMENT

Analgesia if level of consciousness is not impaired:
Avoid NSAIDs.

- Paracetamol, oral, 500 mg to1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
    - Maximum dose: 15 mg/kg/dose.

If no response to paracetamol:

- Morphine, IV, to a total maximum dose of 10 mg (see Appendix II, for individual dosing and monitoring for response and toxicity).

In all patients presenting with aneurysmal subarachnoid haemorrhage while waiting for transfer to neurosurgical facility and in consultation with neurosurgeon:

- Nimodipine, oral, 60 mg 4 hourly for 21 days.

REFERRAL

All patients with minimal impairment of consciousness level for angiography and appropriate neurosurgical management. Patients initially deemed unsuitable for further investigation, may be referred at a later stage, should their condition improve.

14.2 DEMENTIA

E51.2/E52/E63.9/F00.0-2/F00.9/F01.0-3/F01.8-9/F03

DESCRIPTION

Progressive loss of cognitive function, usually of insidious onset. Initial presentation may be with mild personality or memory changes, before more pronounced defects become evident. Investigate patients for potentially reversible causes:

» Metabolic:
  - Hypothyroidism.
  - Vitamin B_{12} deficiency.
  - Pellagra.
  - Thiamine deficiency (Wernicke's syndrome).
» Medications and drugs:
  - Alcohol abuse.
  - Many medicines with CNS side-effects.
» Infections:
  - Syphilis.
  - HIV.
» Surgical:
  - Chronic subdural haematoma.
  - Normal pressure hydrocephalus.
» Severe depression (may mimic dementia).

Conditions which may worsen already existing dementia include:

» electrolyte disturbances and dehydration.
» infections.
» medicine toxicity.

GENERAL MEASURES

Appropriate care and support, according to the level of impairment.
Ambulatory care is preferred to hospitalisation, if feasible.
Family counselling and support.
Use a palliative care approach: involve a multidisciplinary care team early and plan for advanced dementia care.

MEDICINE TREATMENT

Management is mainly symptomatic.

<u>To control restless patients:</u>

- Haloperidol, oral, 0.75–1.5 mg 8 hourly with a higher dose at night, if required.

Note:
» There is uncertainty of benefit versus harm of long-term use of antipsychotics in dementia, but antipsychotics may be of benefit in severe behavioural and psychological symptoms.
» Inform the family of a possible elevated risk of mortality with prolonged use of antipsychotics.
» If there is no improvement, stop the antipsychotic.
» Initiate treatment at a low dose and titrate to the lowest effective dose for the shortest possible time. Reassess the person at least every 6 weeks, to check whether they still need medication.

LoE:IIIa[xix]

For pellagra:
- Nicotinamide, oral, 100 mg 8 hourly.

Wernicke's syndrome: E51.2 + (F02.8*)
- Thiamine, IM, 500 mg immediately and daily for 3 to 5 days.
  - Follow with thiamine, oral, 100 mg 8 hourly.

CAUTION
Thiamine should preferably be administered prior to intravenous glucose to prevent permanent neurological damage.
Do not delay the dextrose administration in a hypoglycaemic patient.

Prophylaxis in patients at risk (alcoholism, malnutrition): Z29.2
- Thiamine, IM, 200 mg daily or oral, 100 mg 8 hourly for 14 days.

LoE:IIb[xx]

Treat other commonly associated nutritional deficiencies:
If confirmed Vitamin B_{12} deficiency, manage as Section2.1.2: Anaemia, megaloblastic.

14.3 DELIRIUM
See Section20.8: Delirium with perceptual disturbances.

14.4 EPILEPTIC SEIZURES
G40.6-7; G41; 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[xxi]

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[xxii]

Not all persons who have an epileptic seizure have epilepsy. Specific criteria must be met to diagnose epilepsy (see Section14.6: 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 (first level in Figure 1). The evolution of the seizure (how it starts and progresses clinically) directs special investigations to determine the cause of the seizure and related management.

LoE:IVb[xxiii]

SEIZURE TYPES

Focal seizures:

The epileptic activity arises from a particular 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.

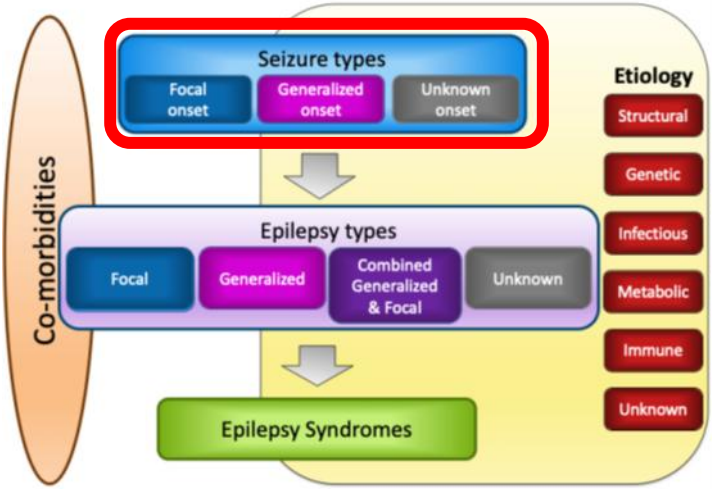

Figure 1. International League Against Epilepsy classification of seizure types *(Source: Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L. ILAE classification of epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017, 58 (4): 512-521)*

LoE:IVb[xxiv]

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.

- **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 Section14.6: 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[xxv]

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

14.5 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 recognized. Diagnosis is confirmed on EEG. Treat as for convulsive status epilepticus below. See Section14.5.1: Epileptic seizures and status epilepticus in adolescents (13 – 18 years) and adults. Identify and manage all underlying causes.

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

14.5.1 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 Section6.4.2: Eclampsia) » electrolyte abnormalities (e.g., in hyperemesis gravidarum) » stroke » reduced blood concentrations 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 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[xxvi]

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 (see figure 2).

» Do not place anything (spoon or spatula, etc.) in the patient's mouth.

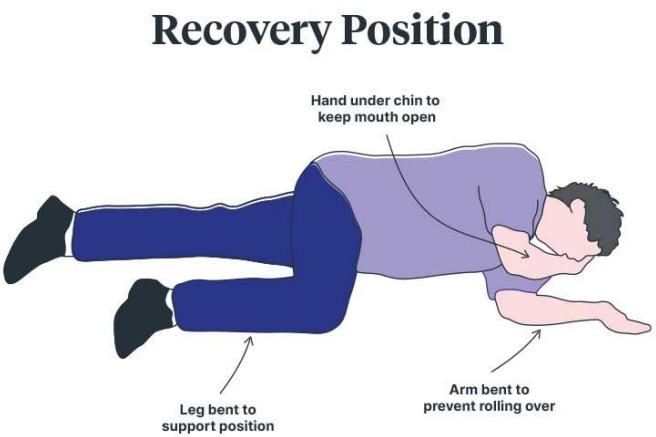

Figure 2: Recovery position for adults experiencing a seizure
Source: Ausmed: Adult Basic Life Support

LoE:IVb[xxvii]

» 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 1 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 by 5 minutes of its onset, commence urgent medicine treatment.

MEDICINE TREATMENT

Aim 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.

TABLE 1: 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) If IV access: • Lorazepam, IV, 4 mg, administered not faster than 2 mg/minute. *LoE:IIb[xxviii]* **OR** • Midazolam, IV, 10 mg. *LoE:IIb[xxix]* **OR** • Diazepam, IV, 10 mg administered over at least 5 minutes (not faster than 2mg/min). **OR** *LoE:IIb[xxx]* • Clonazepam, IV, 1 mg. *LoE:IIIb[xxxi]* If no IV access: • Midazolam, 10 mg, IM or buccal, using the parenteral formulation, while continuing to establish IV access If no IV access and no midazolam is available: • Clonazepam, IM, 1 mg. *LoE:IVb[xxxii]* **OR** • Diazepam, rectal, 0.2 – 0.5 mg/kg as a single dose (maximum 20 mg/dose). *LoE:IVb[xxxiii]* 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), load with antiseizure medicine.	» 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/overdose (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 ASM levels.

	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.	
ESTABLISHED STATUS EPILEPTICUS (10 – 30 minutes)	**LEVEL 2 INTERVENTION:** (Antiseizure medicine.) If IV access **and not suspected to be drug- or toxin-induced**: • Phenytoin, IV, 20 mg/kg diluted in 200 ml sodium chloride 0.9% **(not dextrose containing fluid)** administered not faster than 50mg/minute (usually 20–30 minutes) with cardiac monitoring. ○ If arrhythmias/hypotension occur, interrupt infusion temporarily and reintroduce at a slower rate. **CAUTION** Do not use phenytoin to manage suspected drug- or toxin-induced seizures. Cardiac monitoring is mandatory to ensure safe use. *LoE:IVb*[xxxiv] **Note:** » **Do not use phenytoin if seizures are suspected to be drug- or toxin-induced.** To manage, proceed to level 3 intervention, refractory status epilepticus, and address the acute poisoning (see Chapter 19: Poisoning). » If phenytoin toxicity is suspected (e.g. in a patient on chronic phenytoin treatment), proceed to level 3 intervention, refractory status epilepticus. If no IV access, consider: » Levetiracetam oral, crushed and given by nasogastric tube, 60 mg/kg as a single dose. (Maximum dose: 4500 mg.)	» Prepare for intubation/ventilation. » Arrange referral to higher level of care.

	LoE:IVb[xxxv]	
REFRACTORY STATUS (30 – 60 minutes)	• Propofol, IV, 1–2 mg/kg/dose as a bolus, followed by a continuous infusion at 1.2 mg/kg/hour. If necessary, titrate to effect by increasing infusion rate by 0.3 to 0.6 mg/kg/hour every 5 minutes (maximum rate of 12 mg/kg/hour or maximum total dose of 4 mg/kg/hour over 48 hours). LoE:IVb[xxxvi] **OR** • Midazolam, IV, 0.1 – 0.2 mg/kg bolus, followed by 0.05 – 0.5 mg/kg/hour infusion, titrated to effect. LoE:IVb[xxxvii] **Note:** » To prevent recurrent seizures if epilepsy is diagnosed or suspected, continue treatment with the most appropriate antiseizure medication during the infusion and weaning of propofol or midazolam. » Continue propofol or midazolam infusion for 12−24 hours after the last clinical or electrographic seizure, then wean the infusion.	» Admit to high- or intensive-care unit, if possible. » Employ a neuroprotective ventilation strategy (See Chapter 23: Adult Critical Care): – If it is necessary to ventilate, maintain PaCO2 in the low-normal range, i.e. 4.0–4.5 kPa. » Monitor: – heart rate, acid-base status, – respiratory rate, blood gas analysis, – blood pressure, SaO2, – electrolytes, neurological status, – blood glucose, fluid balance, – antiseizure medication blood concentrations, osmolality.

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 Section20.8: 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 (see Section14.6: Epilepsy) and requires ongoing ASMs.
» 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

» Refractory status.
» Need for more intensive care than can be provided at the facility.

14.6 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, or
» 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) or
» Diagnosis of an epilepsy syndrome.

Note:

» 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 [MR1] [JR2] [MR3] 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 3, 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.

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.

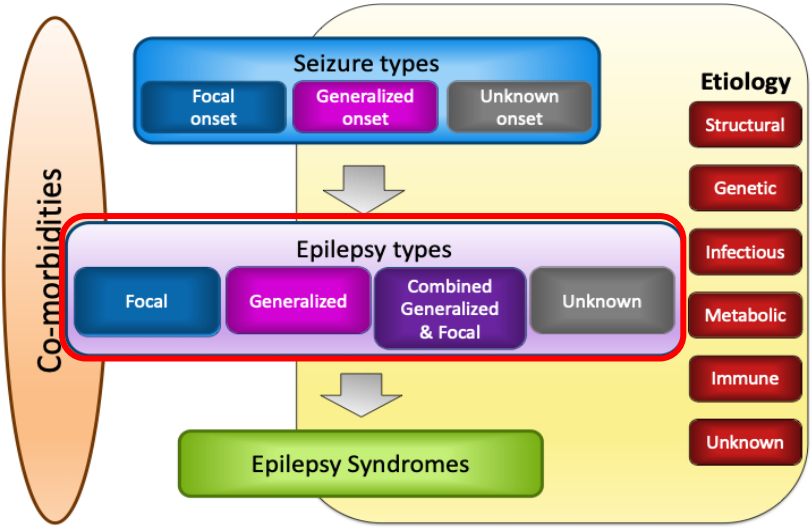

Figure 3. International League Against Epilepsy classification of seizure types *(Source: Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L. ILAE classification of epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. 2017, 58 (4): 512-521)*

LoE:IVb[xxxviii]

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 Section14.4: 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.

14.6.1 EPILEPSY IN ADOLESCENTS AND ADULTS

G40.0-9

DESCRIPTION

See Section14.6: Epilepsy.

DIAGNOSTIC CRITERIA

» The diagnosis of epilepsy is usually made clinically.
» 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 (essential in immunocompromised patients), and 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).

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

» 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 ASMs. See Chapter 7: Family planning.
» In pregnant women, women of child-bearing potential (i.e. women < 55 years of age), and young girls who are likely to need to continue treatment into their child-bearing years, initiate treatment with a lower risk ASM.
  – Lamotrigine and levetiracetam are the safer ASM 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 who have infrequent seizures, and no previous history of seizures requiring hospitalisation or status epilepticus.
  – Levetiracetam may be used if there is a poor response or adverse effects to lamotrigine, or in high-risk patients with frequent seizures, a previous history of hospitalization for seizures or status epilepticus.
» Valproate **must not** be used in pregnant women, women of child-bearing potential and young girls who are likely to need to continue 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 leaning

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 ASM.

» During pregnancy women may experience an increased number of seizures.

- This may be due to sleep deprivation, increased emotional stress and changes in ASM plasma concentrations.
- ASM plasma concentrations may decrease during pregnancy due to decreased absorption from nausea and vomiting, increased volume of distribution and increased clearance.
- There is increased hepatic metabolism of lamotrigine and increased renal clearance of levetiracetam in pregnancy, which return to normal post-partum; increase the dose if necessary, according to clinical response.

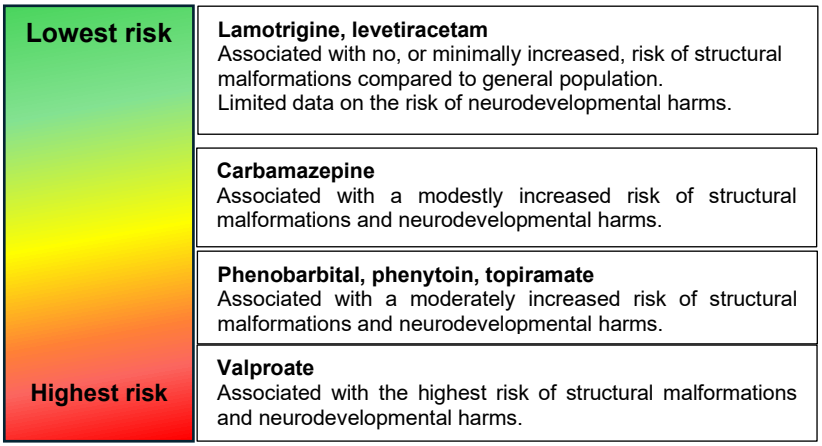

Figure 4. Risk of congenital structural malformations and neurodevelopment harms associated with various antiseizures medicines.
Increasing risk refers to increasing number of pregnancies or children affected.
(Adapted from Pennell PB. *Neurotherapeutics*. 2016 and Medicines & Healthcare products Regulatory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

LoE:IVb[xxxix]

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 of child-bearing potential.

LoE:IIIb[xl]

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 with HIV on ART because of fewer medicine interactions.
» Phenytoin, phenobarbital and carbamazepine are enzyme inducing ASMs. 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.

» Metabolism of lamotrigine is induced by lopinavir/ritonavir and atazanavir/ritonavir. The dose of lamotrigine may need to be increased when patients are switched to, or 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 at least 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

Acute treatment

Manage acute seizure and status epilepticus as per seizures/status epilepticus (see Sections 14.4: Epileptic seizures, and 14.5: Status epilepticus).

Maintenance Treatment

» Refer to Table 2 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 general 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 officer in consultation with a specialist.

Medicine interactions

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.

LoE:IVb[xli]

» 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 Table 2, however 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.

Table 2: Epilepsy treatment in adolescents and adults

Epilepsy type		Population	1st line	2nd line	3rd line *(specialist consultation)*	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	Consider combination treatment or add-on topiramate.	Avoid carbamazepine in people with HIV on ART due to drug-drug interactions.
		Pregnant women and women of child-bearing potential	Lamotrigine	Levetiracetam	Consider Carbamazepine **OR** Combination of lamotrigine and levetiracetam **OR** add-on topiramate	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	Discuss with specialist Consider: Combination therapy **OR** Add-on topiramate	Valproate should not be used unless lamotrigine and levetiracetam are poorly tolerated or ineffective. If valproate used in girls 10 years and older - see note below on acknowledgement of risk form.
		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	Refer for specialist assessment and intervention	Valproate should not be used unless lamotrigine or levetiracetam alone or in combination are ineffective or poorly tolerated.
	Myoclonic *Confirm diagnosis and discuss management*	Adolescent boys, men and women not able to have children	Valproate	Lamotrigine	Discuss with specialist Consider levetiracetam **OR**	These seizures may be aggravated by phenytoin or carbamazepine. Lamotrigine may be effective but may also exacerbate myoclonic seizures.

	with a specialist				Consider combination therapy.	If valproate used in girls 10 years and older - see note below on acknowledgement of risk form.
		Pregnant women and women of child-bearing potential	Lamotrigine	Levetiracetam	Discuss with specialist Consider combination therapy	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	Discuss with specialist Consider levetiracetam **OR** Consider combination therapy.	These seizures may be aggravated by phenytoin or carbamazepine If valproate used in girls 10 years and older - see note below on acknowledgement of risk form.
		Pregnant women and women of child-bearing potential	Lamotrigine	Levetiracetam	Discuss with specialist Consider combination therapy **OR** Consider valproate	Valproate should not be used unless lamotrigine or levetiracetam alone or in combination are ineffective or poorly tolerated. If valproate is used, see note below on "Acknowledgement of risk form" and effective family planning. These seizures may be aggravated by phenytoin or carbamazepine
Combined generalised and focal epilepsy OR Unknown/unclassified Discuss clinical presentation and management with a specialist in all cases.						

NOTE:

- 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, acknowledgment of risk must be obtained annually, even if not of child-bearing potential. Girls aged 10 years and older should receive effective family planning 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[xiii]

Medicine Treatment

- Lamotrigine, oral (Doctor initiated).
  - Dose-titrate using table below.

Table 3: Dosing table for lamotrigine as monotherapy or add-on therapy:

	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.
Lamotrigine as add on therapy to existing regimen			
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.

LoE:IVb[xliii]

CAUTION - LAMOTRIGINE

Lamotrigine may cause Stevens-Johnson Syndrome.

LoE:IVb[xliv]

- Carbamazepine, oral

o Start with 100 mg 12 hourly.
o Increase by 100–200 mg/day at weekly intervals according to seizure control and adverse events.
o Usual maximal dose: 600 mg 12 hourly. *LoE:IIIb*[xiv]

- Levetiracetam, oral

o Initially 250 mg 12 hourly, increasing to a therapeutic dose of 500 mg 12 hourly.
o 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).

- Valproate, oral

o Usual starting dose: 200–300 mg 12 hourly.
o 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.

Only consider continuing phenytoin in patients already well controlled on phenytoin, and in whom phenytoin is well tolerated.

o Usual starting and maintenance dose in adults: 300 mg once daily.
o Dose increases above 300 mg should be done in no more than 50 mg increments at intervals no shorter than 2 weeks.
o Doses > 300 mg/day of phenytoin are potentially toxic and could lead to permanent cerebellar damage. Caution and frequent monitoring of drug levels are essential at doses > 300 mg daily.

LoE:IV[b]

Poorly controlled epilepsy

» Ensure diagnosis of epilepsy and seizure type is confirmed and exclude imitators of epileptic seizures.
» 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 abuse 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 therapy unchanged (unless dose adjustment is necessary

because of a drug interaction). Reassess the patient within 2 weeks.

REFERRAL

» People with epilepsy who have not responded to two trials of ASM monotherapy at therapeutic drug concentrations and require consideration of combination therapy.
» Epilepsy with unexplained neurological symptoms or signs.

Information on the seizures 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?

14.7 HEADACHE AND FACIAL PAIN SYNDROMES

14.7.1 MIGRAINE

G43.0-3/G43.8-9

DESCRIPTION

A migraine is an episodic headache, usually located unilaterally and throbbing/ pulsating in nature, which may occur with or without an aura. Migraines are usually accompanied by nausea and/or vomiting, photophobia (sensitivity to light) and phonophobia (sensitivity to noise). There are several variants of migraine.

GENERAL MEASURES

Reassure patient that this is a benign condition.
Attempt to identify any precipitating factors or food triggers from the patient's history.

MEDICINE TREATMENT

Acute treatment

Initiate therapy during the migraine attack or at the onset of the headache.

Analgesia:

- Paracetamol, oral, 500 mg to1 g, 4 to 6 hourly as required (to a maximum of 4 g in 24 hours).
  - Maximum dose: 15 mg/kg/dose.

OR

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

For nausea:

- Metoclopramide, oral/IM, 10 mg 8 hourly, as required.

Prophylaxis (Z29.2)

Regular, daily, prophylactic therapy is advised if:

» attacks are frequent, i.e. more than 2–3 per month, or
» severe, causing a significant amount of disability, or
» attacks are long lasting, or
» patient poorly tolerates therapy for acute attacks.

- Amitriptyline, oral, 10–25 mg at bedtime. *LoE:IIIa[xlvi]*
  - Up-titrate dose to adequate clinical response.
  - Doses greater than 75 mg are seldom required.

OR *LoE:IIb[xlvii]*

Poor response or contraindication to amitriptyline:

- β-blocker, e.g.:
- Propranolol, oral, 40 mg 12 hourly.
  - Titrate dose to adequate response
  - Maximum dose: 120–240 mg daily. *LoE:IIIb[xlviii]*

REFERRAL

Inadequate response to treatment.

14.7.2 CLUSTER HEADACHE

G44.0

DESCRIPTION

Repetitive episodes of excruciating headache typically of short duration (up to 2 hours) in clusters for weeks to months at a time. Typically, the headache is of sudden onset, unilateral during the specific cluster, and quickly reaches a climax. Associated redness of the eye with lacrimation and rhinorrhoea occurs.

MEDICINE TREATMENT

- Oxygen inhalation may abort some episodes. *LoE:IIIb[xlix]*

Analgesics are ineffective.

To induce rapid remission in patients with episodic cluster headache:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5–10 days.
  - Tapering is not necessary when the above duration is used.

LoE:IVb[1]

Prophylaxis

- Verapamil, oral, 40–80 mg 12 hourly.

REFERRAL

Inadequate response to treatment.

14.7.3 TRIGEMINAL NEURALGIA

G50.0

See Section26.1.4: Management of neuropathic pain.

14.7.4 TENSION HEADACHE

G44.2

DESCRIPTION

Tension headaches are described as a tight band around the head and are generally worse in the afternoon. Usually occurs over the back of the head but may extend over the entire head.

GENERAL MEASURES

Consider use of relaxation techniques.
Exclude medication overuse headache (see Section14.5.5: Medication overuse headache).

MEDICINE TREATMENT

- Amitriptyline, oral, 10–75 mg at night.

REFERRAL

» Atypical pain and/or focal neurological signs and symptoms, suggestive of alternate diagnosis.
» Poor response to therapy.

14.7.5 MEDICATION OVERUSE HEADACHE

G44.4

DESCRIPTION

Medication overuse headache generally occurs for ≥ 15 days per month for more than 3 months and develops as a consequence of regular overuse of analgesics for acute pain-relief. The headache develops or markedly worsens during medication overuse, and usually, but not invariably, resolves after the overuse is stopped. LoE:IVb[ii]

GENERAL MEASURES

Stop all analgesics.
Counsel patient regarding the link between overuse of analgesics and the development of and/or worsening of the headache syndrome.
The headache usually resolves after the overuse is stopped but may transiently worsen.

MEDICINE TREATMENT

- Amitriptyline, oral, 10 mg at night. LoE:IIIb[iii]
  - Increase to a maximum of 75 mg at night.
  - May be used during withdrawal of acute or symptomatic headache treatment.

14.7.6 IDIOPATHIC INTRACRANIAL HYPERTENSION (PSEUDOTUMOUR CEREBRI)

G93.2

DESCRIPTION

Patients present with symptoms (chronic headache, visual disturbance or loss due to papilloedema and tinnitus) and signs (papilloedema) of raised intracranial pressure without structural intracranial abnormality and with normal CSF composition.

Diagnosis

All patients should have neuroimaging (CT scan).

» If this is normal, i.e. the absence of structural lesions or hydrocephalus, perform a lumbar puncture and measure intracranial pressure.
» Diagnosis is confirmed by the presence of raised CSF pressure > 20 cm H_20.

GENERAL MEASURES

Stop medicines associated with benign intracranial hypertension (e.g. doxycycline, corticosteroids, combined oral contraceptives).
Regular monitoring of visual fields is crucial.
Weight loss.
Repeated lumbar punctures with measurement of opening pressure (do lumbar puncture with patient in left lateral position).

Consider surgery if there is progression of visual defects, despite medical therapy, visual loss at onset, or severe papilloedema.

MEDICINE TREATMENT

Discuss all cases with a specialist.

For visual involvement, persistent headaches, or severe papilloedema:

- Acetazolamide, oral, 250 mg 12 hourly
  - Increase, as required, by 250 mg daily every week to the maximum tolerated dose (not exceeding 4 g daily).

OR

LoE:IIIb[iii]

- Furosemide, oral, 40 mg daily.

REFERRAL

» For neuro-imaging, if not available locally.
» Visual symptoms or deterioration of visual fields for opthalmology evaluation.
» Patients not responding to therapy or in need of surgical management.

14.8 INFECTIOUS AND PARASITIC CONDITIONS

14.8.1 MENINGITIS

A32.1† + (G01*)/A39.0† + (G01*)/G00.0-3/G00.8-9/G03.0-2/G03.8-9
**N. meningitidis*, *H. influenzae* Type B and listeriosis are notifiable medical conditions.

DIAGNOSIS

Computed tomography should be done before lumbar puncture in patients with:
» focal neurological signs,
» new seizures,
» papilloedema, or
» reduced level of consciousness.

In cases where lumbar puncture is delayed or cannot be done (e.g. uncontrolled significant bleeding tendency), commence empiric antibiotic therapy after taking samples for blood cultures. Attempt the lumbar puncture later, if possible.

GENERAL MEASURES

Observe patient closely with regular monitoring of vital signs and neurological state.
Pay close attention to hydration status.
Nurse patients in a quiet, semi-dark surrounding.
Repeated lumbar punctures are of no benefit in uncomplicated bacterial meningitis.

Prompt initiation of antibiotic therapy is associated with improved outcomes in patients with bacterial meningitis.

MEDICINE TREATMENT

All patients require sufficient analgesia:

- Paracetamol, oral, 500 mg to1 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.
  - May be increased to a maximum daily dose of 400 mg.

Antibiotic therapy

Empiric therapy for bacterial meningitis, until sensitivity results are available:

- Ceftrixone, W IV, 2 g 12 hourly for 10 days.

LoE:IIIb^{iv}

Adjunctive corticosteroids are not recommended as trials in low-middle income countries have not demonstrated benefit.

Meningococcal meningitis A39.0† + (G01*)

For confirmed meningococcal disease only:

- Benzylpenicillin (penicillin G), A IV, 20–24 MU daily in 4–6 divided doses for one week.

AND

Eradicate nasopharyngeal carriage with a single dose of ciprofloxacin 500 mg after completing course of benzylpenicillin. This is not required if the patient received an initial, pre-referral dose of ceftriaxone.

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

Severe penicillin allergy: (Z88.0)

- Meropenem, W IV, 2 g 8 hourly for 7 days.

LoE:IIIb^{iv}

Prophylaxis of contacts:

Only for close household contacts and for healthcare workers who resuscitate patients before they received appropriate treatment.

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

Pneumococcal meningitis G00.1

Conditions causing cerebrospinal fluid (CSF) leaks increase the risk for this type of infection, e.g. skull fractures, congenital defects, neurosurgery.

If sensitive to penicillin:

- Benzylpenicillin (penicillin G), A IV, 20–24 MU daily in 4–6 divided doses for 10 days.

If resistant to penicillin:

- Ceftriaxone, W IV, 2 g 12 hourly for at least 10 days.

Severe penicillin allergy: (Z88.0)

- Meropenem, W IV, 2 g 8 hourly for 10 days.

Note: Consult a microbiologist/infectious diseases specialist.

Haemophilus influenzae G00.0

- Ceftriaxone, W IV, 2 g 12 hourly for 10 days.

Severe penicillin allergy: (Z88.0)

- Meropenem, W IV, 2 g 8 hourly for 10 days.

Note: Consult a microbiologist/infectious diseases specialist.

***Listeria monocytogenes* meningitis** A32.1†

- Ampicillin, A IV, 3 g 6 hourly for 21 days. *LoE:IIIb*[iv]

AND

- Gentamicin, A IV, 5 mg/kg daily for 7 days (may be prolonged if response is poor). See Appendix II for guidance on prescribing.

Severe penicillin allergy: (Z88.0)
Consult a specialist.

REFERRAL

» For neuro-imaging: patients not responding or worsening in condition, i.e. decrease in consciousness and cranial nerve palsies, despite appropriate therapy. This is especially urgent in patients with tuberculous meningitis, who may develop hydrocephalus and require an urgent shunting procedure.
» Patients with shunts.

14.8.1.1 TUBERCULOUS MENINGITIS (TBM)

A17.0† + (G01*)

DIAGNOSIS

CSF findings are extremely variable. Generally, lymphocytes predominate, however, polymorphs predominate initially in about a third of patients.
Protein is usually > 1 g/L and glucose is usually low.

In cases where the differential diagnosis between bacterial and tuberculous meningitis is in doubt, lumbar puncture should be repeated 2–3 days later

while still on ceftriaxone. If the aetiology is bacterial, considerable improvement in CSF findings may be expected, but with untreated tuberculous meningitis, the cell counts and protein levels will be the same or higher as the original CSF findings; and the glucose level will be the same or lower.

MEDICINE TREATMENT

Treat with standard combination tuberculosis therapy according to National protocol and extend duration of therapy to 9 months (2 months intensive phase, 7 months continuation phase). See Section16.9: Tuberculosis, Pulmonary for details.

In HIV-negative individuals:
Corticosteroid use may be of benefit in reducing neurological deficit in patients with grade II to III disease (focal neurological disease, depressed levels of consciousness, or a Glasgow Coma Scale of 14 or less).

- Dexamethasone, IV, dosing as follows:

Weeks	Dosing regimen
Initial dose	0.3-0.4 mg/kg/day for 2 weeks.
Week 3	0.2 mg/kg daily.
Week 4	0.1 mg/kg daily.
Week 5 to 8	4 mg/day, tapering daily dose by 1 mg each week.

OR

- Corticosteroids (intermediate-acting) e.g.: *LoE:IIa*[lvii]
- Prednisone, oral, 60 mg daily for 2 weeks.
  - Then taper gradually over the next 6 weeks (see Appendix II for an example of a dose reduction regimen). *LoE:IVb*[lviii]

In people with HIV: *LoE:IIa*[lix]
Note: There is uncertainty whether the use of corticosteroids is beneficial in PLWH with TBM. *LoE:IIa*[lx]

14.8.1.2 CRYPTOCOCCAL MENINGITIS

GENERAL MEASURES

People living with HIV (see Section10.2.4: Cryptococcosis)
» In PWH the aim is to suppress the infection until immune restoration occurs with antiretroviral therapy.

HIV-negative patients
» In HIV-negative patients the aim is to cure the infection.

14.8.1.2.1 CRYPTOCOCCAL MENINGITIS, HIV-INFECTED

See Section10.2.4: Cryptococcosis.

14.8.1.2.2 CRYPTOCOCCAL MENINGITIS, HIV-NEGATIVE

B45.1 + (G02.1*)

MEDICINE TREATMENT

Initial therapy:

LoE:IIIb[lxi]

- Amphotericin B, IV, 1 mg/kg daily.
  - Ensure adequate hydration to minimise nephrotoxicity (See Appendix II for preventing, monitoring, and management of toxicity).
  - Duration of initial IV therapy:
    - Treat intravenously for 4 weeks, provided that there are no neurological complications and follow up CSF culture at 2 weeks is negative.
    - In patients with neurological complications or persistent positive culture: increase the initial phase of therapy to 6 weeks in consultation with a specialist.

AND

LoE:IIb[lxii]

- Fluconazole, oral, 800 mg daily for 2 weeks, followed by 400 mg daily for 2 months.

Maintenance therapy:

- Fluconazole, oral, 200 mg daily for a minimum of 1 year.

Follow all patients closely for relapses.

LoE:IVb[lxiii]

Therapeutic lumbar puncture:

This should be considered as the intracranial pressure is often elevated with a communicating hydrocephalus. See Section10.2.4: Cryptococcosis.

14.8.2 VIRAL MENINGOENCEPHALITIS

A86/B00.4† + (G05.1*)

DESCRIPTION

Patients present with headache, neck stiffness, and encephalitic symptoms which may include fever, personality or behavioural changes, hallucinations and seizures. Lumbar puncture typically shows mildly elevated protein, normal glucose and mild pleocytosis (< 500), mainly lymphocytes (early on polymorphs may predominate). Treatment for herpes simplex encephalitis should be commenced in all patients until this has been excluded (see below).

MEDICINE TREATMENT

Analgesia:

- Paracetamol, oral, 500 mg to1 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 immediately then 8 hourly with meals, if needed.

LoE:IVb[lxiv]

OR

- Morphine, IV, to a total maximum dose of 10 mg (see Appendix II, for individual dosing and monitoring for response and toxicity).

Herpes simplex encephalitis

Clinical features are fever, change in behaviour and seizures, which may be either focal or generalised.

Evidence of mucocutaneous involvement is usually not present. Lumbar puncture shows the above features of viral meningoencephalitis. Evidence of encephalitis involving medial temporal lobe region on MRI/CT neuro-imaging or on EEG is strongly supportive of the diagnosis and positive HSV PCR test on CSF is diagnostic.

- Aciclovir, IV, 10 mg/kg 8 hourly for 14 days (21 days in immunocompromised patients).
  - Start therapy as early as possible, i.e. before results are available.
  - A negative herpes PCR usually excludes the diagnosis unless the specimen was taken within 72 hours of onset of symptoms, when false negatives have been described.

Treat seizures appropriately, see Section14.6: Epilepsy. *LoE:IIa*[lxv]

All suspected cases of herpes encephalitis should be discussed with a specialist.

REFERRAL

» For neuro-imaging: patients not responding or worsening in condition, i.e. decrease in consciousness and cranial nerve palsies, despite appropriate therapy.
» Patients with shunts.

14.8.3 MENINGOVASCULAR SYPHILIS (NEUROSYPHILIS)

A52.1 + (G01*)

DIAGNOSIS

Lumbar puncture typically shows lymphocytosis with mildly elevated protein and low/normal glucose.
Serum syphilis serology: a negative TPHA or FTA excludes the diagnosis; RPR may be negative in some cases.
CSF syphilis serology: a CSF VDRL positive result is highly specific for neurosyphilis but may be negative in approximately 50%. A negative CSF FTA-ABS excludes the diagnosis of neurosyphilis.

MEDICINE TREATMENT

- Benzylpenicillin (penicillin G), A IV, 20 MU daily in 4–6 divided doses for 10 days.

LoE:IVb

A serum RPR response (4-fold decline in titre) after 6 months is predictive of treatment success for neurosyphilis.

LoE:IIIb[ixvi]

Severe penicillin allergy: (Z88.0)
Refer for consideration of desensitisation and subsequent treatment with benzylpenicillin at a referral centre.

14.8.4 BRAIN ABSCESS

G06.0

DIAGNOSIS

Patient may present with focal neurological signs and signs of infection. Neurological signs may not always be prominent. Neuro-imaging usually confirms diagnosis. Patients may have concomitant infection of ears, paranasal sinuses or lower respiratory tract.

MEDICINE TREATMENT

Empiric antibiotic therapy

- Ceftriaxone, W IV, 2 g 12 hourly.

AND

- Metronidazole, A oral, 400 mg 8 hourly **or** IV, 500 mg 8 hourly.

Adjust according to antimicrobial sensitivity after surgical drainage.

REFERRAL
All, as patients require urgent neurosurgery opinion and treatment.

14.8.5 ANTIMICROBIAL USE IN PATIENTS WITH HEAD INJURIES
S02.10-11/ /S06.11/S06.21/S06.31/S06.41/S06.51/S06.61/S06.71/S06.81/S06.91/ S09.9

MEDICINE TREATMENT
Basal skull fractures
Antibiotic prophylaxis is not indicated.

Penetrating brain injuries
Antibiotics are given for therapy.

- Ceftriaxone, (W) IV, 2 g 12 hourly for 7 days. *LoE:IVb*

14.8.6 NEUROCYSTICERCOSIS
B69.0 + (G99.8*)

DIAGNOSIS
Patients may present with seizures and/or focal neurological deficit. Typical cystic lesions are seen on neuroimaging. Old, calcified lesions are inactive and do not require treatment.

GENERAL MEASURES
Health education.
Surgery for treatable ventricular blockage or spinal or intraocular cysts.

MEDICINE TREATMENT
For active or viable cysts only:

- Albendazole, oral, 12 hourly for 8 days.
  - ≥ 60 kg: 400 mg.
  - < 60 kg: 7.5 mg/kg to a maximum of 800 mg daily.

Note: Do not use in pregnancy due to teratogenicity.

LoE:IIb[lxvii]

AND

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 60 mg daily for 8 days. *LoE:IVb[lxviii]*

Anticonvulsants, if required. See Section14.6: Epilepsy. *LoE:IIIb[lxix]*

REFERRAL
Uncontrolled seizures despite antiparasitic and anticonvulsant therapy.

14.9 MOVEMENT DISORDERS

DESCRIPTION
Abnormalities of movement/initiation of movement, divided into those with reduction of movement (hypokinesia or bradykinesia), or those with excessive movements (hyperkinesia).

14.9.1 PARKINSONISM, PRIMARY

14.9.1.1 IDIOPATHIC PARKINSON DISEASE
G20

DESCRIPTION
Parkinsonism is a syndrome characterised by tremor, rigidity, bradykinesia, 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.

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

GENERAL MEASURES
General supportive therapy and advice about lifestyle modification, physiotherapy and occupational therapy.

MEDICINE TREATMENT
Note: Set therapeutic targets so that the patient is functioning as well as possible.

Bradykinesia, rigidity and postural disturbance:
- Carbidopa/levodopa, 25/100 mg (1 tablet), oral, 8 hourly, increase gradually according to clinical response.
  - Maximum dose of 200/800 mg daily (8 tablets).
  - Increase dose in consultation with a specialist.

REFERRAL
» Alternative diagnosis suspected (e.g. secondary Parkinsonism)
» No improvement or poor control with treatment.
» Increasing on/off phenomenon.
» Dyskinesias.

14.9.2 PARKINSONISM, SECONDARY

G21.0-4/G21.8-9/G24.0

DESCRIPTION

Secondary parkinsonism is caused by certain medicines (typical and atypical antipsychotics, anti-emetics, anticonvulsants (phenytoin, valproate) and SSRIs), nervous system disorders, or other systemic illnesses.

GENERAL MEASURES

Primary approach in drug-induced parkinsonism should be to stop the offending medicine if possible.

Refer to psychiatric services for review of antipsychotic treatment in patients requiring treatment for parkinsonism (see Section15.5.2: Schizophrenia spectrum disorders).

MEDICINE TREATMENT

Anticholinergics have a limited role in this setting and should be used with caution.

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50 mg 8 hourly, increase gradually according to clinical response.
  - Usual dose: 150–250 mg daily.
  - Maximum dose: 400 mg daily.

LoE:IVb[lxx]

Note: Anticholinergic side effects are common and may be exacerbated by antipsychotics.

OR

- Carbidopa/levodopa, 25/100 mg (1 tablet), oral, 8 hourly.

Acute dystonic reaction: G24.0

Usually follows administration of dopamine-antagonistic drug, e.g. metoclopramide and phenothiazines.

- Anticholinergic agent, e.g.:
- Biperiden, IM/IV, 2 mg.
  - Repeat as necessary.

OR

- Promethazine, deep IM, 25–50 mg.
  - Decrease dose in the elderly to 25 mg.

LoE:IVb

14.9.3 ESSENTIAL TREMOR

G25.0

GENERAL MEASURES

Exclude and manage alternate causes, such as drugs, thyrotoxicosis and hyperadrenergic states. Occasionally a patient may present with essential

tremor and an additional neurological condition, which may make the diagnosis difficult.

MEDICINE TREATMENT

If tremor is severe and interfering with normal daily activity:

- Propranolol, oral,
  - Start at 20 mg daily and titrate as needed up to 80 mg 8 hourly.
  - Monitor for symptomatic bradycardia and/or hypotension. *LoE:IIIb*[lxxi]

14.9.4 CHOREA

G25.5

DESCRIPTION

Chorea is a hyperkinetic movement disorder characterized by involuntary brief, random, and irregular contractions conveying a feeling of restlessness to the observer. Chorea may be caused by hereditary neurodegenerative diseases; structural damage to deep brain structures; or be associated with autoimmune disorders, metabolic derangement, or certain drugs and hormones.

Aetiology is classified as:

» Rarer primary (idopathic or hereditary) – Huntington's chorea,; or
» More common secondary (acquired) – Sydenham's chorea, hemiballismus secondary to infarction, diabetes (hyperglycemia).

Symptoms include involuntary, random, irregular movements.

GENERAL MEASURES

Exclude potential underlying causes initially.
A careful history should include age of onset, time course (acute or insidious), past medical history, history of recent infection with group A beta-haemolytic streptococcus (GABHS), family history, and drug exposure.
Neuroimaging should be performed for new-onset cases, especially when asymmetric.
A variety of laboratory tests may be useful depending on the clinical context.

MEDICINE TREATMENT

Treat the underlying cause, if relevant.

First-generation antipsychotic agents (typical neuroleptics) may reduce chorea although there is little evidence to support their efficacy, and they are increasingly avoided due to increased risk of side effects.

- Haloperidol, oral, 0.75–5 mg 8–12 hourly. (Specialist consultation.)

REFERRAL
The need to refer may be based on the underlying cause and diagnostic workup.
Refer primary choreas for genetic counselling.

LoE:IVb

14.10 NEUROPATHY
See Section26.1.4: Management of neuropathic pain.

14.11 MYELOPATHY, ACUTE
G95.9

DESCRIPTION
Patients present with a sudden onset of paraparesis, with associated sensory loss, i.e. a sensory level may be found. Incontinence and autonomic instability may be present.

GENERAL MEASURES
Do cervical and thoracic spine films, with chest X-ray to exclude obstructive lesions before performing a lumbar puncture.

REFERRAL
All patients for urgent imaging.

14.12 MULTIPLE SCLEROSIS
G35

DESCRIPTION
A demyelinating disease of the central nervous system, characterised by relapsing and remitting episodes of unifocal or multifocal neurological dysfunction. Diagnosis is confirmed by imaging. The CSF may show oligoclonal bands and raised IgG index.
Recovery between acute flares of illness is common, although a general stepwise deterioration from baseline is usually found.

GENERAL MEASURES
Consult with neurologist for diagnosis and treatment.

REFERRAL
All patients.

14.13 MYASTHENIA GRAVIS

G70.0

DESCRIPTION

Myasthenia gravis is an autoimmune neuromuscular disorder characterised by fluctuating motor weakness involving ocular, bulbar, limb, and/or respiratory muscles.

The weakness is due to an antibody-mediated, immunologic attack directed at proteins in the postsynaptic membrane of the neuromuscular junction (acetylcholine receptors or receptor-associated proteins).

Consider this in patients with new onset weakness and fatiguability, particularly involving muscles of the eyes and those involved in swallowing.

MEDICINE TREATMENT

Discuss both diagnosis and treatment with a specialist.

- Pyridostigmine, oral, 60 mg 5 times daily.

LoE:IVb[lxxii]

Corticosteroids and azathioprine should only be used in consultation with a specialist.

14.14 OEDEMA, CEREBRAL

DESCRIPTION

Swelling of brain parenchymal tissue, due to vasogenic, cytotoxic and osmotic causes. Only the vasogenic causes, such as brain tumours and inflammation, respond to corticosteroids.

14.14.1 BRAIN OEDEMA DUE TO TUMOURS AND INFLAMMATION

G93.6

GENERAL MEASURES

Supportive management. See Section14.1.1: Stroke.

Treat the underlying cause. This is especially important where brain oedema is associated with systemic conditions, such as electrolyte disturbances and organ failure.

Patients with primary brain tumours or brain metastases should be considered for definitive treatment of the tumour, which includes surgery and/or radiotherapy.

MEDICINE TREATMENT

- Dexamethasone, IV, 4 mg 6 hourly, initially.

OR

- Betamethasone, oral/IV, 4 mg 6 hourly.
  - Discontinue if no response has occurred after 48 hours.
  - Taper dose according to response and duration of therapy.

14.14.2 BRAIN OEDEMA DUE TO TRAUMATIC INJURY

S06.10-11 + External Cause Code (V,W,X,Y)

GENERAL MEASURES

Refer patient for neurosurgical opinion, if indicated.
Supportive management. See Section14.1.1: Stroke.
Note: DVT prophylaxis with heparin may be contraindicated due to increased risk of bleeding.

The following measures should be used in patients with raised intracranial pressure:

» head elevation and position,
» airway and ventilation control,
» sedation and analgesia,
» control of fever,
» control of hypertension, and
» prevention of seizures.

Currently, no evidence supports the use of hyperventilation in this setting.

MEDICINE TREATMENT

For raised intracranial pressure, pending a definitive neurosurgical procedure only:

- Mannitol 15–25%, IV, 0.25–1 g/kg administered over 30–60 minutes.
  - Monitor neurological response and urine output.
  - Beware of hypovolaemia and electrolyte disturbances, especially hypokalaemia.

Note: Corticosteroids should not be used in this setting as they have a harmful effect.

14.15 SPINAL CORD INJURY, ACUTE

T09.3

GENERAL MEASURES

There is insufficient evidence for the use of high dose corticosteroids in this clinical setting.

For symptomatic management of:

» Constipation – see Section24.1.2: Constipation.
» Urinary retention – see Section7.3.6: Overactive bladder.
» High risk of pressure sores – See Primary Health Care STG & EML, Section5.19: Pressure ulcers/ sores.
» Spasticity – refer patients for multi-disciplinary rehabilitation.

REFERRAL

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

References:

[i] Tissue plasminogen activator: Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al.; Stroke Thrombolysis Trialists' Collaborative Group. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014 Nov 29;384(9958):1929-35. https://www.ncbi.nlm.nih.gov/pubmed/25106063

Tissue plasminogen activator: Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischaemic stroke. Cochrane Database Syst Rev. 2014 Jul 29;(7):CD000213. https://www.ncbi.nlm.nih.gov/pubmed/25072528

Tissue plasminogen activator: Alteplase (window period 3 hours versus 4.5 hours): National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Alteplase – Window period for treating hyper acute ischaemic stroke, February 2018. http://www.health.gov.za/

Tissue plasminogen activator: National Department of Health. Essential Drugs Programme - Tertiary and Quaternary EML, December 2019. http://www.health.gov.za/

Tissue plasminogen activator (Alteplase, IV – window period): National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Alteplase for hyper acute ischaemic stroke, January 2018. http://www.health.gov.za/

Tissue plasminogen activator (Alteplase, IV – window period): Emberson J, Lees KR, Lyden P, Blackwell L, Albers G, Bluhmki E, et al.; Stroke Thrombolysis Trialists' Collaborative Group. Effect of treatment delay, age, and stroke severity on the effects of intravenous thrombolysis with alteplase for acute ischaemic stroke: a meta-analysis of individual patient data from randomised trials. Lancet. 2014 Nov 29;384(9958):1929-35 https://www.ncbi.nlm.nih.gov/pubmed/25106063

Tissue plasminogen activator: Nicola Logallo, Vojtech Novotny, Jörg Assmus, Christopher E Kvistad, Lars Alteheld, Ole Morten Rønning, Bente Thommessen,Karl-Friedrich Amthor, Hege Ihle-Hansen, Martin Kurz, Håkon Tobro, Kamaljit Kaur, Magdalena Stankiewicz, Maria Carlsson, Åse Morsund,Titto Idicula, Anne Hege Aamodt, Christian Lund, Halvor Næss, Ulrike Waje-Andreassen, Lars Thomassen. Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial. Lancet Neurology 2017; 16: 781–88. https://www.ncbi.nlm.nih.gov/pubmed/28780236

Tissue plasminogen activator; Alteplase IV: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[ii] Aspirin, oral (acute stroke): Sandercock PA, Counsell C, Tseng MC, Cecconi E. Oral antiplatelet therapy for acute ischaemic stroke. Cochrane Database Syst Rev. 2014 Mar 26;(3):CD000029. https://www.ncbi.nlm.nih.gov/pubmed/24668137

Aspirin, oral (acute stroke): Rothwell PM, Algra A, Chen Z, Diener HC, Norrving B, Mehta Z. Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: time-course analysis of randomised trials. Lancet. 2016 Jul 23;388(10042):365-375. https://www.ncbi.nlm.nih.gov/pubmed/27209146

[iii] Aspirin: Sandercock PA, Counsell C, Tseng MC, Cecconi E. Oral antiplatelet therapy for acute ischaemic stroke. Cochrane Database Syst Rev. 2014 Mar 26;3:CD000029.http://www.ncbi.nlm.nih.gov/pubmed/24668137

[iv] Simvastatin 40 mg, oral (secondary prevention of ischaemic events): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. www.health.gov.za/

Simvastatin 40 mg, oral (secondary prevention of ischaemic events): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Simvastatin 40 mg, oral (secondary prevention of ischaemic events): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Simvastatin 40 mg, oral (secondary prevention of ischaemic events): Contract circular HP09-2016SD. http://www.health.gov.za/

[v] Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Chastain DB, Stover KR, Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. J Clin Transl Endocrinol. 2017 Feb 22;8:6-14. https://www.ncbi.nlm.nih.gov/pubmed/29067253

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. www.health.gov.za/

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of

256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Contract circular HP09-2016SD. http://www.health.gov.za/

Atorvastatin, oral (drug-drug interaction with protease inhibitors): University of Liverpool. HIV drug interaction database. https://www.hiv-druginteractions.org/

[vi] Simvastatin 40 mg, oral (amlodipine drug interaction): Lexicomp: Drug Interactions database. [Accessed 7 February 2018] Available at: https://www.uptodate.com/drug-interactions

[vii] High dose statins (management of adverse drug reactions): NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181

[viii] Warfarin: Lansberg MG, O'Donnell MJ, Khatri P, Lang ES, Nguyen-Huynh MN, Schwartz NE, Sonnenberg FA, Schulman S, Vandvik PO, Spencer FA, Alonso-Coello P, Guyatt GH, Akl EA; American College of Chest Physicians. Antithrombotic and thrombolytic therapy for ischemic stroke: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012 Feb;141(2 Suppl):e601S-36S. http://www.ncbi.nlm.nih.gov/pubmed/22315273

[ix] Blood pressure management (acute stroke): Bath PM, Krishnan K. Interventions for deliberately altering blood pressure in acute stroke. Cochrane Database Syst Rev. 2014 Oct 28;(10):CD000039. https://www.ncbi.nlm.nih.gov/pubmed/25353321

[x] Long-acting calcium channel blocker/Thiazide diuretic: Bath PM, Krishnan K. Interventions for deliberately altering blood pressure in acute stroke. Cochrane Database Syst Rev. 2014 Oct 28;10:CD000039. http://www.ncbi.nlm.nih.gov/pubmed/25353321

Long-acting calcium channel blocker/Thiazide diuretic: He J, Zhang Y, Xu T, Zhao Q, Wang D, Chen CS, Tong W, Liu C, Xu T, Ju Z, Peng Y, Peng H, Li Q, Geng D, Zhang J, Li D, Zhang F, Guo L, Sun Y, Wang X, Cui Y, Li Y, Ma D, Yang G, Gao Y, Yuan X, Bazzano LA, Chen J; CATIS Investigators. Effects of immediate blood pressure reduction on death and major disability in patients with acute ischemic stroke: the CATIS randomized clinical trial. JAMA. 2014 Feb 5;311(5):479-89. http://www.ncbi.nlm.nih.gov/pubmed/24240777

[xi] Early BP Lowering (within 7 days of stroke onset): Wang H, Tang Y, Rong X, Li H, Pan R, Wang Y, Peng Y. Effects of early blood pressure lowering on early and long-term outcomes after acute stroke: an updated meta-analysis. PLoS One. 2014 May 22;9(5):e97917. https://www.ncbi.nlm.nih.gov/pubmed/24853087

[xii] Blood pressure management (24 hours after acute stroke): Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. American Heart Association Stroke Council. 2018 Guidelines for the Early Management of Patients With Acute Ischemic Stroke: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. Stroke. 2018 Mar;49(3):e46-e110. https://www.ncbi.nlm.nih.gov/pubmed/29367334

[xiii] Warfarin: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[xiv] Aspirin: Thijs V, Lemmens R, Fieuws S. Network meta-analysis: simultaneous meta-analysis of common antiplatelet regimens after transient ischaemic attack or stroke. Eur Heart J. 2008 May;29(9):1086-92.http://www.ncbi.nlm.nih.gov/pubmed/18349026

[xv] Simvastatin 40 mg, oral (secondary prevention of ischaemic events): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. www.health.gov.za/

Simvastatin 40 mg, oral (secondary prevention of ischaemic events): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Simvastatin 40 mg, oral (secondary prevention of ischaemic events): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Simvastatin 40 mg, oral (secondary prevention of ischaemic events): Contract circular HP09-2016SD. http://www.health.gov.za/

[xvi] Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Chastain DB, Stover KR, Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. J Clin Transl Endocrinol. 2017 Feb 22;8:6-14. https://www.ncbi.nlm.nih.gov/pubmed/29067253

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): National Department of Health. Affordable Medicines, EDP-Primary Health Care. Cost-effectiveness analysis of high, intermediate, and low dose statins for the secondary prevention of cardiovascular disease, 31 January 2018. www.health.gov.za/

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170 000 participants in 26 randomised trials. The Lancet 2010; 376(9753): 1670-81. https://www.ncbi.nlm.nih.gov/pubmed/21067804

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Naci H, Brugts JJ, Fleurence R, Ades A. Dose-comparative effects of different statins on serum lipid levels: a network meta-analysis of 256,827 individuals in 181 randomized controlled trials. European journal of preventive cardiology 2013; 20(4): 658-70. https://www.ncbi.nlm.nih.gov/pubmed/23529608

Atorvastatin 10 mg, oral (secondary prevention of ischaemic events – patients on protease inhibitors): Contract circular HP09-2016SD. http://www.health.gov.za/

Atorvastatin, oral (drug-drug interaction with protease inhibitors): University of Liverpool. HIV drug interaction database. https://www.hiv-druginteractions.org/

[xvii] Simvastatin 40 mg, oral (amlodipine drug interaction): Lexicomp: Drug Interactions database. [Accessed 7 February 2018] Available at: https://www.uptodate.com/drug-interactions

[xviii] High dose statins (management of adverse drug reactions): NICE: Cardiovascular disease: risk assessment and reduction, including lipid modification. Clinical guideline, 18 July 2014. www.nice.org.uk/guidance/cg181

[xix] Haloperidol (risk in dementia): Ma H, Huang Y, Cong Z, Wang Y, Jiang W, Gao S, Zhu G. The efficacy and safety of atypical antipsychotics for the treatment of dementia: a meta-analysis of randomized placebo-controlled trials. J Alzheimers Dis. 2014;42(3):915-37. https://www.ncbi.nlm.nih.gov/pubmed/25024323

Haloperidol (risk in dementia): National Institute for Health and Clinical Excellence. Guideline - Dementia: assessment, management and support for people living with dementia and their carers, 20 June 2018. https://www.nice.org.uk/guidance/ng97

Haloperidol (risk in dementia): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[xx] Thiamine oral/IM: Day E, Bentham PW, Callaghan R, Kuruvilla T, George S. Thiamine for prevention and treatment of Wernicke-Korsakoff Syndrome in people who abuse alcohol. Cochrane Database Syst Rev. 2013 Jul 1;7:CD004033. http://www.ncbi.nlm.nih.gov/pubmed/23818100

Thiamine oral/IM: National Department of Health, Essential Drugs Programme: Primary Health Care STGs and EML, 2018. http://www.health.gov.za/

[xxi] Epileptic Seizure (Definition): International League Against Epilepsy. Diagnostic Manual of the epilepsies. Epigraph Vol. 18 Issue 2, Fall 2016. https://www.epilepsydiagnosis.org

[xxii] Epileptic Seizure (Definition): International League Against Epilepsy. Epilepsy Imitators. https://www.epilepsydiagnosis.org/epilepsy-imitators.html

[xxiii] Epileptic Seizure (Definition): International League Against Epilepsy. Diagnostic Manual of the epilepsies. Epigraph Vol. 18 Issue 2, Fall 2016. https://www.epilepsydiagnosis.org

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.

[xxiv] Epileptic Seizure (Definition): 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.

[xxv] Epileptic Seizure (Definition): International League Against Epilepsy. Diagnostic Manual of the epilepsies. Epigraph Vol. 18 Issue 2, Fall 2016. https://www.epilepsydiagnosis.org

[xxvi] Valproate – caution in pregnancy: European Medicines Agency - Pharmacovigilance Risk Assessment Committee. Assessment report EMA/198940/2018 - valproate exposure in pregnancy, 8 February 2018. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Valproate_2017_31/Position_provided_by_CMDh/WC500250221.pdf

Valproate – caution in pregnancy: Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. Pregnancy outcomes in women with epilepsy: a systematic review and meta-analysis of published pregnancy registries and cohorts. Epilepsy Res. 2008 Sep;81(1):1-13. https://www.ncbi.nlm.nih.gov/pubmed/18565732

[xxvii] Epileptic Seizure (Recovery Position): Ausmed Adult Basic Life Support. https://www.ausmed.com/learn/articles/basic-life-support

[xxviii] Lorazepam IV/IM (status epilepticus): Prasad M, Krishnan PR, Sequeira R, Al-Roomi K. Anticonvulsant therapy for 2014 Sep 10;(9):CD003723. https://www.ncbi.nlm.nih.gov/pubmed/25207925

Lorazepam, IV/IM (status epilepticus): NICE. Epilepsies: diagnosis and management: Clinical guideline [CG137], published January 2012 and updated February 2016. https://www.nice.org.uk/guidance/cg137

Lorazepam, IV/IM (Rate of adminisration): University of Cape Town, Faculty of Health Sciences, Division of Clinical Pharmacology. (2024). South African Medicines Formulary (SAMF). SAMF website. https://samf-app.com

[xxix] Midazolam IM/IV: Silbergleit R, Durkalski V, Lowenstein D, Conwit R, Pancioli A, Palesch Y, Barsan W; NETT Investigators. Intramuscular versus intravenous therapy for prehospital status epilepticus. N Engl J Med. 2012 Feb 16;366(7):591-600. http://www.ncbi.nlm.nih.gov/pubmed/22335736

Midazolam IM/IV: NICE. Epilepsies: diagnosis and management: Clinical guideline [CG137], published January 2012 and updated February 2016. https://www.nice.org.uk/guidance/cg137

NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

[xxx] Diazepam IV (status epilepticus): Prasad M, Krishnan PR, Sequeira R, Al-Roomi K. Anticonvulsant therapy for 2014 Sep 10;(9):CD003723. https://www.ncbi.nlm.nih.gov/pubmed/25207925
Diazepam, IV (status epilepticus): NICE. Epilepsies: diagnosis and management: Clinical guideline [CG137], published January 2012 and updated February 2016. https://www.nice.org.uk/guidance/cg137
NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

[xxxi] Clonazepam IV (status epilepticus): Alvarez V, Lee JW, Drislane FW, Westover MB, Novy J, Dworetzky BA, Rossetti AO. Practice variability and efficacy of clonazepam, lorazepam, and midazolam in status epilepticus: A multicenter comparison. Epilepsia. 2015 Aug;56(8):1275-85. https://www.ncbi.nlm.nih.gov/pubmed/26140660
NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

[xxxii] Clonazepam (IM): D'Anto J, Beuchat I, Rossetti AO, Novy J. Clonazepam Loading Dose in Status Epilepticus: Is More Always Better? CNS Drugs. 2023 Jun;37(6):523-529. doi: 10.1007/s40263-023-01012-9. Epub 2023 Jun 8. PMID: 37291410; PMCID: PMC10276784.
NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

[xxxiii] Diazepam (Rectal): Glauser T, Shinnar S, Gloss D, Alldredge B, Arya R, Bainbridge J, Bare M, Bleck T, Dodson WE, Garrity L, Jagoda A, Lowenstein D, Pellock J, Riviello J, Sloan E, Treiman DM. Evidence-Based Guideline: Treatment of Convulsive Status Epilepticus in Children and Adults: Report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr. 2016 Jan-Feb;16(1):48-61. doi: 10.5698/1535-7597-16.1.48. PMID: 26900382; PMCID: PMC4749120.
Diazepam (Rectal): NICE. Epilepsies: diagnosis and management: Clinical guideline [CG137], published January 2012 and updated February 2016. https://www.nice.org.uk/guidance/cg137

[xxxiv] Phenytoin (avoid in poisoning): Shah AS, Eddleston M. Should phenytoin or barbiturates be used as second-line anticonvulsant therapy for toxicological seizures? Clin Toxicol (Phila). 2010 Oct;48(8):800-5. https://www.ncbi.nlm.nih.gov/pubmed/20923393
Phenytoin (avoid in poisoning): Chen HY, Albertson TE, Olson KR. Treatment of drug-induced seizures. Br J Clin Pharmacol. 2016 Mar;81(3):412-9. https://www.ncbi.nlm.nih.gov/pubmed/26174744

[xxxv] Levetiracetam (NGT): White R, Bradnam V. Handbook of Drug Administration via Enteral Feeding Tubes. Pharmaceutical Press. 2007

[xxxvi] Propofol, IV: Prabhakar H, Bindra A, Singh GP, Kalaivani M. Propofol versus thiopental sodium for the treatment of refractory status epilepticus. Cochrane Database Syst Rev. 2012 Aug 15;8:CD009202. http://www.ncbi.nlm.nih.gov/pubmed/22895985
Propofol, IV: NICE Clinical Guideline 137. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. Issued Jan 2012; modified Jan 2015. http://guidance.nice.org.uk/cg137

[xxxvii] Midazolam, IV: NICE Clinical Guideline 137. The epilepsies: the diagnosis and management of the epilepsies in adults and children in primary and secondary care. Issued Jan 2012; modified Jan 2015. http://guidance.nice.org.uk/cg137

[xxxviii] Epilepsy (Classification): 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

[xxxix] Risk of congenital structural malformations and neurodevelopment harms: Pennell PB. Neurotherapeutics. 2016 and Medicines & Healthcare products Regulatory Agency safety leaflet).

[xl] Valproate – caution in pregnancy: European Medicines Agency - Pharmacovigilance Risk Assessment Committee. Assessment report EMA/198940/2018 - valproate exposure in pregnancy, 8 February 2018. http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Valproate_2017_31/Position_provided_by_CMDh/WC500250221.pdf
Valproate – caution in pregnancy: Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. Pregnancy outcomes in women with epilepsy: a systematic review and meta-analysis of published pregnancy registries and cohorts. Epilepsy Res. 2008 Sep;81(1):1-13. https://www.ncbi.nlm.nih.gov/pubmed/18565732

[xli] Anti-epileptic drug-drug interactions: National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, 2019. http://www.health.gov.za/

[xlii] Epilepsy (Medicine Treatment): NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

[xliii] Lamotrigine, oral (dose titration): University of Cape Town, Faculty of Health Sciences, Division of Clinical Pharmacology. (2024). South African Medicines Formulary (SAMF). SAMF website. https://samf-app.com
Lamotrigine, oral (dose titration): South African Health Product Regulatory Authority. Approved Professional Information Package. Lamotrigine. Available at https://pi-pil-repository.sahpra.org.za/wp-content/uploads/2025/02/PI-Approved-Lamilepsy-31012025.pdf
Lamotrigine, oral (dose titration): Western Cape Department of Health. Lamotrigine dose titration protocol. 2019.

[xliv] Lamotrigine, drug-drug interactions with ART (adults): National Department of Health, Essential Drugs Programme: Adult Hospital Level STGs and EML, 2019. http://www.health.gov.za/
Lamotrigine, drug-drug interactions with ART (adults): National Department of Health. 2019 ART Clinical Guidelines for the Management of HIV in Adults, Pregnancy, Adolescents, Children, Infants and Neonates. https://www.knowledgehub.org.za/elibrary/2019-art-clinical-guidelines-management-hiv-adults-pregnancy-adolescents-children-infants

[xlv] Carbamazepine, oral: Gigli GL, Placidi F, Diomedi M, Maschio M, Silvestri G, Scalise A, Marciani MG. Nocturnal sleep and daytime somnolence in untreated patients with temporal lobe epilepsy: changes after treatment with controlled-release carbamazepine. Epilepsia. 1997 Jun;38(6):696-701. http://www.ncbi.nlm.nih.gov/pubmed/9186252

[xlvi] Migraine prophylaxis indications: Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000 Sep 26;55(6):754-62. Erratum in: Neurology 2000 Jan 9;56(1):142. https://www.ncbi.nlm.nih.gov/pubmed/10993991

[xlvii] Amitriptyline, oral (migraine prophylaxis): National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Migraine prophylaxis, June 2018. http://www.health.gov.za/
Amitriptyline, oral (dose for migraine prophylaxis): Couch JR; Amitriptyline Versus Placebo Study Group. Amitriptyline in the prophylactic treatment of migraine and chronic daily headache. Headache. 2011 Jan;51(1):33-51. https://www.ncbi.nlm.nih.gov/pubmed/21070231
Amitriptyline, oral (dose for migraine prophylaxis): Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. Headache. 2012 Jun;52(6):930-45. https://www.ncbi.nlm.nih.gov/pubmed/22671714

[xlviii] Beta-blocker (migraine prophylaxis): National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Migraine prophylaxis, June 2018. http://www.health.gov.za/
Beta-blocker (migraine prophylaxis): Jackson JL, Cogbill E, Santana-Davila R, Eldredge C, Collier W, Gradall A, et al. A Comparative Effectiveness Meta-Analysis of Drugs for the Prophylaxis of Migraine Headache. PLoS ONE 2015;10(7):1-60. https://www.ncbi.nlm.nih.gov/pubmed/26172390

[xlix] Oxygen: Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016 Jul;56(7):1093-106. doi: 10.1111/head.12866. PMID: 27432623.

[l] Corticosteroids, oral (Therapeutic group): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[li] Medication overuse headache (classification): Headache Classification Committee of the International Headache Society (IHS).The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia. 2013 Jul;33(9):629-808. https://www.ncbi.nlm.nih.gov/pubmed/23771276

[lii] Amitriptyline, oral: Descombes S, Brefel-Courbon C, Thalamas C, Albucher JF, Rascol O, Montastruc JL, Senard JM. Amitriptyline treatment in chronic drug-induced headache: a double-blind comparative pilot study. Headache. 2001 Feb;41(2):178-82. https://www.ncbi.nlm.nih.gov/pubmed/11251703

[liii] Acetazolamide oral: Piper RJ, Kalyvas AV, Young AM, Hughes MA, Jamjoom AA, Fouyas IP. Interventions for idiopathic intracranial hypertension. Cochrane Database Syst Rev. 2015 Aug 7;(8):CD003434. https://www.ncbi.nlm.nih.gov/pubmed/26250102
Acetazolamide, oral: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.
NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee; Wall M, McDermott MP, Kieburtz KD, Corbett JJ, Feldon SE, Friedman DI, Katz DM, Keltner JL, Schron EB, Kupersmith MJ. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. JAMA. 2014 Apr 23-30;311(16):1641-51. doi: 10.1001/jama.2014.3312. PMID: 24756514; PMCID: PMC4362615.
ten Hove MW, Friedman DI, Patel AD, Irrcher I, Wall M, McDermott MP; NORDIC Idiopathic Intracranial Hypertension Study Group. Safety and Tolerability of Acetazolamide in the Idiopathic Intracranial Hypertension Treatment Trial. J Neuroophthalmol. 2016 Mar;36(1):13-9. doi: 10.1097/WNO.0000000000000322. PMID: 26587993.

[liv] Empiric antibiotic therapy:Proulx N, Fréchette D, Toye B, Chan J, Kravcik S. Delays in the administration of antibiotics are associated with mortality from adult acute bacterial meningitis. *QJM.* 2005 Apr;98(4):291-8. http://www.ncbi.nlm.nih.gov/pubmed/15760921
Empiric antibiotic therapy: Koster-Rasmussen R, Korshin A, Meyer CN. Antibiotic treatment delay and outcome in acute bacterial meningitis. J Infect. 2008 Dec;57(6):449-54. http://www.ncbi.nlm.nih.gov/pubmed/19000639

[lv] Meropenem, IV (severe penicillin allergy - bacterial meningitis): Gaeta F, Valluzzi RL, Alonzi C, Maggioletti M, Caruso C, Romano A. Tolerability of aztreonam and carbapenems in patients with IgE-mediated hypersensitivity to penicillins. J Allergy Clin Immunol. 2015 Apr;135(4):972-6. https://www.ncbi.nlm.nih.gov/pubmed/25457154

[lvi] Ampicillin, IV + gentamicin, IV (Listeriosis meningitis): Charlier C, Perrodeau É, Leclercq A, Cazenave B, Pilmis B, Henry B, Lopes A, Maury MM, Moura A, Goffinet F, Dieye HB, Thouvenot P, Ungeheuer MN, Tourdjman M, Goulet V,

de Valk H, Lortholary O, Ravaud P, Lecuit M; MONALISA study group. Clinical features and prognostic factors of listeriosis: the MONALISA national prospective cohort study. Lancet Infect Dis. 2017 May;17(5):510-519. https://www.ncbi.nlm.nih.gov/pubmed/28139432

Ampicillin, IV + gentamicin, IV (Listeriosis meningitis): Thønnings S, Knudsen JD, Schønheyder HC, Søgaard M, Arpi M, Gradel KO, Østergaard C; Danish Collaborative Bacteraemia Network (DACOBAN). Antibiotic treatment and mortality in patients with Listeria monocytogenes meningitis or bacteraemia. Clin Microbiol Infect. 2016 Aug;22(8):725-30. https://www.ncbi.nlm.nih.gov/pubmed/27345176

[lvii] Dexamethasone, IV : Prasad K, Singh MB. Corticosteroids for managing tuberculous meningitis. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD002244. http://www.ncbi.nlm.nih.gov/pubmed/18254003

Dexamethasone, IV: Thwaites GE, Nguyen DB, Nguyen HD, Hoang TQ, Do TT, Nguyen TC, Nguyen QH, Nguyen TT, Nguyen NH, Nguyen TN, Nguyen NL, Nguyen HD, Vu NT, Cao HH, Tran TH, Pham PM, Nguyen TD, Stepniewska K, White NJ, Tran TH, Farrar JJ. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. N Engl J Med. 2004 Oct 21;351(17):1741-51. https://www.ncbi.nlm.nih.gov/pubmed/15496623

[lviii] Corticosteroids, oral (Therapeutic group): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[lix] Prednisone, oral: Prasad K, Singh MB. Corticosteroids for managing tuberculous meningitis. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD002244. http://www.ncbi.nlm.nih.gov/pubmed/18254003

[lx] Dexamethasone, IV (HIV-infected TBM): Prasad K, Singh MB. Corticosteroids for managing tuberculous meningitis. Cochrane Database Syst Rev. 2008 Jan 23;(1):CD002244. http://www.ncbi.nlm.nih.gov/pubmed/18254003

[lxi] Amphotericin B, IV (1 mg dose): Molloy SF, Kanyama C, Heyderman RS, Loyse A, Kouanfack C, Chanda D, Mfinanga S, Temfack E, Lakhi S, Lesikari S, Chan AK, Stone N, Kalata N, Karunaharan N, Gaskell K, Peirse M, Ellis J, Chawinga C, Lontsi S, Ndong JG, Bright P, Lupiya D, Chen T, Bradley J, Adams J, van der Horst C, van Oosterhout JJ, Sini V, Mapoure YN, Mwaba P, Bicanic T, Lalloo DG, Wang D, Hosseinipour MC, Lortholary O, Jaffar S, Harrison TS; ACTA Trial Study Team. Antifungal Combinations for Treatment of Cryptococcal Meningitis in Africa. N Engl J Med. 2018 Mar 15;378(11):1004-1017. https://www.ncbi.nlm.nih.gov/pubmed/29539274

[lxii] Amphotericin B, IV (duration of treatment in HIV-uninfected): Perfect JR, Dismukes WE, Dromer F, Goldman DL, Graybill JR, Hamill RJ, Harrison TS, Larsen RA, Lortholary O, Nguyen MH, Pappas PG, Powderly WG, Singh N, Sobel JD, Sorrell TC. Clinical practice guidelines for the management of cryptococcal disease: 2010 update by the infectious diseases society of America. Clin Infect Dis. 2010 Feb 1;50(3):291-322. https://www.ncbi.nlm.nih.gov/pubmed/20047480

[lxiii] Amphotericin B: Southern African HIV Clinicians Society: Guideline for the prevention, diagnosis and management of cryptococcal meningitis among HIV-infected persons:2013 update. S Afr J HIV Med 2013;14(2):76-86. [Online][Accessed 8March2015] http://www.sajhivmed.org.za/index.php/hivmed/article/view/82

Fluconazole: Southern African HIV Clinicians Society: Guideline for the prevention, diagnosis and management of cryptococcal meningitis among HIV-infected persons:2013 update. S Afr J HIV Med 2013;14(2):76-86. [Online][Accessed 8March2015] http://www.sajhivmed.org.za/index.php/hivmed/article/view/82

[lxiv] Ibuprofen: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[lxv] Aciclovir, IV (Herpes simplex encephalitis – duration of therapy): Tunkel AR, Glaser CA, Bloch KC, Sejvar JJ, Marra CM, Roos KL, Hartman BJ,Kaplan SL, Scheld WM, Whitley RJ; Infectious Diseases Society of America. The management of encephalitis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Infect Dis. 2008 Aug 1;47(3):303-27. https://www.ncbi.nlm.nih.gov/pubmed/18582201

Aciclovir, IV (Herpes simplex encephalitis – duration of therapy): Sköldenberg B, Forsgren M, Alestig K, Bergström T, Burman L, Dahlqvist E, Forkman A, Frydén A, Lövgren K, Norlin K, et al. Acyclovir versus vidarabine in herpes simplex encephalitis. Randomised multicentre study in consecutive Swedish patients. Lancet. 1984 Sep 29;2(8405):707-11. https://www.ncbi.nlm.nih.gov/pubmed/6148470

Aciclovir, IV (Herpes simplex encephalitis – duration of therapy): Whitley RJ, Alford CA, Hirsch MS, Schooley RT, Luby JP, Aoki FY, Hanley D, Nahmias AJ, Soong SJ. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. N Engl J Med. 1986 Jan 16;314(3):144-9. https://www.ncbi.nlm.nih.gov/pubmed/3001520

Aciclovir, IV (Herpes simplex encephalitis – duration of therapy): Solomon T, Michael BD, Smith PE, Sanderson F, Davies NW, Hart IJ, Holland M, Easton A, Buckley C, Kneen R, Beeching NJ; National Encephalitis Guidelines Development and Stakeholder Groups. Management of suspected viral encephalitis in adults--Association of British Neurologists and British Infection Association National Guidelines. J Infect. 2012 Apr;64(4):347-73. https://www.ncbi.nlm.nih.gov/pubmed/22120595

[lxvi] Serum RPR titre (predictor of treatment success): Marra CM, Maxwell CL, Tantalo LC, Sahi SK, Lukehart SA. Normalization of serum rapid plasma reagin titer predicts normalization of cerebrospinal fluid and clinical abnormalities after treatment of neurosyphilis. Clin Infect Dis. 2008 Oct 1;47(7):893-9. https://www.ncbi.nlm.nih.gov/pubmed/18715154

[lxvii] Albendazole: Abba K, Ramaratnam S, Ranganathan LN. Anthelmintics for people with neurocysticercosis. Cochrane Database Syst Rev. 2010 Jan 20;(1):CD000215. http://www.ncbi.nlm.nih.gov/pubmed/20091504

Albendazole: Garcia HH, Pretell EJ, Gilman RH, Martinez SM, Moulton LH, Del Brutto OH, Herrera G, Evans CA, Gonzalez AE; Cysticercosis Working Group in Peru. A trial of antiparasitic treatment to reduce the rate of seizures due to cerebral cysticercosis. N Engl J Med. 2004 Jan 15;350(3):249-58. http://www.ncbi.nlm.nih.gov/pubmed/14724304

[lxviii] Corticosteroids, oral (Therapeutic group): South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[lxix] Prednisone: Vazquez VA, Sotelo J. The course of seizures after treatment for cerebral cysticercosis.*N Engl J Med.* 1992;327:696-701. http://www.ncbi.nlm.nih.gov/pubmed/1495522

[lxx] Orphenadrine: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

[lxxi] Propranolol: Zesiewicz TA, Elble RJ, Louis ED, Gronseth GS, Ondo WG, Dewey RB Jr, Okun MS, Sullivan KL, Weiner WJ. Evidence-based guideline update: treatment of essential tremor: report of the Quality Standards subcommittee of the American Academy of Neurology. Neurology. 2011 Nov 8;77(19):1752-5. https://www.ncbi.nlm.nih.gov/pubmed/26678329

Zesiewicz TA, Kuo SH. Essential tremor. BMJ Clin Evid. 2015 Dec 15;2015. pii: 1206. https://www.ncbi.nlm.nih.gov/pubmed/26678329

Propanolol: Jefferson D, Jenner P, Marsden CD. Relationship between plasma propranolol concentration and relief of essential tremor. J NeurolNeurosurg Psychiatry. 1979 Sep;42(9):831-7. http://www.ncbi.nlm.nih.gov/pubmed/501384

[lxxii] Pyridostigmine: South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

SOUTH AFRICAN ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 14: NEUROLOGICAL DISORDERS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2020-4)

The Adult Hospital Level Neurological Disorders chapter underwent detailed clinical editing and editorial changes for clarity.

Medicine amendment recommendations, with supporting evidence and rationale are listed below.
Kindly review the medicine amendments in the context of the respective standard treatment guideline (STG) and supporting medicine reviews. All reviews and costing reports may be accessed at: https://www.health.gov.za/nhi-edp-stgs-eml/.

TABLE A: AMENDMENTS

SECTION		MEDICINE/MANAGEMENT			ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
14.1.1 STROKE		**General Measures**			Editorial update to specify patient population
		Blood pressure management: Hydrochlorothiazide			Dose aligned to the Hypertension STG in the cardiovascular conditions chapter (Section 3.6: Hypertension)
		Hyper-acute management: Recombinant tissue plasminogen activator (rtPA) time window			Retained
		Direct oral anticoagulants (DOACs)			Not Added
		Medicine Treatment			Editorial update to ensure adequate swallowing ability
14.2 DEMENTIA		**Restless Patients:** Haloperidol, Oral:			Retained with amendment in dosage range
		Wernicke's syndrome: Thiamine, IM			Retained with amendment in dose
		Other commonly associated nutritional deficiencies: Vitamin B12 Testing:			Retained
14.4 EPILEPTIC SEIZURES		Types of seizures			Detail on seizure types added and expanded
14.5 STATUS EPILEPTICUS	**14.5.1 Epileptic Seizures and status epilepticus in Adolescents (13 – 18 years) and Adults**	**EARLY STATUS EPILEPTICUS (5 – 10 minutes)** **LEVEL 1 INTERVENTION:** Benzodiazepines	**If no IV access:**	Midazolam, IM or buccal	Retained
				Diazepam, rectal	Added
				Clonazepam, IM	Added
			If IV access:	Lorazepam, IV	Retained
				Midazolam, IV	Retained
				Clonazepam, IV	Retained
				Diazepam, IV	Retained
		ESTABLISHED STATUS EPILEPTICUS (10 – 30 minutes) **LEVEL 2 INTERVENTION:** Antiseizure medicine	**If no IV access**	Levetiracetam NGT	Added
			If vascular access	Phenytoin, IV	Retained – Moved to level 2 intervention

SECTION		MEDICINE/MANAGEMENT			ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
		REFRACTORY STATUS (30 – 60 minutes)	Propofol, IV		Retained
			Midazolam, IV		Retained
			Thiopental, IV		Removed
14.6.1 EPILEPSY IN ADOLESCENTS AND ADULTS		**Focal Epilepsy:** With and without evolution to bilateral tonic-clonic seizures		**First line:** Lamotrigine	Retained, moved to first-line: Adolescent boys, men and women not able to have children
				Second Line: Carbamazepine	Retained, moved to second-line: Adolescent boys, men and women not able to have children
				Second Line: Levetiracetam	Added: Adolescent boys, men and women not able to have children
				Third Line: *(specialist consultation):* Consider combination treatment or add-on topiramate	Added: Adolescent boys, men and women not able to have children
				First line: Lamotrigine	Retained: Pregnant women and women of child-bearing potential
				Second Line: Levetiracetam	Added: Pregnant women and women of child-bearing potential
				Third Line: *(specialist consultation):* Carbamazepine OR Combination lamotrigine and levetiracetam OR add-on topiramate	Added as third-line option: Pregnant women and women of child-bearing potential
		Generalised Epilepsy: Tonic-clonic, atonic, clonic or tonic seizures		**First line:** Lamotrigine (low-risk)	Retained: Adolescent boys, men and women not able to have children.
				First line: Levetiracetam(high-risk)	Added: Adolescent boys, men and women not able to have children.
				Carbamazepine	Deleted
				Second Line: Lamotrigine or levetiracetam (whichever not used as first line) OR Valproic acid	Added: Adolescent boys, men and women not able to have children.
				Third Line: *(specialist consultation):* Discuss with specialist Consider: Consider combination therapy OR add-on topiramate	Added: Adolescent boys, men and women not able to have children.

SECTION	MEDICINE/MANAGEMENT		ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
		First Line: Lamotrigine (low risk)	Retained: Pregnant women and women of child-bearing potential
		First Line: Levetiracetam (high-risk)	Added: Pregnant women and women of child-bearing potential
		Second Line: Levetiracetam or lamotrigine (whichever not used as first line) OR Consider combination therapy with lamotrigine and levetiracetam	Added: Pregnant women and women of child-bearing potential
		Third Line *(specialist consultation):* Refer for specialist assessment and intervention	Added: Pregnant women and women of child-bearing potential
	Myoclonic Confirm diagnosis and discuss management with a specialist	**First line:** Valproic acid	Retained: Adolescent boys, men and women not able to have children
		Second Line: Lamotrigine	Added: Adolescent boys, men and women not able to have children
		Third Line *(specialist consultation):* Discuss with specialist Consider levetiracetam OR Consider combination therapy	Added: Adolescent boys, men and women not able to have children
		First line: Lamotrigine	Added: Pregnant women and women of child-bearing potential
		Second Line: Levetiracetam	Added: Pregnant women and women of child-bearing potential
		Third Line *(specialist consultation):* Discuss with specialist Consider combination therapy	Added: Pregnant women and women of child-bearing potential
	Absence e.g. Juvenile absence epilepsy or persistent childhood absence epilepsy	**First line:** Valproic acid	Retained: Adolescent boys, men and women not able to have children
		Second Line: Lamotrigine	Retained, moved to second-line: Adolescent boys, men and women not able to have children
		Third Line *(specialist consultation):* Discuss with specialist Consider levetiracetam	Added: Adolescent boys, men and women not able to have children

SECTION	MEDICINE/MANAGEMENT		ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
		OR Consider combination therapy.	
		First line: Lamotrigine	Added: Pregnant women and women of child-bearing potential
		Second Line: Levetiracetam	Added: Pregnant women and women of child-bearing potential
		Third Line *(specialist consultation):* Discuss with specialist Consider combination therapy OR Consider sodium valproate	Added: Pregnant women and women of child-bearing potential
	Only consider continuing phenytoin in patients already well controlled on phenytoin, and in whom phenytoin is well tolerated	Phenytoin, oral	Only consider continuing phenytoin in patients already well controlled on phenytoin, and in whom phenytoin is well tolerated
14.7.2 CLUSTER HEADACHE	Oxygen Inhalation		Retained
14.7.6 IDIOPATHIC INTRACRANIAL HYPERTENSION (PSEUDOTUMOUR CEREBRI)	Acetazolamide, oral		Amended (Up Titration for maximum dose added)
14.9.1.1 IDIOPATHIC PARKINSON DISEASE	Dopamine agonists (Pramipexole extended-release tablets)		Not added
14.9.4 CHOREA	Clinical, medicine management & referral criteria		Expanded
	Haloperidol, Oral		Retained with amendment in dosage range
14.13 MYASTHENIA GRAVIS	Clinical description		Expanded to include clinical symptoms
14.14.1 BRAIN OEDEMA DUE TO TUMOR AND INFLAMMATION	Evidence Base for Medicine Management		Not Added
	Dexamethasone, IV		Retained, with no amendment in dosage
14.14.2 BRAIN OEDEMA DUE TO TRAUMATIC INJURY	Evidence Base for Medicine Management		Not Added
OTHER:	Endoscopic Cystoventriculostomy and Ventriculo-Cysternostomy for patients with Hydrocephalus (Adult and Paediatric) Referral to Specialist Neurosurgeon for surgical treatment		Not Added
14.15 (previously 14.1.3) SPINAL CORD INJURY, ACUTE	Management of sequalae of high risk of pressure sores		Added cross reference to PHC STG
	Symptomatic management of spasticity		Added with referral note for multi-disciplinary rehabilitation
	Symptomatic management of management of patients with cervical spinal cord injury		Added with referral note for multi-disciplinary rehabilitation

TABLE B: AMENDMENTS 2025

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/ NOT ADDED/ RETAINED
14.1.1 STROKE Secondary prevention:	Statin	Choice of statin for secondary prevention amended

Paracetamol[1] dosing has been amended in the chapter with dosage range amended and maximum dose reiterated and aligned to AHL Chapter 25: Pain. Additionally, the maximum daily dose for Tramadol has also been aligned to the AHL Chapter 25: Pain.

14.1.1 STROKE

General Measures

In cases of cryptogenic stroke in young patients, it is important to consider neurosyphilis as a possible cause, given that about 15% of untreated neurosyphilis patients and nearly 3% of all syphilis patients present with a stroke, particularly those under 50 years of age.[2] Therefore, the age for conducting serology to exclude meningovascular syphilis was set at < 45 years also in line with risk factors for ischaemic stroke in young adults mentioned later under general measures.

The following editorial update was made to the STG:

From:
Do serology to exclude meningovascular syphilis

To:
Do serology to exclude meningovascular syphilis, (in patients < 45 years old who do not have risk factors for stroke).

An external comment received to include a cross reference to palliative care chapter was supported by the Committee.

The STG was updated as follows:

GENERAL MEASURES
Optimise hydration and nutrition; insert nasogastric tube if patient cannot swallow. Take precautions to ensure an open airway if patient is unconscious.
Physiotherapy and good nursing care. Consider rehabilitation for suitable patients and refer if necessary.
Do an ECG to rule out an acute coronary event or atrial fibrillation as precipitants.
Do serology to exclude meningovascular syphilis (in patients <45 years old who do not have risk factors for stroke).
Check lipid profile in ischaemic strokes.
Ischaemic stroke in young adults (< 45 years of age) may be due to atherosclerosis, but also consider:
- Embolic: e.g. rheumatic heart disease, atrial fibrillation, cardiomyopathy, previous myocardial infarction, and, very rarely, patent foramen ovale: history, careful clinical cardiac examination, ECG/CXR, and echocardiography.
- Vessel wall disease: e.g. syphilis, HIV infection, collagen-vascular diseases, TB or bacterial meningitis, and extracranial arterial dissection. Investigate as guided by clinical presentation, but at least perform syphilis and HIV serology, urinalysis (haematuria and/or proteinuria), and ANF/RF. ANCA, and cerebral angiography or carotid Doppler may be indicated. Note that absence of a carotid bruit does not exclude significant carotid stenosis.
- Hypercoagulable states: e.g. antiphospholipid antibody syndrome, thrombotic thrombocytopenic purpura. Useful screening investigations are FBC and, in women, PTT/Anti-phospholipid Ab. Testing and management of thrombophilias should be done in consultation with an expert.

Initiate a palliative care approach if the patient's condition is deteriorating / in case of a massive stroke (See Chapter 24: Medicines Used in Palliative Care).
Ensure adequacy of swallowing ability by dietician or by asking the patient to swallow 10 mL of water.

Blood pressure management (if adequate fluid intake can be ensured)
Hydrochlorothiazide, Oral: *Aligned to the hypertension STG*

[1] South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.
[2] Singh AE, Romanowski B. Syphilis: review with emphasis on clinical, epidemiologic, and some biologic features. Clin Microbiol Rev. 1999; 12(2): 187-209.

Alignment of the dose of Hydrochlorothiazide for the management of blood pressure (if adequate fluid intake can be ensured) was confirmed against the cardiovascular conditions chapter (Section 3.6: Hypertension) as follows:

Hydrochlorothiazide, oral, 12.5 mg daily.

Hyper-acute management:

Recombinant tissue plasminogen activator (rtPA) time window: Retained

An external comment to revise recombinant tissue plasminogen activator (rtPA) time window from 3 to 4.5 hours for the treatment of acute ischaemic stroke was not accepted as an evidence review3 for the same comment reviewed by NEMLC in the previous review cycle (2019), concluded reduced cost-benefit beyond 3 hours.

Refer to evidence review:

Alteplase for stroke - therapeutic window_A

Recommendation: Based on this evidence review, the Adult Hospital Level Committee recommends that rtPA time window not be extended from 3 to 4.5 hours for the treatment of acute ischaemic stroke. rtPA is only to be considered for use at facilities where specialised neuro-radiological services and relevant expertise that are available within the prescribed three hours.

Rationale: Cost-benefit beyond 3 hours decreases and rtPA is expensive. rtPA can only be administered where specialised neuro-radiological services are available. Alteplase is currently included on the Tertiary & Quaternary EML and Provincial PTCs have the mandate to authorise use at appropriate levels by relevant specialists.

Level of Evidence: I Meta analysis, Systematic review, Guidelines, Expert opinion

Review indicator:

Evidence of efficacy	Evidence of harm/safety	Price reduction
		x

VEN status: (T&Q EML)

Vital	Essential	Necessary
	x	

NEMLC MEETING OF 6 DECEMBER 2018:

The NEMLC accepted the Adult Hospital Level Committee's recommendation, above and further recommended that a registry be set up to determine actual use of tPA throughout the country. This would also assist in identifying facilities that provide thrombolytic therapy for management of stroke (and training needs as required).

Bridging Anticoagulation

Direct oral anticoagulants (DOACs): *Not Added*

An external comment to include direct oral anticoagulants (DOACs) as bridging anticoagulation was not accepted for adult secondary level of care, but deferred to the Tertiary and Quaternary expert review committee for review.
The maximum dose of Alteplase, IV, was confirmed and set as 90mg in line with the South African Medicines Formulary[4].

Medicine Treatment

The following update was made to the STG

Hyper-acute management:
Symptom onset ≤ 3 hours:

3 Tissue plasminogen activator: Alteplase (window period 3 hours versus 4.5 hours): National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Alteplase – Window period for treating hyper acute ischaemic stroke, February 2018. http://www.health.gov.za/

4 South African Medicines Formulary, 14th Edition. Division of Clinical Pharmacology. University of Cape Town, 2022.

» Do not give aspirin.
» Refer immediately to hospital that **can provide thrombolytic therapy:**

- Alteplase, IV, 0.9 mg/kg. Total dose should not exceed 90 mg.
    - 10 % of total dose given as a bolus and the remainder continued as an infusion over an hour.

14.2 DEMENTIA

General Measures

An external comment received to involve a palliative care team or interdisciplinary team early and commence advanced care planning for dementia was supported by the Committee; because this implies focus on quality of life throughout care. It is further recommended to involve a multidisciplinary care team early and plan for advanced dementia care

The STG was updated as follows:

GENERAL MEASURES
Appropriate care and support, according to the level of impairment.
Ambulatory care is preferred to hospitalisation, if feasible.
Family counselling and support.
~~Involve a palliative care team~~ Use a palliative care approach: involve a multidisciplinary care team early and plan for advanced dementia care.

To control restless patients

Haloperidol, Oral: *retained with amendment in dosage range*

Haloperidol IM has been discontinued in South Africa. However, oral haloperidol is available locally. The recommendation for the use of oral haloperidol to control restless patients was retained. As the oral haloperidol formulation available is a 1.5mg scored tablet; the dosage range for oral haloperidol was amended for ease of dosing.

The STG was updated as follows:

From:

MEDICINE TREATMENT
Management is mainly symptomatic.

To control restless patients:
- Haloperidol, oral, 0.5–1 mg 8 hourly with a higher dose at night, if required.

To:

MEDICINE TREATMENT
Management is mainly symptomatic.

To control restless patients:
- Haloperidol, oral, 0.75–1.5 mg 8 hourly with a higher dose at night, if required.

Wernicke's syndrome: E51.2 + (F02.8*)
Thiamine, IM: *Retained with amendment in dose*

Refer to the evidence summary for the optimum dose of thiamine for prevention and treatment of Wernicke's encephalopathy:

NEMLC MEETING OF 23 JUNE 2022:
NEMLC accepted the proposal to amend the dose of thiamine from "100mg" to "200mg", aligned with available RCT evidence, for the prevention of Wernicke's encephalopathy. NEMLC also deliberated on the route of administration and recommended that for the prevention of Wernicke's encephalopathy, that thiamine should be administered intramuscularly and not by the intravenous route.

Review of the evidence for the optimum dose of thiamine for prevention and treatment of Wernicke's encephalopathy showed that no good quality evidence could be identified to support a dose of thiamine 500mg three times a day although recommended in most guidelines[5]; and that thiamine 500mg once daily may be sufficient for 3-5 days. In the absence of any evidence updates and no reported harms, the pragmatic solution was to retain thiamine for the treatment of Wernicke's syndrome with an adjustment of dose to 500mg IM immediately and daily for 3 to 5 days.

For prophylaxis in patients at risk (alcoholism, malnutrition) intramuscular (IM) dose was clarified as 200mg daily and route of administration restricted to IM and not extended to intravenous as IM indicated as preferred route of administration in package information leaflet[6].

The STG was updated, with inclusion of a caution box for the administration of thiamine, as follows

FROM:

Wernicke's syndrome: E51.2 + (F02.8*)
- Thiamine, IV, 500 mg 12 hourly for 3 days, followed by 500 mg daily for 3–5 days.
  - Follow with oral thiamine 100 mg 8 hourly.

To:

Wernicke's syndrome: E51.2 + (F02.8*)
- Thiamine, IM, 500 mg immediately and daily for 3 to 5 days.
  - Follow with thiamine, oral, 100 mg 8 hourly

CAUTION
Thiamine should preferably be administered prior to intravenous glucose to prevent permanent neurological damage.
Do not delay the dextrose administration in a hypoglycaemic patient.

Prophylaxis in patients at risk (alcoholism, malnutrition): Z29.2
- Thiamine, IM/~~IV~~ 200mg daily or oral, 100 mg 8 hourly for 14 days.

Level of Evidence: Low to Moderate Certainty Evidence

Treat other commonly associated nutritional deficiencies
Vitamin B_{12} Testing: *Retained*
The availability of Vitamin B_{12} tests was queried with the National Health Laboratory Services (NHLS). The test is freely available at all levels of care without restrictions.

5 Latt N, Dore G. Thiamine in the treatment of Wernicke encephalopathy in patients with alcohol use disorders. Intern Med J. 2014;44(9):911-5.10.1111/imj.12522
6 South African Health Product Regulatory Authority. Professional Information for Medicines for Human Use. A-Lennon Vitamin B Complex. Available at: https://pi-pil-repository.sahpra.org.za/

14.4 EPILEPTIC SEIZURES, 14.5 STATUS EPILEPTICUS, AND 14.6 EPILEPSY

The Epilepsy Subcommittee was constituted in October 2024 following the receipt of numerous external comments on the draft epilepsy sections of the Primary Healthcare (PHC) and Adult Hospital level (AHL) Standard Treatment Guidelines (STGs) and Essential Medicines List (EML). Additionally, and as an overarching issue, NEMLC was concerned with the Paediatric Hospital recommendation of sodium valproate as first line treatment for generalised tonic-clonic seizures, absence seizures, and children with HIV due to the concerns regarding sodium valproate use in pregnancy and women and men of child-bearing potential.

The purpose of the Epilepsy Subcommittee was to align the STGs on epilepsy across all levels of care (i.e. primary, secondary, and tertiary/quaternary care) and age groups (i.e. children, adolescents and adults) to ensure a continuum of care, using the medicines currently on the EML, and to identify gaps in EML treatment.

Table 1: Medicine Amendments outlines the medicine changes to the AHL STGs and EML.

This is to be read in conjunction with the Epilepsy Subcommittee Report and updated STGs; which summarises the process of updating the STGs and EMLs and highlight rationale for changes.

14.7.2 CLUSTER HEADACHE

Oxygen inhalation: *Retained*
An external comment, without supporting evidence, was received to add the following statement: '100% oxygen mask for 10 minutes' to the existing STG recommendation for oxygen therapy for cluster headaches.

The American headache society evidence-based guidelines[7] mention two class I randomised controlled trials with a level A recommendation for efficacy of oxygen. The rates and duration of oxygen therapy varied in the studies mentioned in the guidelines. Therefore, oxygen inhalation was retained in the STG without specifying rate or duration of therapy. An AGREE II appraisal was conducted, in duplicate, on the guideline and summarised below.

AGREE II Appraisal Summary

Guideline: Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016 Jul;56(7):1093-106. doi: 10.1111/head.12866. PMID: 27432623	
Domain 1: Scope and purpose	72%
Domain 2: Stakeholder involvement	6%
Domain 3: Rigour of development	63%
Domain 4: Clarity of presentation	86%
Domain 5: Applicability	42%
Domain 6: Editorial independence	88%

Overall Assessment: 75%
Level of Evidence: Low to Moderate Certainty Evidence

14.7.6 IDIOPATHIC INTRACRANIAL HYPERTENSION (PSEUDOTUMOUR CEREBRI)

Acetazolamide, oral: *Amended* (Up titration for maximum dose added)

Following an external comment highlighting a gap in instruction on reaching the maximum acetazolamide dose; the STG was amended to include an up titration of acetazolamide to the maximum allowable daily dose. Acetazolamide

[7] Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016 Jul;56(7):1093-106. doi: 10.1111/head.12866. PMID: 27432623.

has been used to treat idiopathic intracranial hypertension with doses ranging from 250 to 500 mg twice daily; increasing the dose as tolerated by 250 mg every week to reach a desired clinical effect or a maximum dose of 4 g/day[8].

The maximum allowable dose was revised from 2 grams daily to 4 grams daily. Two RCTs were also reviewed regarding tolerated doses. Wall[9] et al stopped dose escalation if there was a measurable improvement in papilledema and visual field (according to prespecified criteria). ten Hove[10] et al only stopped dose escalation if participants reported symptoms interfering with activities of daily living. Both RCTs showed that acetazolamide appears to have an acceptable safety profile at dosages up to 4 g daily in the treatment of idiopathic intracranial hypertension.

Therefore, maximum dose was set at 4 grams daily but wording included for maximum tolerated dose, not exceeding 4 grams.

Level of Evidence: RCT: IIIb

The STG was updated as follows:

MEDICINE TREATMENT

Discuss all cases with a specialist.

For visual involvement, persistent headaches, or severe papilloedema:

- Acetazolamide, oral, 250 mg 12 hourly~~maximum dose 2 g daily~~
    - Increase, as required, by 250mg daily every week to the maximum tolerated dose (not exceeding 4g daily)

OR

Furosemide, oral, 40 mg daily.

14.9.1.1 IDIOPATHIC PARKINSON DISEASE

Dopamine agonists (Pramipexole extended-release tablets): *Not added*

An external recommendation was received for the inclusion of dopamine agonists specifically pramipexole extended-release tablets for ease of use (once daily dosing), substantial clinical effect, generally well tolerated, delay in dyskinesias and prolonged monotherapy which possibly improves depression. Dopamine agonists were not added as as they are approved for use as management at T&Q level of care[11].

14.9.4 CHOREA

Clinical, medicine management and referral criteria: *Expanded*

The STG was expanded including clinical, medicine management and referral criteria as follows:

From:

G25.5

DESCRIPTION

Involuntary random, irregular movements.

Aetiology is classified as:

» primary – Huntington's chorea,; or

» secondary – Sydenham's chorea, hemiballismus secondary to infarction, diabetes (hyperglycemia)

MEDICINE TREATMENT

[8] Up to Date. Idiopathic intracranial hypertension (pseudotumor cerebri): Prognosis and treatment. 2021. Available at: https://www.uptodate.com/contents/idiopathic-intracranial-hypertension-pseudotumor-cerebri-prognosis-and-treatment?search=acetazolamide%20and%20dosing%20&source=search_result&selectedTitle=2%7E94&usage_type=default&display_rank=2.

[9] NORDIC Idiopathic Intracranial Hypertension Study Group Writing Committee; Wall M, McDermott MP, Kieburtz KD, Corbett JJ, Feldon SE, Friedman DI, Katz DM, Keltner JL, Schron EB, Kupersmith MJ. Effect of acetazolamide on visual function in patients with idiopathic intracranial hypertension and mild visual loss: the idiopathic intracranial hypertension treatment trial. JAMA. 2014 Apr 23-30;311(16):1641-51. doi: 10.1001/jama.2014.3312. PMID: 24756514; PMCID: PMC4362615.

[10] ten Hove MW, Friedman DI, Patel AD, Irrcher I, Wall M, McDermott MP; NORDIC Idiopathic Intracranial Hypertension Study Group. Safety and Tolerability of Acetazolamide in the Idiopathic Intracranial Hypertension Treatment Trial. J Neuroophthalmol. 2016 Mar;36(1):13-9. doi: 10.1097/WNO.0000000000000322. PMID: 26587993.

[11] National Essential Medicines List Committee (NEMLC). TERTIARY AND QUATERNARY LEVEL. ESSENTIAL MEDICINES LIST. Reviewed Items. June 2022.

Treat the underlying cause, if relevant.

- Haloperidol, oral, 0.5–5 mg 8–12 hourly (Specialist consultation).

To:
G25.5

DESCRIPTION
Chorea is a hyperkinetic movement disorder characterized by involuntary brief, random, and irregular contractions conveying a feeling of restlessness to the observer. Chorea may be caused by hereditary neurodegenerative diseases; structural damage to deep brain structures; or be associated with autoimmune disorders, metabolic derangement, or certain drugs and hormones.

Aetiology is classified as:
Rarer primary (idopathic or hereditary) – Huntington's chorea,; or
More common secondary (acquired) – Sydenham's chorea, hemiballismus secondary to infarction, diabetes (hyperglycemia)

Symptoms include involuntary, random, irregular movements.

GENERAL MEASURES
Exclude potential underlying causes initially.
A careful history should include age of onset, time course (acute or insidious), past medical history, history of recent infection with group A beta-hemolytic streptococcus (GABHS), family history, and drug exposure.
Neuroimaging should be performed for new-onset cases, especially when asymmetric.
A variety of laboratory tests may be useful depending on the clinical context.

MEDICINE TREATMENT
Treat the underlying cause, if relevant.

First-generation antipsychotic agents (typical neuroleptics) may reduce chorea although there is little evidence to support their efficacy, and they are increasingly avoided due to increased risk of side effects.
- Haloperidol, oral, 0.75–5 mg 8–12 hourly (Specialist consultation).

REFERRAL
The need to refer may be based on the underlying cause and diagnostic workup.
Refer primary choreas for genetic counselling.

Haloperidol, Oral: *retained with amendment in dosage range*

As the oral haloperidol formulation available is a 1.5mg scored tablet; the dosage range (lower end) for oral haloperidol was amended for ease of dosing.
Level of Evidence: LOW Certainty Evidence: Expert Opinion for the use of Haloperidol for the Management of Chorea

14.13 MYASTHENIA GRAVIS

Clinical description: *Expanded to include clinical symptoms*

The STG was expanded as follows:

From:

DESCRIPTION
Consider this in patients with new onset weakness and fatiguability. particularly involving the eyes and the swallowing muscles.

MEDICINE TREATMENT
Discuss both diagnosis and treatment with a specialist.
- Pyridostigmine, oral, 60 mg 5 times daily.

Corticosteroids and azathioprine should only be used in consultation with a specialist.

To:

G70.0

DESCRIPTION

Myasthenia gravis is an autoimmune neuromuscular disorder characterised by fluctuating motor weakness involving ocular, bulbar, limb, and/or respiratory muscles.
The weakness is due to an antibody-mediated, immunologic attack directed at proteins in the postsynaptic membrane of the neuromuscular junction (acetylcholine receptors or receptor-associated proteins).
Consider this in patients with new onset weakness and fatiguability, particularly involving muscles of the eyes and those involved in swallowing.

MEDICINE TREATMENT

Discuss both diagnosis and treatment with a specialist.

- Pyridostigmine, oral, 60 mg 5 times daily.

Corticosteroids and azathioprine should only be used in consultation with a specialist.

14.14.1 BRAIN OEDEMA DUE TO TUMORS AND INFLAMMATION

Dexamethasone, IV: *retained, with no amendment in dosage*

The STG recommends Dexamethasone, IV, 4 mg 6 hourly, initially. External comment was received to consider twice daily dosing instead, due to the risk of corticosteroid-induced adrenal suppression and insomnia. It was noted that treatment with dexamethasone for this indication was not intended as a palliative care approach and that short term IV therapy in hospital was unlikely to result in adrenal suppression and insomnia. The proposed amendment was therefore not supported by the Committee.

Evidence Base for Medicine Management: *Not Added*

In response to an external comment, the evidence base for medicine management for STGs 14.14.1 brain oedema due to tumors and inflammation was considered. However, it was noted that evidence citations for historic recommendations are generally not included in the current STGs, due to space constraints and therefore the evidence base was not included.

14.14.2 BRAIN OEDEMA DUE TO TRAUMATIC INJURY

Evidence Base for Medicine Management: *Not Added*

The evidence base for medicine management for STG 14.12.2 brain oedema due to traumatic injury was considered. However, it was noted that evidence citations for historic recommendations are generally not included in the current STGs, due to space constraints and therefore the evidence base was not included.

OTHER

The following addition suggested by an external commentator was not accepted for inclusion as it likely falls into tertiary management or outside the scope of the EML.

Chapter 14: Neurological Disorders:
Endoscopic Cystoventriculostomy and Ventriculo-Cysternostomy for patients with Hydrocephalus (Adult and Paediatric)
Referral to Specialist Neurosurgeon for surgical treatment.
Surgical Treatment:
・ Hydrocephalus is a chronic medical condition that occurs in individuals who are unable to reabsorb cerebrospinal fluid (CSF) created within the ventricles of the brain. Treatment requires excess CSF to be cleared and the clearance

of occlusions;
Choice of treatment procedure:
Recent advancements in both fiber laser and endoscope technologies may enable minimally invasive recanalization of ccluded ventricular catheters.
Hydrocephalus procedure options (different equipment used for each option) :

- Surgical insertion of drainage system – Shunt;
- Endoscopic Third ventriculostomy (ETV);
- Endoscopic Third ventriculostomy (ETV) with Choroid Plexus Cauterization (ETV/CPC);

Cost saving/Value adding to the Public Health Sector:
The Thulium Yag laser provides a rapid, safe, and effective means of clearing obstructed catheters in patients suffering from hydrocephalus, potentially reducing the need for surgical revision.

- Safe technique for laser endoscopic third ventriculostomy;
- Good vaporization and haemostasis for Choroid Plexus Cauterization;
- The Thulium Yag laser offers precise surgery with:
  - No deep penetration
  - Safe operation
  - Excellent hemostasis

14.15 SPINAL CORD INJURY, ACUTE

Spinal Cord Injury, Acute STG was moved from section 14.1.3 to 14.15 because section 14.1 relates to cerebrovascular disease. This editorial update is also in keeping with the PHC chapters were 15.12 Spinal Cord Injuries appears as the last STG in the chapter.

Management of sequalae of high risk of pressure sores: *Added cross reference to PHC STG*

Symptomatic management of spasticity: *Added with referral note for multi-disciplinary rehabilitation*

Symptomatic management of patients with cervical spinal cord injury: *Added with referral note for multi-disciplinary rehabilitation*

Only acute spinal cord injury is included in the STG. For the symptomatic management of sequalae of high-risk pressure sores a cross reference to the PHC STG: Skin and dermatology chapter (Section 5.19 Pressure Ulcers/ Sores) was added. Additionally, a referral note for multi-disciplinary rehabilitation was added for the symptomatic management of spasticity and management of patients with cervical spinal cord injury. The referral criterion added on receipt of motivation from RuReSA and Rehabilitation Associations of SA in collaboration with the Department of Health and Rehabilitation Sciences, Stellenbosch University[12] for pressure ulcers/sores and for prevention of pressure sores e.g., wheelchair users should be referred to rehabilitation for wheelchair and transfers training.[13,14]

The STG was updated as follows:

From:
For symptomatic management of:
» Constipation – see section 24.1.2: Constipation.
» Urinary retention – see section 7.3.6: Overactive bladder.

To:
For symptomatic management of:
» Constipation – see section 24.1.2: Constipation.
» Urinary retention – see section 7.3.6: Overactive bladder.
» High risk of pressure sores – See Primary Health Care STG & EML, section 5.19: Pressure ulcers/ sores.
» Spasticity – refer patients for multi-disciplinary rehabilitation.

[12] Arora M, Harvey LA, Glinsky JV, Nier L, Lavrencic L, Kifley A, Cameron ID. Electrical stimulation for treating pressure ulcers. Cochrane Database Syst Rev. 2020 Jan 22;1(1):CD012196. https://pubmed.ncbi.nlm.nih.gov/35244315/.
[13] Harvey LA, Glinsky JV, Bowden JL. The effectiveness of 22 commonly administered physiotherapy interventions for people with spinal cord injury: a systematic review. Spinal Cord. 2016 Nov;54(11):914-923. https://pubmed.ncbi.nlm.nih.gov/27349607/.
[14] Wang J, Ren D, Liu Y, Wang Y, Zhang B, Xiao Q. Effects of early mobilization on the prognosis of critically ill patients: A systematic review and meta-analysis. Int J Nurs Stud. 2020 Oct;110:103708. https://pubmed.ncbi.nlm.nih.gov/32736250/.

REFERRAL

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

2025 UPDATES

14.1.1 STROKE

Following the publication of the chapter, The STG has been amended on the choice of statin for secondary prevention of CVD from Simvastatin 40mg to rosuvastatin 10mg in line with the source chapter AHL Chapter 3: CVS. In addition, the dose of simvastatin has been amended from 10mg to 10-20mg also in line with the source chapter AHL Chapter 3: CVS for patients on amlodipine (not on Protease inhibitors). The STG has been amended as follows:

<table>
<tr><th>AHL Chapter 3: Cardiovascular System</th><th>Chapter 14: Neurological Disorders</th></tr>
<tr><td></td><td>Section: 14.1.1 Stroke</td></tr>
<tr><td>
<table>
<tr><td colspan="2">B: Secondary prevention - existing CVD</td></tr>
<tr><td>» Ischaemic heart disease.
» Atherothrombotic stroke.
» Peripheral vascular disease.</td><td>▪ HMGCoA reductase inhibitors (statins), e.g.:
● Rosuvastatin, oral, 10 mg at night.</td></tr>
<tr><td>» Patients on protease inhibitors.</td><td>• Atorvastatin, oral, 10 mg daily.</td></tr>
<tr><td>» Patients on amlodipine (and not on protease inhibitor).</td><td>• Simvastatin, oral, 10–20 mg at night.</td></tr>
<tr><td>» If patient complains of muscle pain.</td><td>Reduce dose:
▪ HMGCoA reductase inhibitors (statins), e.g.:
• Simvastatin, oral, 10 mg at night.
OR
Consult specialist for further management.</td></tr>
</table>
</td><td>
Secondary prevention:
Measures for secondary prevention may not be appropriate for patients with severe disability.

<u>All patients with a thrombotic stroke, not on anticoagulation and irrespective of the LDL level:</u>
Aspirin, oral, 150 mg daily.
AND
▪ HMGCoA reductase inhibitors (statins), e.g.:
● ~~Simvastatin, oral, 40mg~~ Rosuvastatin, oral, 10 mg at night.

<u>Patients on protease inhibitor:</u>
• Atorvastatin, oral, 10 mg at night.

<u>Patients on amlodipine (and not on a protease inhibitor):</u>
● Simvastatin, oral, 10-20 mg at night.
</td></tr>
</table>