Epilepsy and Related topics

Updates to the Standard Treatment Guidelines and Essential Medicines List:

- Primary Health Care
- Adult Hospital Level
- Paediatric Hospital Level

Prof Lesley Robertson

10 February 2026

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Evidence

Please access the revised chapters and the National Essential Medicines List Committee (NEMLC) reports which detail the evidence (including rationale, references and costings) informing the decision-making on medicine addition, amendments and deletions from the NHI website.

NHI Website: https://www.health.gov.za/nhi-edp-stgs-eml

Knowledge Hub (for webinar recordings access): https://knowledgehub.health.gov.za/webinars

Disclaimer

This presentation is an implementation tool and should be used alongside the most recently published STGs available on the Knowledge Hub.

This information does not supersede or replace the Standard Treatment Guidelines (STGs).

SCAN ME

Epilepsy Subcommittee Report

Epilepsy Subcommittee

Epilepsy Subcommittee

Why was the Epilepsy Subcommittee convened?

01

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)

02

Concerns regarding valproate use in pregnancy and women and men of child-bearing potential, including the Paediatric Hospital recommendation of valproate as first line treatment for generalised tonic-clonic seizures, absence seizures, and children with HIV

Purpose and Functions of the Epilepsy Subcommittee

PURPOSE

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.

FUNCTIONS

- Assess the current epilepsy STGs across all levels of care including EML items indicated for paediatric and adult male and female patients, classification of seizures, and guidance for acute versus maintenance treatment.
- Prepare recommendations for updating of epilepsy chapters of the STGs, across all levels of care by end of March 2025; and
- Assist with the review of bid specifications for national tenders as needed.

Key Issues Arising from External Comments and NEMLC Discussions

01 **Need for alignment** across all levels of care on terminology, classification, and treatment choices.

02 **Updates required** in descriptions, general measures, medicine guidance, and referral criteria.

03 **Treatment algorithms challenged**, with concerns about medicine choices and need for clearer options.

04 **Valproate concerns**: Continued use in girls and women of child-bearing potential despite SAHPRA risk-form processes and first-line recommendations may reinforce prescribing

05 **Lamotrigine titration issues**: Long initiation period makes it less acceptable to some stakeholders as first-line therapy.

06 **High demand for levetiracetam**, including access at PHC.

International Guidelines

INTERNATIONAL LEAGUE AGAINST EPILEPSY (ILAE)[1]

- The ILAE classification system, which has been incorporated into the WHO ICD-11 nomenclature, was used to reorganise the guidance.

NICE 2022 GUIDELINE (UPDATED JANUARY 2025)[2]

- Used to inform changes to the indications and hierarchy of choice of the antiseizure medicines (ASMs) already on the EML.
- Although resources differ between countries, NEMLC did not recommend a GRADE-ADOLOPMENT of the NICE 2022 guideline as no new medicines were being added to the NEML.

1. International League Against Epilepsy. EpilepsyDiagnosis.org. 30 June 2024. Available at https://www.epilepsydiagnosis.org/
2. NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

Restructuring to Four New Sections

Epileptic Seizures
(PHC, Adult Hospital and Paediatric Hospital Level)

Status Epilepticus
(PHC, Adult Hospital and Paediatric Hospital Level)

Febrile Seizures
(PHC and Paediatric Hospital Level)

Epilepsy
(PHC, Adult Hospital and Paediatric Hospital Level)

Epileptic Seizures and Status Epilepticus

Epileptic Seizures and Status Epilepticus Previous STGs

Key Issues across levels of care

Positioning

Positioned after the epilepsy section in AH STG, implying that epileptic seizures are always caused by epilepsy.

Description

Description varied between levels of care, with Adult Hospital providing no description of differing seizure types, aetiologies or differential diagnosis although Paediatric Hospital emphasised the need to find the cause of the seizure and used ILAE terminology.

Treatment

Medicine treatment differed between STGs in terms of timing and doses of benzodiazepines and other antiseizure medicines.

Epileptic Seizures and Status Epilepticus Revised STGs

01 Provide a generic description of epileptic seizures, differential diagnoses, and important causes to exclude.

02 Briefly describe different seizure types with link to ILAE website.

03 Separate management into a) children < 13 years of age and b) adolescents and adults.

04 Separate treatment of convulsive status epilepticus using ILAE time points of 5 minutes (t1 abnormally prolonged seizure) and 30 minutes (t2 when a seizure may cause long-term consequences) and level 1, 2 and 3 interventions.

05 Provide post-seizure guidance to include the post-ictal phase and active follow-up.

06 Refine treatment algorithms to clarify dosing and administration. Expand vascular access in children to include the intraosseous route.

Epileptic Seizures and Status Epilepticus Key Medicine Management Changes

Repeat IV phenytoin dose removed across all age groups due to safety concerns.

Post-seizure initiation of oral phenytoin 300 mg removed; replaced with broader guidance to continue the most appropriate ASM during propofol/midazolam weaning only if epilepsy is suspected/diagnosed.

Phenobarbital IV repeat dosing modified for children <13 years—give as two half-doses to reduce risk of respiratory depress

Option of levetiracetam administration via NGT added at all service levels

Phenytoin and benzodiazepines now recommended **sequentially**, not simultaneously, in Adult STGs.

Phenobarbital IM added at PHC level (if product is available).

Epileptic Seizures and Status Epilepticus Identified Gaps

Access to Schedule 5 Medication

- PHC Nurses and Clinical Associates cannot prescribe Schedule 5 medicines (e.g., benzodiazepines, full phenobarbital doses) except for obstetric analgesia.
- Verbal prescriptions from doctors to pharmacists must be followed by written prescriptions within 7 days; no legal provision exists for nurses to receive verbal orders.
- Most Emergency Medicine Services (EMS) staff often have only Basic Life Support training and are not authorised to administer Schedule 5 medicines.

Children <13 years of age

- Phenobarbital via NGT (20 mg/kg) cannot be safely repeated due to delayed therapeutic levels and overdose risk.
- Levetiracetam via NGT may be used after phenobarbital if needed.
- No IV second-line treatment available at PHC level (IV/IM phenobarbital only via Section 21; phenytoin IV requires cardiac monitoring).
- In hospitals, phenytoin IV is the only second-line IV option; no alternative exists where phenytoin is contraindicated (e.g., suspected cardio-toxic poisoning).

Adolescents and Adults

- At PHC level, no second- level intravenous intervention.
- At hospital level, no intravenous alternative to phenytoin, IV.

Epilepsy

Epilepsy
Previous STGs

Key Issues across levels of care

Treatment based on **special populations (e.g. WOCBP, HIV)** rather than epilepsy type, limiting tailored care.

Adult PHC & AHL

PHC

Strong general guidance, but **minimal information on epilepsy types**; limited paediatric treatment options and **absence seizures default to referral**.

Paediatric STGs recommended **valproate 1st line for generalised seizures**, raising concerns as children transition to child-bearing potential.

Valproate

Paediatric Hospital Level

Detailed epilepsy types and syndromes with type-specific treatment but **limited general clinical guidance**.

Levetiracetam syrup and topiramate are only available at Paediatric Hospital level and tertiary and quaternary levels (for treatment resistant epilepsy).

Access Gaps

Incosistencies

Misalignment existed between the PHC, AHL and Paediatric Hospital STGs.

Epilepsy
Revised STGs

Separate guidance for children (<13 years) and adolescents/adults due to dosing and level-of-care differences.

Paediatric Hospital STG table expanded to include epilepsy syndromes, recommended medicines, and drugs to avoid. **Dosing for syndromes excluded**, as these cases require **specialist-led management**

01

02

03

04

Treatment now structured by **ILAE epilepsy classification**, not by special populations.

Medicine choices (1st–3rd line) aligned with **NICE 2022** but adapted for South African public-sector feasibility.

References:
- International League Against Epilepsy. EpilepsyDiagnosis.org. 30 June 2024. Available at https://www.epilepsydiagnosis.org/
- NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

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Focal Epilepsy
Key Medicine Management Changes

Lamotrigine is now 1st-line for all ages based on high-quality evidence showing superiority over carbamazepine, valproate, and topiramate, though slow titration is a concern for those with ongoing seizures.

Carbamazepine becomes 2nd-line for patients without child-bearing potential/HIV, chosen mainly for affordability despite being inferior to levetiracetam for treatment failure and adverse effects.

Levetiracetam is 2nd-line when child-bearing potential or HIV is relevant, with evidence showing equivalence to lamotrigine; not 1st-line due to cost and possible neuropsychiatric effects.

Topiramate removed as 2nd-line monotherapy due to lack of advantage over carbamazepine and safety concerns; may be used **as 3rd-line add-on** under specialist guidance.

Valproate remains excluded for focal epilepsy except as 2nd-line add-on per NICE, due to significant safety risks in pregnancy and people of child-bearing potential.

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References:
- Nevitt et al. (2022). Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Database of Systematic Reviews. DOI: 10.1002/14651858.CD011412.pub4.
- NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

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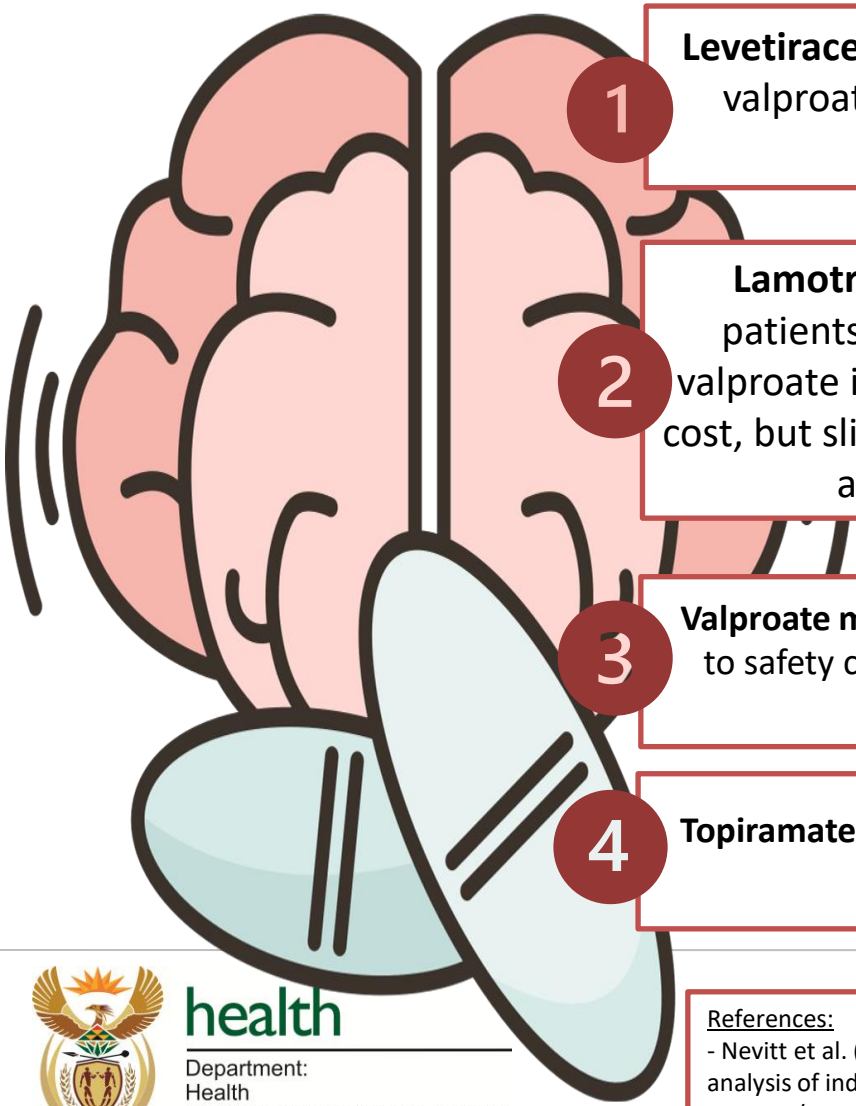
Generalised Epilepsy with Tonic-clonic Seizures
Key Medicine Management Changes



1. **Levetiracetam is now a 1st-line option**, showing no difference from valproate in treatment failure for any reason and offering rapid seizure control at similar cost.

2. **Lamotrigine remains a 1st-line option**, suitable for "low-risk" patients who can tolerate slower titration; similar outcomes to valproate in terms of side effects and treatment failure and is low in cost, but slightly less effective vs valproate on network meta-analyses and therefore cannot be a stand-alone 1st option.

3. **Valproate moved to 2nd-line** for patients with no child-bearing potential due to safety concerns, moderate-certainty evidence, and the impracticality of NICE's two-specialist approval process in South Africa.

4. **Topiramate not recommended as monotherapy but** may be used **as 3rd-line add-on therapy** under specialist guidance.

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References:
- Nevitt et al. (2022). Antiepileptic drug monotherapy for epilepsy: a network meta-analysis of individual participant data. Cochrane Database of Systematic Reviews. DOI: 10.1002/14651858.CD011412.pub4.

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Generalised Epilepsy with Myoclonic Seizures
Key Medicine Management Changes

Evidence base is weak, Recommendation of valproate as 1st line was influenced by NICE guidance and expert opinion

Levetiracetam recommended as 1st line for girls of child-bearing potential, because of safety considerations rather than efficacy.

Myoclonic seizures usually occur in epilepsy syndromes, often associated with severe to profound intellectual disability, where child-bearing potential is not a concern. Therefore, it does not seem reasonable to withhold valproate in these patients.

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References
- NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217
- International League Against Epilepsy. EpilepsyDiagnosis.org. 30 June 2024. Available at https://www.epilepsydiagnosis.org/

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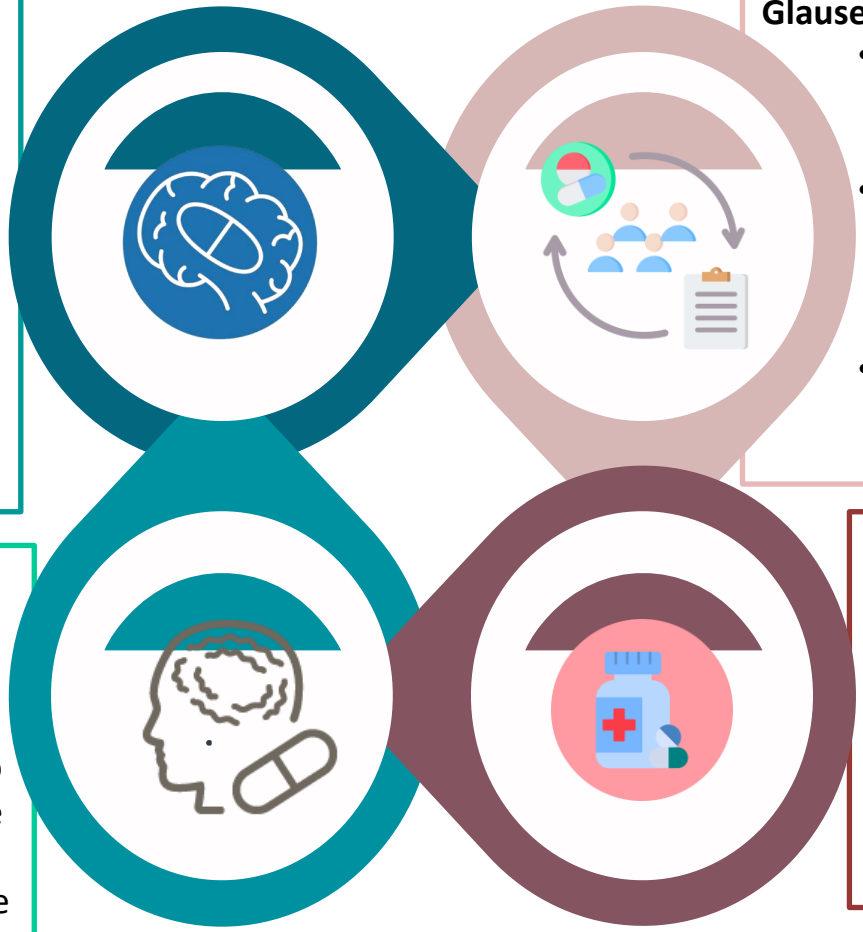
Generalised Epilepsy with Absence Seizures
Key Medicine Management Changes

Valproate = 1st line (only if no child-bearing potential). Based on high-quality childhood absence epilepsy (CAE) Randomised Control Trial (RCT) (Glauser 2013) showing valproate efficacy similar to ethosuximide and superior to lamotrigine. Ethosuximide has high cost and not available in public sector.

Lamotrigine recommended for girls who may need treatment beyond age 10 (to avoid valproate in child-bearing years) but **not preferred 1st line** due to lower efficacy and long response time (3–6 months). Evidence for efficacy of lamotrigine in juvenile absence epilepsy has been deferred by the subcommittee to a future review cycle.



Glauser et al. key findings (CAE):

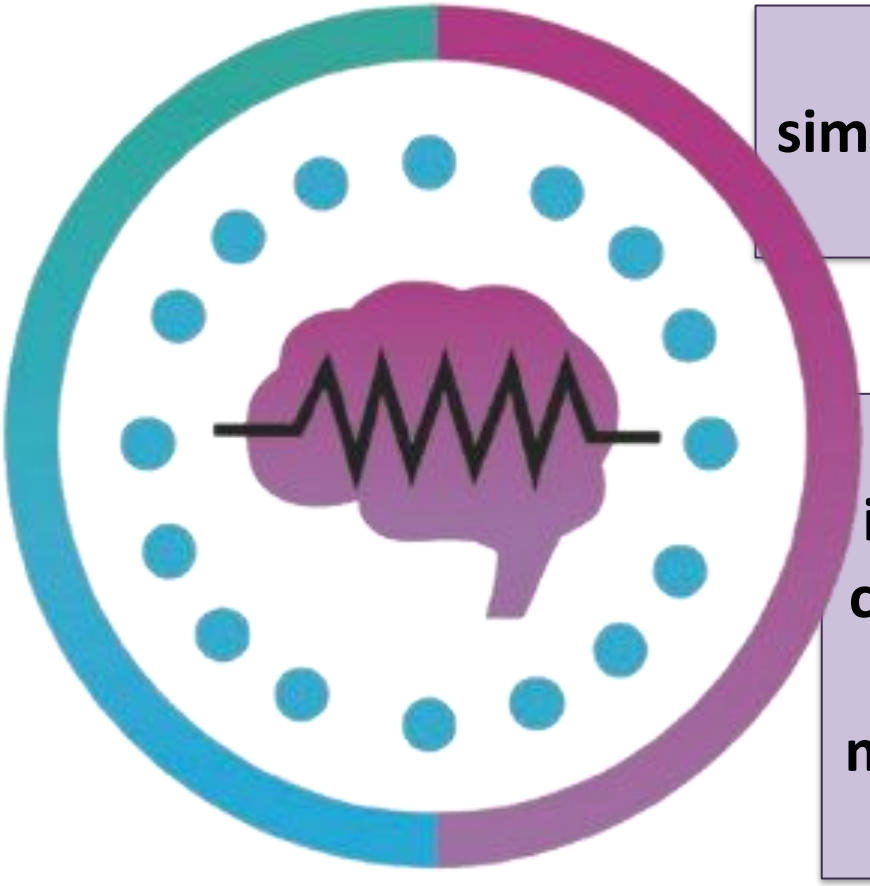
- **Efficacy:** Valproate ~58% at 16–20 weeks vs lamotrigine 30%; similar to ethosuximide.
- **Adverse effects:** Similar rates between ethosuximide and valproate; lamotrigine lowest.
- **Inattention:** Highest with valproate; lowest with lamotrigine.

Levetiracetam = 3rd line (or 2nd line in those with child-bearing potential) due to only weak evidence from one small RCT assessed by NICE guidance.

References:

- Glauser T, Ben-Menachem E, Bourgeois B, Cnaan A, Guerreiro C, Kälviäinen R, Mattson R, French JA, Perucca E, Tomson T; ILAE Subcommission on AED Guidelines. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. Epilepsia. 2013 Mar;54(3):551-63. doi: 10.1111/epi.12074. Epub 2013 Jan 25. PMID: 23350722.
- NICE. Epilepsies in children, young people and adults. April 2022 (Updated 2025) Available at https://www.nice.org.uk/guidance/ng217

Epilepsy Syndromes
Key Medicine Management Changes



Description of the syndromes simplified to be more relevant to non-specialists.

Medicine recommendations now included, to facilitate access to care close to home and enable discussion between PHC/ district hospital medical practitioners and specialists, which may occur remotely.

Subcommittee Deliberations

Valproate Risk/Benefit Summary

Why Valproate Is High-Risk (Especially in Girls & Women of Childbearing Potential)

- Major concerns: **birth defects (≈10%)** and **neurodevelopmental disorders (30–40%)** with exposure in pregnancy.
- Real-world data show **no reduction** in prescribing and little to no use of SAHPRA risk-acknowledgement forms despite multiple warnings.
- WC study: **459 pregnancies exposed** over 2 years → large potential harm.

Why Prescribing Persists

- Valproate often used for **rapid seizure control**, acute psychiatric presentations, and where alternatives are slow/complex to titrate.
- Prescribers may lack confidence with lamotrigine titration; system barriers (clinic load, inconsistent follow-up).
- Fear of seizure worsening when switching stable patients.

Reasons Against Removing Valproate Completely

- **Best or only effective treatment** for some epilepsies (e.g., CAE, myoclonic seizures, Lennox-Gastaut, Dravet).
- Many children either outgrow these epilepsies or will **never reach child-bearing potential**.
- Seizure control remains essential to reduce **morbidity and mortality**.

Valproate Use in Boys & Men

- **Reproductive risks much lower** than in women; evidence of harm is **weak and inconsistent**.
- No strong link to congenital malformations; potential fertility effects may improve when switching to lamotrigine/levetiracetam.
- Regulatory bodies (e.g., European Medicines Agency) advise **not stopping treatment suddenly**.

References:

- Mehta et al. (2021). Understanding and Responding to Prescribing Patterns of Valproic acid-Containing Medicines in Pregnant Women and Women of Childbearing Age in Western Cape, South Africa. Drug Safety 44:41–51 DOI: 10.1007/s40264-020-00987-4
- Johnson Y et.al. Department of Health Pharmacy Division in collaboration with the University of Western Cape.
- Esposto et al. (2025). Valproic acid discontinuation in girls and women of childbearing age with epilepsy: An Italian multicenter retrospective study on prescribing patterns and outcomes. Epilepsia. 00:1–11 DOI: 10.1111/epi.18281
- NICE. Valproic acid use in men: as a precaution, men and their partners should use effective contraception. 5 September 2024. Available at: https://www.gov.uk/drug-safety-update/valproic acid-use-in-men-as-a-precaution-men-and-their-partners-should-use-effective-contraception

Ensuring Adherence with SAHPRA Valproate Requirements

Need to improve use of **SAHPRA risk acknowledgement forms** for girls & women of child-bearing potential (WOCBP).

Options discussed:

- **Simplify the form** (EDP–SAHPRA discussions).
- **Restrict valproate initiation to specialists/ hospitals**
- **Train pharmacists not to dispense** without a signed form.

Unclear whether WC simplified form has improved prescribing, counselling or contraception use.

Challenge: PHC needs access to valproate for boys/men and bipolar disorder, and to ensure continuity of treatment.

Proposed approach: Pharmacists at all levels only dispense to girls & WOCBP if a **signed form/motivation** is attached; ensure **forms available at all clinics**.

Stay tuned for a **live demo** of the SAHPRA valproate risk form after this presentation

Reference: https://www.sahpra.org.za/document/valproic acid-annual-risk-acknowledgement-form/

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Other Considerations

Cost

- Lamotrigine is the least expensive option
- Using 2024 tender prices and defined daily dosing (DDD), cost of levetiracetam is similar to valproate (Refer to table 7 in Epilepsy subcommittee report).
- Therefore, expanding use of levetiracetam as a replacement for valproate is unlikely to affect overall expenditure.

Education & Training

- Limited expertise in diagnosing and managing epilepsy, especially at PHC level.
- Strengthened basic and in-service training is strongly recommended.
- BPNA's (British Paediatric Neurology Association) Paediatric Epilepsy Training course endorsed by ILAE for global roll-out.
- ILAE's Epilepsy Training in Adult Medicine (ETAM) course piloted for broader use in Africa.
- NDoH webinars help to disseminate the STGs, however additional training platforms are needed for wider reach.

Reference:
https://www.health.gov.za/wp-content/uploads/2025/06/Epilepsy-Subcommittee-Report-Version-0.1-26-May-2025.pdf

Other Considerations

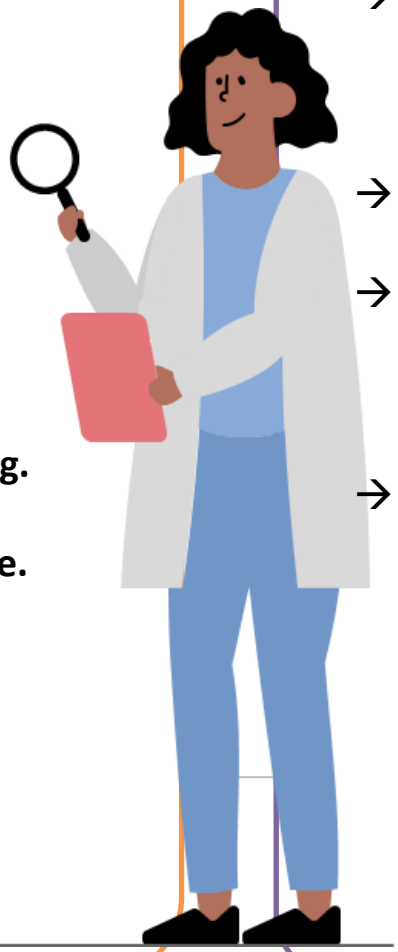
Medicine Treatment recommendations

→ **No new medicines added, but indications and hierarchy revised.**

→ **Need to strengthen guidance regarding:**

- **Post seizure follow up/ after care.**
- **Management of co-morbid neuropsychiatric neurodevelopmental, neurocognitive and other mental health conditions.**
- **Psychosocial and intersectoral care needs to reduce disability and improve wellbeing.**

→ **Considerations around affordability when expanding use of levetiracetam vs lamotrigine.**



Monitoring & Evaluation

→ **Medicine use monitoring should be linked to treatment outcome monitoring**, e.g., epilepsy rehospitalisation rates.

→ May require **new national health indicators** specific to epilepsy.

→ Affordable Medicines Directorate engaging NDoH stakeholders on the expansion of national indicators to include epilepsy.

→ Stakeholder discussions also highlight the need to **strengthen education and training programmes.**

Future Reviews and Research Recommendations

Review definitions of and clinical approach to low- versus high-risk subgroups of generalised epilepsy with tonic-clonic seizures

Re-evaluate previous reviews on use of IV valproate in status epilepticus

Affordability of expanding levetiracetam vs lamotrigine use.

Epilepsy has functional implications that require screening and intervention from a rehabilitation multidisciplinary team to prevent a disability. NEMLC advised that a thorough review regarding occupational therapy and epilepsy be conducted in the next review cycle

Review motivation and evidence for IV levetiracetam, however not yet registered in South Africa.

Evidence for efficacy of lamotrigine in juvenile absence epilepsy.

Need for rescue therapy in specific high-risk cases where the diagnosis of epilepsy is not confirmed is still to be discussed by the subcommittee.

Further research to establish best biopsychosocial practice in South Africa in terms if person-centred outcomes (prevention of seizures and improvement of quality of life)

Acknowledgements

Epilepsy Subcommittee Members

Member	Affiliation
Adj. Prof L Robertson (Chairperson)	Psychiatrist: Sedibeng District Health Services & Department of Psychiatry, University of the Witwatersrand
Dr A Gray (Vice-Chair)	Pharmacist: Division of Pharmacology, Discipline of Pharmaceutical Sciences, University of KwaZulu-Natal.
A/Prof K Cohen	Pharmacologist: Division of Clinical Pharmacology, Department of Medicine, University of Cape Town
A/Prof T Crowley	Professional Nurse: School of Nursing, University of Western Cape
Dr MV Gule	Neurologist, Groote Schuur Hospital & University of Cape Town
Ms S McGee	Insight Actuaries and Consultants
A/Prof U Mehta	Pharmacist and Pharmacovigilance Consultant: University of Cape Town
Dr J Mohale	Family Physician: Chris Hani Health District & Walter Sisulu University
Dr G Reubenson	Paediatrician: Rahima Moosa Mother and Child Hospital & Department of Paediatrics, University of the Witwatersrand
Dr S Rossouw (resigned)	Neurologist: Livingstone Hospital, Eastern Cape
Dr T Ruder	Paediatrician: Division of Community Paediatrics, School of Public Health, University of Witwatersrand
Dr J Taylor	Pharmacology Registrar: Division of Clinical Pharmacology, Department of Medicine, University of Cape Town
Prof J Wilmshurst	Paediatric Neurologist: Head of Paediatric Neurology, Red Cross War Memorial Children's Hospital

Oversight Group Members

Dr Jane Riddin

National Department of Health
Essential Drugs Program

Ms K MacQuilkan*

Consultant: Health Technology Assessment and Policy (NDoH)

Dr M Reddy*

Consultant: Health Technology Assessment and Policy (NDoH

* Acknowledgement to SAMRC, Health Systems Research Unit

THANK YOU!!

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