health
Department:
Health
REPUBLIC OF SOUTH AFRICA

SOUTH AFRICAN ADULT HOSPITAL LEVEL ESSENTIAL MEDICINES LIST
AHL CHAPTER 7: NEPHROLOGICAL/ UROLOGICAL DISORDERS
NEMLC RECOMMEDATIONS FOR MEDICINE AMENDMENTS (2020-2024 REVIEW CYCLE)

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).

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED
7.1 Nephrology disorders	Dose adjustments in CKD	New guidance added
7.1.1 Chronic kidney disease (CKD)	Description of CKD	Amended
	Common causes of CKD	Amended
	Prognosis of CKD by GFR and albuminuria categories	Reference for Figure 7.1 amended
	Salt intake restriction	Guidance amended
	Dietary Protein limit	Guidance removed
	Proteinuria screening	Guidance amended
	Furosemide,oral,IV	Dose and directions amended
	Calcium,oral	Retained, dose wording amended
	Aluminium hydroxide, oral	Short term treatment added
	Hyperparathyroidism	Timing of initiation of therapy retained
- Anaemia associated with CKD in patients on dialysis programmes	Erythropoietin Stimulating Agents (ESAs)	Added as a therapeutic class
	Epoetin alfa and epoetin beta	Retained as the example of class in the STG
	Methoxy polyethylene glycol epoetin beta	Added as a therapeutic alternative
	Darbepoetin alfa	Added as a therapeutic alternative
	Erythropoeitin IV/SC	Prescriber level retained
-Referral	Nephrotic-range proteinuria	Referral for possible kidney biopsy added
7.1.2 Glomerular disease and nephritic syndrome	Amlodipine,oral	Retained
	Furosemide,oral	Retained, moved to first-line diuretic alternative
	Hydrochlorothiazide,oral	Retained
7.1.3 Nephrotic Syndrome	Nephrotic-range proteinuria	Definition amended
7.1.4 Acute Kidney Injury	Acute dialysis	Indications amended
	Metabolic acidosis	Definition amended
	Hyperkalaemia	Definition and guidance on management amended
	Calcium gluconate 10%, slow IV	Retained, Directions for use amended
	Dextrose 50%, IV	Retained, Directions for use amended
	Salbutamol nebulisation	Retained, dose and administration guidance added
	Sodium polystyrene sulfonate, oral/rectal	Retained
	Lactulose, oral	Retained
	Sorbitol, oral	Not added
7.2.2 Hypokalaemia:	Description	Amended
	Potassium chloride, oral	Retained, Potassium chloride oral solution added
	Potassium, IV	Retained
7.2.3 Hypernatraemia	Description	Amended
7.2.4 Hyponatraemia:	Description	Retained, caution revised
7.3.1 Haematuria	Praziquantel, oral	Retained, dosing guidance amended

7.3.2 Urinary Tract Infection (UTI) Complicated community acquired cystitis	Ciprofloxacin, oral	Retained, treatment duration amended
7.3.5 Benign prostatic hyperplasia - Dose titration to clinical effect	Alpha blocker, oral	Retained as a therapeutic class
	Doxazosin, oral, immediate-release (1mg)	Added as an example of class
	Doxazosin, oral, long-acting (4mg)	Added to the therapeutic interchange database
	Tamsulosin, oral (0.4mg)	Added to the therapeutic interchange database
	Terazosin, oral (1 and 5mg)	Added to the therapeutic interchange database
	Alfuzosin, oral (10mg)	Added to the therapeutic interchange database
	Silodosin, oral (4mg)	Added to the therapeutic interchange database
7.3.5 Benign prostatic hyperplasia *-standard maintenance dose*	Alpha blocker, oral	Retained as a therapeutic class
	Doxazosin, oral, immediate-release (4mg)	Added as an example of class
	Doxazosin, oral, long-acting (4mg)	Added to the therapeutic interchange database
	Tamsulosin, oral (0.4mg)	Removed as an example of class and added to the therapeutic interchange database
	Terazosin, oral (10mg)	Retained in the therapeutic interchange database
	Alfuzosin, oral (10mg)	Retained in the therapeutic interchange database
	Silodosin, oral (8mg)	Retained in the therapeutic interchange database

7.1. NEPHROLOGY DISORDERS

Dose adjustments in CKD: New guidance added

Some principles of dosing medication in patients with chronic kidney disease (CKD) and acute kidney injury (AKI) have been added to the STG guidance. The 2021 CKD Epidemiology Collaboration (CKD-EPI) measure of eGFR has been added as a reliable measure of eGFR in the STG. It has acceptable performance characteristics and potential consequences that do not disproportionately affect any one group of individuals[1].

The STG has been amended as follows:

CAUTION
Check all medicines for possible dose adjustment based on eGFR~~/CrCl~~

Principles of dosing medication in patients with Chronic Kidney Disease (CKD) and Acute Kidney Injury (AKI)

In the setting of kidney failure all prescribed medications should be reviewed regularly to ensure that they are safe and at the correct dose for the estimated glomerular filtration rate [eGFR]. Currently, the most reliable measure of eGFR is CKD-EPI in adults and Schwartz equation for children. Nephrotoxic drugs should be avoided in the setting of any kidney dysfunction. Prior to starting any medication, review for previous drug allergies and adverse events. Monitoring of drug toxicity and levels is important where available (e.g. aminoglycoside).

In AKI, the eGFR is not reliable as kidney function changes rapidly. Therefore, it is essential to monitor eGFR and doses of medications regularly.

[1] Inker LA, Eneanya ND, Coresh J, et al., for the Chronic Kidney Disease Epidemiology Collaboration. New Creatinine- and Cystatin C-Based Equations to Estimate GFR without Race.N Engl J Med. 2021 November 4, 385 (19):1737-1749.

~~The doses of many medicines need to be adjusted in renal impairment.~~ Recommendations for medicines that require dose adjustment in renal impairment can be found in the South African Medicine Formulary (SAMF), package insert, and from many online resources e.g.: http://www.globalrph.com/index_renal.htm

7.1.1 CHRONIC KIDNEY DISEASE (CKD)

Description: Amended

The description has been amended in line with the KDIGO 2012 CKD Guidelines[2]. New nomenclature is "kidney disease" which encompasses both acute kidney injury and chronic kidney disease. The word “chronic renal disease” has been replaced with the word “chronic kidney disease” throughout the chapter.

Common causes of CKD: Table 7.1 has been amended to include additional causes of CKD.

The STG has been amended as follows:

DESCRIPTION

Evidence of structural damage (proteinuria/haematuria) or loss of kidney function (eGFR <60 mL/min/1.73 m^2), present for >3 months. ~~Structural or functional kidney damage present for >3 months, with or without a decreased estimated glomerular filtration rate (eGFR).~~

Markers of kidney damage include:

- proteinuria; (UPCR = urine protein to creatine ratio; UACR = urine albumin to creatine ratio)
  - Severely increased: UPCR >0.05 g/mmol (>0.500 g/g); UACR > 30 mg/mmol (300 mg/g)
  - Moderately increased: UPCR 0.015-0.05 g/mmol (0.15-0.5 g/g); UACR 3 -30 mg/mmol (30-300 mg/g)
  - Normal or mildly increased: UPCR <0.015 g/mmol (<0.15 g/g); UACR <3 mg/mmol (<30 mg/g)
  - ~~ACR-urine (albumin creatinine ratio) ≥30 mg/g or ≥3 mg/mmol; PCR-urine (protein creatinine ratio) >0.05 g/mmol~~
- urine dipstick positive for blood and/or protein (for females with haematuria: exclude current menstrual cycle)
- increased serum creatinine or low eGFR <60 mL/min/1.73 m^2
- abnormal kidneys on ultrasound, e.g. polycystic, small in size and scarring
- abnormalities on ~~renal~~kidney biopsy
- electrolyte abnormalities due to tubular disorders
- history of ~~kidney~~ renal transplant

eGFR calculator online access:
https://www.kidney.org/apps/professionals/egfr-calculator

Table 7.1: Common causes of CKD

Category	Example
Vascular	Hypertension, renal artery stenosis, vasculitis etc.
Glomerular diseases	Diabetes, autoimmune diseases (e.g. lupus nephritis), chronic systemic infections (e.g. HIV, HBV, syphilis), drugs, neoplasia
Tubulointerstitial diseases	UTI, drug-induced interstitial nephritis (e.g. rifampicin, allopurinol, fluoroquinolones, sulphonamides, beta-lactam antibiotics, proton pump inhibitors, nonsteroidal anti-inflammatory drugs)
Structural	Polycystic kidney/s ~~renal artery stenosis, small or enlarged kidneys~~, renal masses, obstruction (stones, strictures)
Others	Congenital

Level of Evidence: Low certainty

[2] Eknoyan G, Lameire N. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-150.

Prognosis of CKD by GFR and albuminuria categories: *Reference for Figure 7.1 amended*

The reference for figure 7.1: Prognosis of CKD by GFR and albuminuria categories has been amended to the latest version of KDIGO guidelines 2024[3]. It is to be noted that not all the sections of the STG were reviewed in line with the updated KDIGO guidelines due to the limited timelines for finalisation of the chapter for publication. Further updates are to be prioritised in the next review cycle.

The STG has been amended as follows:

Figure 7.1: Prognosis of CKD by GFR and albuminuria categories: KDIGO 2024~~12~~

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				ACR* <30 mg/g <3 mg/mmol	ACR* 30–300 mg/g 3–30 mg/mmol	ACR* >300 mg/g >30 mg/mmol
eGFR categories (ml/min per 1.73m²) - description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60 –89			
	G3a	Mildly to moderately decreased	45–59			Refer
	G3b	Moderately to severely decreased	30–44		Refer	Refer
	G4	Severely decreased	15–29	Refer	Refer	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

ACR: albumin to creatinine ratio in urine specimen.

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red: very high risk; A1, A2, A3 = categories of albuminuria; G1, G2, G3a, G3b, G4, G5 = categories of eGFR

~~Adapted from: Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney Int. 2014 Jan;85(1):49-61. https://www.ncbi.nlm.nih.gov/pubmed/24284513~~

GENERAL MEASURES

Salt intake: Guidance amended.

Guidance to limit total sodium chloride intake (including salt in food) in order to reduce blood pressure and improve volume control has been updated in the STG in alignment with the updated guidelines[4,5,6]. In addition, examples of nephrotoxic drugs/agents to avoid have been added.

The STG has been amended as follows:

» Limit total salt intake (including salt in food) ~~to < 2300 mg per day of sodium chloride~~. Consult with dietician as required.

[3] Stevens PE, Ahmed SB, Carrero JJ, Foster B, Francis A, Hall RK, Herrington WG, Hill G, Inker LA, Kazancıoğlu R, Lamb E. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney international. 2024 Apr 1;105(4):S117-314.

[4] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024 Apr;105(4S):S117-S314. doi: 10.1016/j.kint.2023.10.018. PMID: 38490803.

[5] 5 ways to 5 grams | Heart & Stroke Foundation | South Africa [Internet]. Heart & Stroke Foundation | South Africa. 2018 [cited 2024 Aug 1]. Available from: https://heartfoundation.co.za/topical_articles/5-ways-to-5-grams/

[6] Why should I limit the salt in my food? - MyDynamics [Internet]. MyDynamics. 2021 [cited 2024 Aug 1]. Available from: https://www.mydynamics.co.za/nutrition/why-should-i-limit-the-salt-in-my-food/

» Avoid nephrotoxic ~~medicine~~ drugs/agents like NSAIDs, aminoglycoside antibiotics and radiocontrast media.
» Regular exercise~~,~~and target BMI (BMI <25 kg/m^2) according to South African ~~calculations~~ reference ranges.

Level of Evidence: Low certainty

Dietary Protein limit: Guidance removed

The recommendation to limit dietary protein intake to 0.8 g/kg/day has been removed from the STG, A Systematic Review of 17 RCT's (n=2996) where 10 studies compared a low protein (0.5 to 0.6 g/kg/day) diet with a normal protein(≥ 0.8 g/kg/day) diet in participants with CKD categories 3a and 3b (9 studies) or 4 (one study), found that there was little or no difference in the numbers of participants who died from all causes (5 studies 1680 participants: RR 0.77, 95% CI 0.51 to 1.18; 13 fewer deaths per 1000). In addition, a low protein diet was found to make little or no difference in the number of participants who reached End-Stage Kidney Disease (ESKD) compared with a normal protein diet (6 studies, 1814 participants: RR 1.05, 95% CI 0.73 to 1.53; 7 more per 1000 reached ESKD)[7].

The STG has been amended as follows:

~~» Limit dietary protein intake to 0.8 g/kg/day.~~

Level of Evidence: Moderate certainty

Proteinuria screening: Guidance amended

In the STG guidance for proteinuria screening, the definition of significant proteinuria has been amended to equal a spot urine PCR of >0.15 g/mmol in line with guideline recommendations[1]. The recommendation to perform a UACR if the spot urine protein measures less than 1+ has been retained.

The STG has been amended as follows:

» Screen for proteinuria.
  - If urine dipstick 1+ or greater, repeat on a properly collected midstream urine specimen on another occasion.
  - If proteinuria persists, quantify protein with a spot urine protein creatinine ratio. Significant proteinuria = spot urine PCR of >0.15 g/mmol.
  - If urine dipstick < 1+, ACR.

Rehabilitation support: added

Aligned with PHC STGs and EML, Inspiratory muscle training shown to improve inspiratory and expiratory muscles and functional capacity[8]. Multidisciplinary care likely decreases rapid progression of renal disease[9] and exercise shown to improve sleep quality amongst adults and children with end-stage kidney disease[10].

[7] Hahn D, Hodson EM, Fouque D. Low protein diets for non-diabetic adults with chronic kidney disease. Cochrane Database Syst Rev. 2020 Oct 29;10(10):CD001892. doi: 10.1002/14651858.CD001892.pub5. PMID: 33118160; PMCID: PMC8095031.

[8] de Medeiros AIC, Fuzari HKB, Rattesa C, Brandão DC, de Melo Marinho PÉ. Inspiratory muscle training improves respiratory muscle strength, functional capacity and quality of life in patients with chronic kidney disease: a systematic review. J Physiother. 2017 Apr;63(2):76-83. https://pubmed.ncbi.nlm.nih.gov/28433237/

[9] Hsu HT, Chiang YC, Lai YH, Lin LY, Hsieh HF, Chen JL. Effectiveness of Multidisciplinary Care for Chronic Kidney Disease: A Systematic Review. Worldviews Evid Based Nurs. 2021 Feb;18(1):33-41. https://pubmed.ncbi.nlm.nih.gov/33247619/

[10] Natale P, Ruospo M, Saglimbene VM, Palmer SC, Strippoli GF. Interventions for improving sleep quality in people with chronic kidney disease. Cochrane Database Syst Rev. 2019 May 26;5(5):CD012625. https://pubmed.ncbi.nlm.nih.gov/31129916/

MEDICINE TREATMENT

Metformin,oral and risk of lactic acidosis: Guidance retained.
Additional references have been included in the chapter to support the current STG guidance to discontinue metformin in avoidance of lactic acidosis when the eGFR <30 mL/minute/1.73 m^2 [11,12].

Furosemide,oral,IV: Dose and *directions amended*
For the management of fluid overload and oedema, the dose of furosemide has been amended from an oral dose of 40mg 12 hourly to a dose of 20mg upto 160mg oral/IV in divided doses[13]. Additional guidance through an external comment has also been added to first establish an effective dose of furosemide and ascertain that the prescribed dose results in urination within 1-2 hours of intake until urination ensues. In addition, guidance has been added to dose furosemide at specific times in the morning and afternoon (eg 8 AM and 2 PM) to avoid a nighttime dose.

The STG has been amended as below:

Fluid overload and oedema

- Furosemide, oral or IV, 20 to 80mg daily, as a single or divided doses, initiating at the lowest effective dose and titrating upwards. Dose may be increased to 160mg IV or oral daily in divided doses.
- First establish an effective dose and ascertain if urination occurs within 1-2 hours of intake. If urination does not occur within 1-2 hours, the dose should be increased further until urination ensues.
- Diuretic action starts within 60 minutes of dose, hence divided doses should be given in the morning and afternoon eg 8AM and 2PM. ~~40 mg 12 hourly~~

LoE:IVb[i]

When fluid overloaded and eGFR <60 mL/minute/1.73 m^2, start:

- Furosemide, oral or IV, 40 mg in divided doses (eg. 8 a.m. and 2 p.m.) ~~12 hourly.~~
  - Titrate to a maximum of 500 mg in divided doses (eg. 8 a.m. and 2 p.m.)
  - Furosemide is ineffective when patients are on dialysis and anuric.

Level of Evidence: Low certainty

Calcium, oral: *Retained, dose wording amended*
For the management of hypocalcaemia and hyperphosphatemia, the STG recommended dose for calcium has been amended to exclusively refer to the elemental calcium requirements in relation to calcium-phosphate product.

The STG has been amended as follows:

Calcium (elemental), oral, (Calcium carbonate),500 mg 8 hourly with meals if calcium-phosphate product <4.4 $mmol^2/L^2$.

Aluminium hydroxide, oral: Short term treatment added
In patients not on dialysis, an external comment, to add aluminium hydroxide if the calcium-phosphate product >4.4 $mmol^2/L^2$ for two weeks only, then switching to calcium carbonate, oral, has been accepted[14]. This aims to achieve adequate control of serum phosphorus without development of hypercalceamia and in addition, to avoid long term aluminium retention toxicity. This recommendation is based on local practice at Tygerberg Hospital.

[11] Salpeter SR, Greyber E, Pasternak GA, Salpeter EE. Risk of fatal and nonfatal lactic acidosis with metformin use in type 2 diabetes mellitus. Cochrane Database Syst Rev. 2010 Apr 14;2010(4):CD002967. doi: 10.1002/14651858.CD002967.pub4. PMID: 20393934; PMCID: PMC7138050.

[12] Orloff et al. Safety and efficacy of metformin in patients with reduced renal function: a systematic review. Diabetes Obes Metab 2021. 23(9): 2035-2047.

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

[14] Mudge DW, Johnson DW, Hawley CM, Campbell SB, Isbel NM, van Eps CL, Petrie JJ. Do aluminium-based phosphate binders continue to have a role in contemporary nephrology practice? BMC Nephrol. 2011 May 13;12:20. doi: 10.1186/1471-2369-12-20. PMID: 21569446; PMCID: PMC3107169.

The STG has been amended as follows:

Patients with CKD stage 3–5, not on dialysis:
Hyperphosphataemia and/or hypocalcaemia:

- Calcium ~~carbonate~~ (elemental), oral ~~equivalent to elemental calcium~~ (calcium carbonate), ~~approximately~~ 500 mg 8 hourly with meals if calcium phosphate product <4.4 $mmol^2/L^2$.
    - Increase to approximately 1 g 8 hourly with meals if hyperphosphatemia persists.
- Aluminium hydroxide 300mg/5ml, oral, 10 mL with meals if calcium-phosphate product >4.4 $mmol^2/L^2$, for two weeks only, then switch to calcium carbonate~~. Increase to approximately 1 g 8 hourly with meals, if hyperphosphatemia persists.~~

Hypocalcaemia and low or normal serum phosphate:

- Calcium carbonate (elemental), oral (calcium carbonate)~~,equivalent to elemental calcium~~, ~~approximately~~ 500 mg 8 hourly ~~between~~ two hours after meals, increase to approximately 1 g 8 hourly between meals.

Level of Evidence: Very low certainty

Hyperparathyroidism: Timing of initiation of therapy retained
The KDIGO guidelines recommends maintaining the PTH between 2 and 9 times ULN in dialysis patients[15]. Therefore, for hyperparathyroidism, the STG currently recommends initiating therapy when PTH levels >2 times upper limit of normal (ULN) range: (Specialist initiated). A comment to initiate therapy when the PTH level is >9 times the ULN was not accepted.
Level of Evidence: Low certainty

Anaemia with CKD in patients on dialysis programmes
Erythropoietin Stimulating Agents (ESAs): *added as a therapeutic class*
Epoetin alfa and epoetin beta: *retained as the example of class in the STG*
Methoxy polyethylene glycol epoetin beta: *added as a therapeutic alternative*
Darbepoetin alfa: *added as a therapeutic alternative*

Refer to the medicine review:

ESAs for Anaemia in CKD_Class review_A(

Recommendation: The NEMLC has recommended that ESAs be recommended as a therapeutic group for patients with anaemia of chronic kidney disease (*strong recommendation).*
Rationale: Epoetin alfa and epoetin beta; methoxy polyethylene glycol epoetin beta and darbepoetin alfa are equally effective in increasing haemoglobin and preventing blood transfusions in chronic kidney disease. Harms and cardiovascular risks are similar and dose proportional. This has been demonstrated in several systematic reviews comparing various agents in various situations.
Level of Evidence: Moderate certainty evidence (Meta-analysis and systematic review; III Guidelines)

NEMLC RECCOMENDATION (MEETING OF 23 JUNE 2022):

The NEMLC accepted the proposal that erythropoiesis-stimulating agents be recommended as a therapeutic class. Furthermore, with the final ratification of the respective nephrology/urology chapter, NEMLC recommended that a circular be disseminated guiding on comparative dosing, dose switching and relevant pragmatic issues.

[15] Eknoyan G, Lameire N. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. 2013;3(1):1-150.

Therapeutic Interchange database

The following updates to the therapeutic interchange database were supported by the Committee:

Section	Indication	Therapeutic class	Strength	Unit	Formulation
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin beta	2000 iu	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin beta	4000 iu	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin beta	6000 iu	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin beta	10000 iu	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin beta	30000 iu	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin alfa	2000 iu/0.5ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin alfa	4000 iu/0.4ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin alfa	6000 iu/0.6ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin alfa	10000 iu/ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Epoetin alfa	40000 iu/ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	50 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	75 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	100 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	120 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	150 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	200 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	250 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Methoxy Polyethylene Glycol-Epoetin Beta	360 mcg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	10 µg/0.4ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	20 µg/0.5ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	30 µg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	40 mcg	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	50 mcg	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	60 µg/0.3ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	80 mcg	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	100 mcg	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on	Erythropoietin Stimulating Agents	Darbepoetin alfa	150 µg/0.3ml	INJ

	dialysis	(ESA)			
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	300 µg/0.6ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	100 mg/5ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	250 µg/0.5ml	INJ
7.1.1 CHRONIC KIDNEY DISEASE (CKD)	Anaemia associated with CKD in patients on dialysis	Erythropoietin Stimulating Agents (ESA)	Darbepoetin alfa	500 µg/0,4ml	INJ

Erythropoietin IV/SC: Prescriber level retained

Erythropoietin Stimulating Agents (ESA) are currently recommended in the STG for patients who are on a dialysis programme and are managed by clinicians with the relevant experience. An external comment to reserve initiation of treatment for only specialists was not supported. In addition, B12 folate deficiency has been added as a factor which may aggravate anaemia.

The STG has been amended as follows:

Definitive treatment, e.g. transplantation, usually improves anaemia. It is important to identify factors likely to aggravate anaemia, e.g. iron deficiency, ~~and~~ infection, and vitamin B12 and folate deficiency.

Nephrotic-range proteinuria: Referral for possible kidney biopsy added

The STG has been amended, adding a recommendation for a referral to a specialist for a possible kidney biopsy in patients with nephrotic-range proteinuria (UPCR >0.35 g/mmol) or nephrotic syndrome. The indication for a biopsy was deemed to be a specialist decision after referral from the district level.

The STG has been amended as follows:

CONSULT WITH A SPECIALIST AT THE LOCAL REFERRAL CENTRE

» Unknown cause of kidney failure.
» Rapid deterioration in kidney ~~renal~~ function.
» Resistant hypertension despite appropriate medication and adherence.
» All patients with persistent proteinuria: on urine dipstick ≥ 1+ or proteinuria >1 g/24 hours (UPCR >0.1 g/mmol).
» Patients with nephrotic-range proteinuria (UPCR >0.35g/mmol) or nephrotic syndrome should be referred for possible kidney biopsy

REFERRAL

» All ESKD ~~ESRD~~ patients who may qualify for long term dialysis programs. See section 7.1.5: Kidney ~~renal~~ replacement therapy.
» CKD stage 3 and above (see ~~prognosis table~~ Figure 7.1: Prognosis of CKD by GFR and albuminuria categories).

7.1.2 GLOMERULAR DISEASE AND NEPHRITIC SYNDROME

Furosemide, oral: Retained, amended to first-line diuretic alternative
Amlodipine, oral: Retained
Hydrochlorothiazide, oral: Retained

For fluid overload if hypertension present, oral furosemide has been recommended as the first choice diuretic in combination treatment with amlodipine. Loop diuretics may provide a greater natriuretic effect than thiazide diuretics[16] [17] [18].

[16] KDIGO. Clinical practice guideline for the management of glomerular diseases.2021 Available from: https://www.kidney-international.org/action/showPdf?pii=S0085-2538%2821%2900562-7

[17] Crew R. J., Radhakrishnan J., Appel G. (2004). Complications of the nephrotic syndrome and their treatment. Clin. Nephrol. 62 245–259. 10.5414/CNP62245

[18] Jo W, Koh ES, Chung S. Therapeutic roles of thiazides and loop diuretics in blood pressure control and renal protection against chronic kidney disease. Clin Hypertens. 2023 May 15;29(1):14. doi: 10.1186/s40885-023-00238-5. PMID: 37183259; PMCID: PMC10184374.

The STG has been amended FROM:

MEDICINE TREATMENT

Fluid overload

- Furosemide, as a slow IV bolus, 80 mg.
  - Avoid unnecessary intravenous fluids.

If hypertension present: I12.0/I12.9

Diastolic BP >100 mmHg or systolic BP >150 mmHg:

- Amlodipine, oral, 5 mg as a single dose.

AND

- Hydrochlorothiazide, oral, 25 mg (if eGFR ≥30 mL/minute).

OR

- Furosemide, oral, 40–80 mg (if eGFR <30 mL/minute).

TO

MEDICINE TREATMENT

Fluid overload

- Furosemide, as a slow IV bolus, 80 mg.
  - Avoid unnecessary intravenous fluids.

If hypertension present: I12.0/I12.9

Diastolic BP >100 mmHg or systolic BP >150 mmHg:

- Amlodipine, oral, 5 mg as a single dose.

AND

- Furosemide, oral, 40–80 mg (if eGFR <30 mL/minute).

OR

- Hydrochlorothiazide, oral, 25 mg (if eGFR ≥30 mL/minute).

Level of Evidence: Very low certainty

7.1.3 NEPHROTIC SYNDROME

Nephrotic-range proteinuria: Definition amended

The definition of nephrotic-range proteinuria has been amended in line with guidelines [19]. In addition, a statement of emphasis included to highlight the need for specialist consultation for the diagnosis of nephrotic syndrome.

The STG has been amended as follows:

DESCRIPTION

Glomerular disease characterised by:

» Nephrotic-range ~~severe~~ proteinuria, i.e.: UPCR >0.3~~2~~5 g/mmol

and

- oedema,
- hypoalbuminaemia, and
- hyperlipidaemia.

The cause cannot be determined accurately without a kidney biopsy. With the exception of diabetic nephropathy, all other causes of nephrotic syndrome require specialist consultation.

Level of Evidence: Low certainty

[19] KDIGO. Clinical practice guideline for the management of glomerular diseases.2021 Available from: https://www.kidney-international.org/action/showPdf?pii=S0085-2538%2821%2900562-7

7.1.4 ACUTE KIDNEY INJURY

Acute dialysis: Indications amended

Pulmonary oedema refractory to medical treatment has been added as an indication for acute dialysis.

Metabolic acidosis: Definition amended

The PH definition of severe metabolic acidosis has been reduced from PH<7.2 to PH<7.15[20]. The STG has also been amended to list *severe metabolic acidosis (PH <7.15) refractory to medical therapy* and *severe hyperkaleamia (Potassium >7 mmol/L) refractory to medical therapy* as independent indications for acute dialysis.

The STG has been amended as follows:

Acute dialysis
Discuss all cases with the referral centre.
Common indications for acute dialysis include:
» Pulmonary oedema refractory to medical therapy ~~and anuria~~ ~~and~~
» Severe metabolic acidosis **(**pH < 7.1~~2~~5) refractory to medical therapy
» Severe hyperkalaemia (>7 mmol/L) refractory to medical therapy
» Uraemic complications, e.g. pericarditis, encephalopathy and bleeding.
» Medication overdose if due to dialysable toxin. See section 19: Exposure to poisonous substances.

LoE:IVb[ii]

Level of Evidence: Low certainty

Hyperkalaemia: Definition amended

The STG has been amended with a change of the definition of hyperkalaemia from Serum K+ >6.5 mmol/L to >6.0 mmol/L [21,22, 23,24]

Serum K^+ >6.0~~5~~ mmol/L.

Level of Evidence: Low certainty

Hyperkalaemia, Emergency measures

Calcium gluconate 10%, slow IV:Guidance amended

When using calcium gluconate for hyperkalaemia, additional dosing guidance was added for consideration of subsequent doses if ECG changes persist.

Dextrose 50%, IV: Guidance amended

The STG has been amended to recommend dextrose 50% IV and insulin sequentially as opposed to using

[20] Gaudry, S., Hajage, D., Martin-Lefevre, L. et al. The Artificial Kidney Initiation in Kidney Injury 2 (AKIKI2): study protocol for a randomized controlled trial. Trials 20, 726 (2019). https://doi.org/10.1186/s13063-019-3774-9

[21] Clase CM, Carrero JJ, Ellison DH, Grams ME, Hemmelgarn BR, Jardine MJ, Kovesdy CP, Kline GA, Lindner G, Obrador GT, Palmer BF, Cheung M, Wheeler DC, Winkelmayer WC, Pecoits-Filho R; Conference Participants. Potassium homeostasis and management of dyskalemia in kidney diseases: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. Kidney Int. 2020 Jan;97(1):42-61. doi: 10.1016/j.kint.2019.09.018. Epub 2019 Oct 10. PMID: 31706619.

[22] Humphrey T, Davids MR, Chothia MY, Pecoits-Filho R, Pollock C, James G. How common is hyperkalaemia? A systematic review and meta-analysis of the prevalence and incidence of hyperkalaemia reported in observational studies. Clin Kidney J. 2021 Dec 2;15(4):727-737. doi: 10.1093/ckj/sfab243. PMID: 35371465; PMCID: PMC8967676.

[23] Chothia MY, Chikte U, Zemlin A, Moodley D, Fitchat N, Wessels A, van Vuuren E, Davids T, Davids MR. Outcomes of hospitalised patients with hyperkalaemia at a South African tertiary healthcare centre. EClinicalMedicine. 2022 Jul 1;50:101536. doi: 10.1016/j.eclinm.2022.101536. PMID: 35818351; PMCID: PMC9270242.

[24] National kidney foundation.Best practices in managing hypekaleamia in patinets with chronic kidney disease.2016.Available from :https://www.kidney.org/sites/default/files/02-10-7259_DBH_Best-Practices-in-Managing-Hyperkalemia-in-CKD.pdf

concurrently, this is in line with clinical guidelines[12, 25].

Salbutamol nebulisation: Dose amended

The dose of salbutamol has been amended from 5mg to a range of 10-20mg in line with guidelines[12]. In addition, administration guidance has been added.

The STG has been amended as follows:

Emergency measures

- Calcium gluconate 10%, slow IV bolus, 10 mL over 10 minutes. Subsequent doses should be considered if ECG changes persist after 5 minutes or recur
- ~~Maximum dose: 40 mL.~~
- Dextrose 50%, IV ~~continuous~~ bolus ~~infusion~~, 100 mL followed by ~~with~~ soluble insulin, 10 units administered ~~over 15-30 minutes~~ as a push over 5 minutes.
  - Monitor blood glucose levels hourly up to 6 hours post-insulin administration.

AND

- Salbutamol nebulisation, 10-20 mg. *LoE:IIb[iii]*
  - Dilute Salbutamol 0.5% (5 mg/mL), solution, 1 mL (5 mg) salbutamol 0.5% solution made up to 4 mL with sodium chloride 0.9%.

Level of Evidence: Moderate certainty

Sodium polystyrene sulfonate, oral/rectal: Retained

Lactulose, oral: Retained

Sorbitol, oral: Not Added

For acute kidney injury, where dialysis is not feasible, the STG currently recommends sodium polystyrene sulfonate, oral in combination with oral lactulose or sodium polystyrene sulfonate (enema) as a short-term measure for the management of hyperkalaemia. An external comment (Expert opinion) to include monotherapy laxatives (lactulose or sorbitol) as an alternative for treating hyperkalaemia associated with acute kidney injury was not recommended due to lack of evidence in support of the comment. Lactulose has been retained in combination with oral sodium polystyrene for this indication.

The STG has been amended as follows:

These are short-term measures - patients should be dialysed or if this is not feasible:

- Sodium polystyrene sulfonate, oral, 15 g with 15 mL lactulose, 6 hourly.

OR

- Sodium polystyrene sulfonate, rectal, 30–60 g as an enema.
  - After 8 hours, wash out with phosphate enema.

  Note: Rectal administration is less effective.

~~OR~~

- ~~Laxatives alone e.g. oral lactulose or sorbitol (dose should be increased until diarrhoea ensues).~~

7.2.2 HYPOKALAEMIA

Description: Amended

Prolonged QT interval and bradycardia have been included as signs of hypokalaemia. Further caution has been added to identify and treat the course of hypokalaemia with potential causes of hypokalaemia added in the STG guidance.

The STG has been amended as follows:

[25] Chothia MY, Humphrey T, Schoonees A, Chikte UME, Davids MR. Hypoglycaemia due to insulin therapy for the management of hyperkalaemia in hospitalised adults: A scoping review. PLoS One. 2022 May 12;17(5):e0268395. doi: 10.1371/journal.pone.0268395. PMID: 35552566; PMCID: PMC9097985.

Signs of hypokalaemia: cardiac arrhythmias as well as ECG abnormalities (Prolonged QT interval, bradycardia ~~ST – segment changes).~~
Identify the cause and treat/remove the cause! It is usually due to gastro-intestinal losses (~~vomiting~~ diarrhoea) or kidney ~~renal~~ losses (diuretic therapy, hyperaldosteronism, vomiting).

Potassium chloride oral: Retained
Potassium chloride oral solution: Added
Potassium, IV: Retained
As the total body potassium deficit in patients with hypokalaemia may be large, in order to rapidly replenish stores, potassium chloride oral solution has been added to the STG as an alternative to potassium oral tablets. The formula for the compounding of potassium chloride solution has been included in Appendix IV: Extemporaneous preparations. Editorial amendments have also been made to the text for better clarity.

The STG has been amended as follows:

For chronic asymptomatic hypokalaemia, look for and manage the cause:
- Potassium chloride, oral, 600 mg, 1–2 tablets 8 hourly.
    - Each 600 mg potassium chloride tablet contains 8 mmol of potassium chloride.
    - Titrate according to response to therapy.
    - Maximum daily dose: 6 g. (i.e.10 tablets per day in divided doses).
    - Review potassium levels after 4 weeks.

OR
- Potassium chloride solution (1g/5ml) 10-30 mL daily in divided doses PO up to 6 g. (See Appendix IV: Extemporaneous preparations for the preparation formula for adults).

Note: Routine supplementation with potassium chloride in patients who are on diuretics is usually inappropriate. Co-administration of ACE-inhibitors and/or spironolactone counteracts the hypokalaemia from furosemide or thiazides. In patients that develop hypokalaemia while using potassium-sparing diuretics or ACEi/ARBs, consider underlying primary hyperaldosteronism.

For mild to moderate hypokalaemia in a non-vomiting patient (potassium level usually 3–3.4 mmol/L):
- Potassium chloride, oral, 1 200 mg (2 tablets) 8 hourly.
    - Each 600 mg potassium chloride tablet contains 8 mmol of potassium chloride.
    - Titrate according to response to therapy.
    - Maximum daily dose: 6 g (i.e.10 tablets per day in divided doses). ~~Maximum daily dose: 6 g.~~
    - Continue treatment until the serum potassium concentration is persistently above 3.5 mmol/L and symptoms or signs have resolved.

OR
Potassium chloride solution (1g/5ml), oral, 10-30 mL daily in divided doses up to 6 g. (See Appendix IV: Extemporaneous preparations for the preparation formula for adults.

For severe, symptomatic hypokalaemia:
- Potassium chloride, IV by peripheral line, 40 mmol in 1 L of 0.9% or 0.45% sodium chloride, mixed thoroughly.
    - Administer over 3 hours, or up to ~~at~~ a maximum rate of 20 mmol per hour ~~over 3 hours~~. Beware of volume overload (See Appendix II, for individual dosing and monitoring for response and toxicity).
    - Repeat as required, monitoring potassium serum levels after each replacement dose.
    - One ~~P~~potassium chloride 15% 10 mL ampoule contains 20 mmol potassium.

7.2.3 HYPERNATREAMIA

Description: Amended
A revised description for hypernatremia has been included in the STG.

The STG has been amended as follows:

In patients who develop hypernatraemia outside of the hospital, it is usually due to ~~inadequate water intake~~ water losses (decreased thirst sensation or inability to drink water (delirium/reduced consciousness), ~~or due to~~ gastro-intestinal losses (diarrhoea ~~vomiting, diarrhoea~~) or renal losses (diabetes insipidus ~~osmotic diuresis, furosemide~~).

In hospitalised, critically ill patients it is usually the result of sodium gain (administration of too much sodium-containing intravenous solutions).

7.2.4 HYPONATRAEMIA

Description: Retained, caution revised

The caution in this section has been revised highlighting to monitor the sodium levels in order to prevent the rapid overcorrection of chronic hyponatraemia. The STG now recommends minimum correction of below Na <8 mmol/L per day[26,27] in line with guidelines.

The STG has been amended as follows:

CAUTION

Rapid correction of chronic hyponatraemia may lead to ~~central pontine myelinolysis~~ osmotic demyelination syndrome, which is often irreversible and fatal. Sodium should be frequently monitored, and increases should be <~~9~~8 mmol/L per day.

Level of Evidence: Low certainty

7.3.1 URINARY TRACT INFECTION (UTI)

Praziquantel oral: *Retained, dose amended*

In line with the PHC STG, the dose for praziquantel oral, has been revised to a weight-based dosing schedule (40mg/kg, as a single dose). The title of Figure 7.3 has been amended to (Approach to haematuria)

Figure 7.3: Approach to haematuria has been amended as follows:

Schistosomiasis (bilharzia) is a common cause of haematuria
Treat with:

- Praziquantel, oral, ~~3g,~~ 40mg/kg, as a single dose

7.3.2 URINARY TRACT INFECTION (UTI)

Gentamicin: *Retained, guidance amended*

For uncomplicated community acquired cystitis, Gentamicin IM has been retained, additional text highlighting that therapeutic drug monitoring is not required has been added.

The STG has been amended as follows:

[26] Verbalis JG, Goldsmith SR, Greenberg A, Korzelius C, Schrier RW, Sterns RH, Thompson CJ. Diagnosis, evaluation, and treatment of hyponatremia: expert panel recommendations. Am J Med. 2013 Oct;126(10 Suppl 1):S1-42. doi: 10.1016/j.amjmed.2013.07.006. PMID: 24074529.

[27] Spasovski G, Vanholder R, Allolio B, Annane D, Ball S, Bichet D, Decaux G, Fenske W, Hoorn EJ, Ichai C, Joannidis M, Soupart A, Zietse R, Haller M, van der Veer S, Van Biesen W, Nagler E. Clinical practice guideline on diagnosis and treatment of hyponatraemia. Intensive Care Med. 2014 Mar;40(3):320-31. doi: 10.1007/s00134-014-3210-2. Epub 2014 Feb 22. Erratum in: Intensive Care Med. 2014 Jun;40(6):924. Hoorn, Ewout [corrected to Hoorn, Ewout J]. PMID: 24562549.

Uncomplicated community acquired cystitis: N30.9
Fosfomycin, oral, 3 g as a single dose.
OR
- Gentamicin, IM, 5 mg/kg as a single dose.
  - **Note:** Gentamicin should not be used in renal impairment or pregnancy (see Appendix II for guidance on prescribing). Therapeutic drug monitoring is not required.

OR
- Nitrofurantoin, oral, 100 mg 6 hourly for 5 days.

Ciprofloxacin, oral: Retained, treatment duration amended
In line with the PHC Chapter 8: Kidney and urological disorders, the duration of treatment for complicated community acquired cystitis has been amended from 10 days to 7 days.

The STG has been amended as follows:

Complicated community acquired cystitis (Non pregnant women)
- Ciprofloxacin, oral, 500 mg 12 hourly for 7~~-10~~ days.

7.3.5 BENIGN PROSTATIC HYPERPLASIA

A: Dose titration to clinical effect
Alpha-blocker, oral: *added as a therapeutic class*
Doxazosin, oral, immediate-release (1mg): *added as an example of class*
Doxazosin, oral, long-acting (4mg): *added to the therapeutic interchange database*
Tamsulosin, oral (0.4mg): *added to the therapeutic interchange database*
Terazosin, oral (1 and 5mg): *added to the therapeutic interchange database*
Alfuzosin, oral (10mg): *added to the therapeutic interchange database*
Silodosin, oral (8mg): *added to the therapeutic interchange database*

B: Standard maintenance dose
Alpha-blocker, oral: *retained as a therapeutic class*
Doxazosin, oral, immediate-release (4mg): *added as an example of class*
Doxazosin, oral, long-acting (4mg): *added to the therapeutic interchange database*
Tamsulosin, oral (0.4mg): *removed as an example of class and added to the therapeutic interchange database*
Terazosin, oral (10mg): *retained in the therapeutic interchange database*
Alfuzosin, oral (10mg): *retained in the therapeutic interchange database*
Silodosin, oral (8mg): *retained in the therapeutic interchange database*

In the NEMLC meeting held 31 March 2022, tamsulosin 0.4mg, was recommended to be removed as an example of the alpha-blocker therapeutic class and was replaced by doxazosin 4mg for the treatment of benign prostatic hyperplasia. Tamsulosin has been added to the therapeutic interchange database due to considerations of cost and supply security. It was noted that the standard doxazosin formulation requires to be slowly up titrated from 1 mg/day to clinical effect, to avoid first-dose orthostatic hypotension[28]. However, the long-acting formulation of doxazosin, standard dose does not. As per circular REF: 2022/03/31/EDP/02, the updated treatment protocol has been disseminated and now includes the dose titration to achieve clinical dose.

The STG amended as follows:

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

Indication: Adult Hospital Level STGs and EML, 2019	Current recommendation in STGs and EML (2019)	Updated recommendation for 2020-2024 version of the STGs and EML
7.3.5 Benign prostatic hyperplasia	▪ Alpha blocker, e.g.: ○ Tamsulosin, oral, 0.4 mg daily.	▪ Alpha blocker, e.g.: • Doxazosin, oral, 4 mg daily. ○ Titrate dose by 1 mg every 2 weeks to clinical effect. ○ Initial dose: 1 mg daily. ○ Usual maintenance dose: 4 mg daily.

The following titration protocol to clinical effect has been recommended.

Alpha-blocker	Dose titration protocol
Doxazosin, immediate release	1mg daily x14days, 2mg daily x14days, 4mg daily
Terazosin	1mg x14 days, 2mg x14 days, 5mg x14 days, 10mg daily
Doxazosin, long-acting	n/a
Tamsulosin	n/a
Alfuzosin	n/a
Silodosin	n/a

The alpha blocker therapeutic class has been amended in the AHL therapeutic interchange database as follows:

7.3.5	**Beningn prost**	**Dose-titratior**	**N40**	**Alpha blocker**	**G04CA**	**Doxazosin**	**1**	**mg**	**oral**
7.3.5	Beningn prosta	Dose-titration	N40	Alpha blocker	G04CA	Doxazosin	4	mg	long-acting
7.3.5	Beningn prosta	Dose-titration	N40	Alpha blocker	G04CA	Tamsulosin	0.4	mg	oral
7.3.5	Beningn prosta	Dose-titration	N40	Alpha blocker	G04CA	Terazosin	1-5	mg	oral
7.3.5	Beningn prosta	Dose-titration	N40	Alpha blocker	G04CA	Alfuzosin	10	mg	oral
7.3.5	Beningn prosta	Dose-titration	N40	Alpha blocker	G04CA	Silodosin	8	mg	oral
7.3.5	**Beningn prost**	**Standard mai**	**N40**	**Alpha blocker**	**G04CA**	**Doxazosin**	**4**	**mg**	**oral**
7.3.5	Beningn prosta	Standard main	N40	Alpha blocker	G04CA	Doxazosin	4	mg	long-acting
7.3.5	Beningn prosta	Standard main	N40	Alpha blocker	G04CA	Tamsulosin	0.4	mg	oral
7.3.5	Beningn prosta	Standard main	N40	Alpha blocker	G04CA	Terazosin	10	mg	oral
7.3.5	Beningn prosta	Standard main	N40	Alpha blocker	G04CA	Alfuzosin	10	mg	oral
7.3.5	Beningn prosta	Standard main	N40	Alpha blocker	G04CA	Silodosin	8	mg	oral

Potassium Chloride 1g/5ml oral solution (5L)

Ingredient	Quantity
Potassium Chloride powder	1 kg
Concentrated Chloroform Water AQ	125 mL
Distilled water up to	5 L

(Adapted with permission from Tygerberg Academic Hospital Department Of Pharmaceutical Services)

***Note**: Different volumes can be prepared. Recalculate based on the above proportions.*

Method

1. Weigh off Potassium Chloride powder.
2. Place in a mixing bowl of a small mixer.
3. Heat 2.5 litres distilled water and add to powder.
4. Mix at low speed.
5. Add 1,5 litres of cold water to mixture.
6. Measure off 125ml concentrated Chloroform water and add to mixture.
7. Place in a 5 litre container prepared for the manufacture of Potassium Chloride.
8. Make up to 5 litres with distilled water.
9. Print stickers and fill in packing card.
10. Pack in 100 ml glass amber bottles.

Storage: store in a glass amber bottle for up to 1 month.

Directions for use: Dilute every 5mL with 60mL of fluid (Juice or water)

How to prepare concentrated Chloroform Water B.P (125ml)

Ingredient	**Quantity**
Alcohol 96 %	75 mL
Chloroform Liquid	12,5 mL
Distilled water up to	125 mL

Method:

1. Measure alcohol 96 % in glass cylinder and pour into amber glass bottle prepared for the manufacture of Chloroform water.
2. Measure chloroform liquid in a glass cylinder and add to the alcohol. Perform this step expeditiously as Chloroform evaporates.
3. Make up the volume with distilled water.
4. Label bottle with Batch number and date of manufacture.