health
Department:
Health
REPUBLIC OF SOUTH AFRICA

2030 NDP

SOUTH AFRICAN PRIMARY HEALTHCARE LEVEL ESSENTIAL MEDICINES LIST
CHAPTER 8: KIDNEY AND UROLOGY CONDITIONS
NEMLC RECOMMENDATIONS FOR MEDICINE AMENDMENTS (2016-2018)

Medicine amendment recommendations, with supporting evidence and rationale are listed below. Kindly review the medicine amendments in the context of the complete kidney and urology chapter.

SECTION	MEDICINE/MANAGEMENT	ADDED/DELETED/AMENDED/NOT ADDED/ RETAINED
8.1 Chronic kidney disease (CKD)		
- *Caution regarding dose adjustment in renal impairment*	n/a	Added
- *Prognosis of CKD by GFR and albuminuria categories*	n/a	Amended to align with KDIGO,2012
- *Proteinuria*	Enalapril, oral	Dose amended from "10 mg" to "20 mg" 12 hourly
8.2 Acute kidney injury		
- *Children: fluid overload*	Furosemide, IV	Retained (fluid overload)
- *Children: hypertension*	Nifedipine, oral	Retained (hypertension)
- *Adults: fluid overload*	Furosemide, IV	Retained (fluid overload)
- *Adults: hypertension*	Amlodipine, oral	Retained as a pre-referral dose
	Furosemide, oral	Retained as a pre-referral dose (eGFR unknown or < 30 mL/min)
	Hydrochlorothiazide, oral	Deleted as a pre-referral dose (eGFR≥30 mL/min)
	Labetalol, oral	Not added as a pre-referral dose
8.3.1 Nephritic syndrome		
- *Children*	Furosemide, IV	Deleted, with cross-referral to section 8.2
	Nifedipine, oral	Deleted, with cross-referral to section 8.2
- *Adults*	Furosemide, IV	Deleted, with cross-referral to section 8.2
	Amlodipine, oral	Deleted, with cross-referral to section 8.2
	Furosemide, oral	Deleted, with cross-referral to section 8.2
	Hydrochlorothiazide, oral	Deleted, with cross-referral to section 8.2
8.4 Urinary tract infection (UTI):		
- *uncomplicated cystitis*	Ciprofloxacin, oral	Retained
	Fosfomyicn, oral	Not added
- *For pregnant women and adolescents:*	Amoxicillin/clavulanic acid 875/125 mg, oral	Deleted
	Nitrofurantoin, oral	Added
8.7 Benign prostatic hyperplasia (BPH)		
	Testosterone-5-alpha reductase inhibitors, oral	Not added
8.9 Enuresis		
	Desmopressin	Not added
8.10 Impotence/ erectile dysfunction		
	Phosphodiesterase type 5 inhibitors, oral	Not added
8.11 Renal calculi		
	NSAIDs, oral	Not added
	Morphine, IV	Retained

8.1 CHRONIC KIDNEY DISEASE (CKD)

Caution regarding dose adjustment in renal impairment: *added*
The following test was added, aligned with the Adult STGs and EML, 2015:

CAUTION

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

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 SAMF, package insert, and from many online resources e.g.:http://www.globalrph.com/index_renal.htm

Level of Evidence: III Guidelines

Prognosis of CKD by GFR and albuminuria categories: *amended to align with KDIGO,2012*

STG was updated as follows, aligned the table with the Kidney Disease: Improving Global Outcomes (KDIGO) Guidelines, 2014, as amended:

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				ACR* <30 mg/g <3mg/mmol	ACR* 30–300 mg/g 3–30 mg/mmol	ACR* >300 mg/g >30 mg/mmol
$eGFR_2$ categories (ml/min per 1.73m) - description and range	G1	Normal or high	≤90		Refer	Refer
	G2	Mildly decreased	60 –89		Refer	Refer
	G3a	Mildly to moderately decreased	45–59		Refer	Refer
	G3b	Moderately to severely decreased	30–44	Refer	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

Level of Evidence: III Guidelines

Proteinuria

Enalapril, oral: *dose amended from 20 mg 12 hourly to 10 mg 12 hourly*

Rationale: Risk of ACE-inhibitors causing or exacerbating hyperkalaemia in CKD, warrants a lower dose of enalapril to be used at primary level of care.

Level of Evidence: III Expert opinion

Kidney Disease Outcomes Quality Initiative (K/DOQI) recommendations of ACE-inhibitors in chronic kidney disease[1]:

Therapeutic class	Medicine	Dose ranges (mg/day)
ACE-inhibitor	Benazepril	20-40 mg
	Captopril	25-150 mg
	Enalapril	10-40 mg
	Fosinopril	20-40 mg
	Lisinopril	20-40 mg
	Perindopril	4-8 mg
	Quinapril	20-80 mg
	Ramipril	2.5-20 mg
	Trandolapril	2-4 mg

[1] Kidney Disease Outcomes Quality Initiative (K/DOQI). K/DOQI clinical practice guidelines on hypertension and antihypertensive agents in chronic kidney disease.Am J Kidney Dis. 2004 May;43(5 Suppl 1):S1-290. https://www.ncbi.nlm.nih.gov/pubmed/15114537

8.2 ACUTE KIDNEY INJURY (AKI)

CHILDREN

If fluid overloaded:

Furosemide, IV: *retained*

If hypertension present*:*

Nifedipine, oral: *retained*

ADULTS

If fluid overloaded/respiratory distress:

Furosemide, IV: *retained as bolus dose*

If hypertension present:

Amlodipine, oral: *retained pre-referral dose*

Furosemide, oral: *retained pre-referral dose*

Hydrochlorothiazide, oral: *deleted pre-referral dose*

Labetalol, oral: *not added as a pre-referral dose*

Labetalol, oral: An external comment to consider labetalol, oral was not accepted as anti-hypertensive(s) are administered as single doses, prior to referral to secondary level for further management of acute kidney injury. Labetalol, oral is currently not included on either the PHC or Adult Hospital Level EML.

eGFR cut-off for administering hydrochlorothiazide: External comment was received to amend eGFR cut-off from *"30 mL/min"* to *"45 mL/minute" (no supporting evidence provided).* This was not accepted. Current recommendation of 30mL/minute is aligned the Adult Hospital Level STGs and EML, 2015[2] and with the KDIGO Guidelines.[3]

Hydrochlorothiazide, oral: External comment that thiazides are inappropriate for AKI was noted. The STG recommends thiazides only if current eGFR > 30 mL/min, aligned with SAMF, 2016. [4]

Level of Evidence: III Guidelines

NEMLC MEETING DISCUSSION: 22 FEBRUARY 2018[5]

- **8.2 Acute kidney injury (AKI):** The need for a pre-referral dose of hydrochlorothiazide, oral in this clinical setting was discussed; as the STG provides for furosemide, oral.
  NEMLC Recommendation: The NEMLC did not accept the PHC Committee's recommendation, but recommended that the pre-referral dose of hydrochlorothiazide be removed from the STG/EML for managing hypertension associated with AKI.
  Rationale: The STG/EML does recommend a pre-referral dose of oral furosemide if current eGFR is unknown or ≥ 30 mL/min.
  Level of Evidence: III Exert opinion

8.3.1 NEPHRITIC SYNDROME

Medicine management was deleted with a cross-referral to section 8.2: Acute kidney injury.

CHILDREN

Furosemide, IV: *deleted*

Nifedipine, oral: *deleted*

[2] Adult Hospital STGs and EML, 2015

[3] 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

[4] SAMF, 2016

[5] NEMLC minutes of the meeting, 22 February 2018

ADULTS
Furosemide, IV: *deleted*
Amlodipine, oral: *deleted*
Furosemide, oral: *deleted*
Hydrochlorothiazide, oral: *deleted*

8.4 URINARY TRACT INFECTION (UTI)

Uncomplicated cystitis
Ciprofloxacin, oral: *retained*
Fosfomyicn, oral: *not added*
External comment raising concerns of collateral damage if uncomplicated cystitis is routinely treated with quinolones was duly noted; as well as associated adverse reactions (tendonitis associated with quinolones). However, available local susceptibility study showed that UTI pathogens had similar susceptibility profiles for fosfomycin (95.5%; 95% CI 92.6 to 98.4); the 3 fluoroquinolones, ciprofloxacin, levofloxacin and norfloxacin (94.1%; 90.8 to 97.4); nitrofurantoin (91.7%; 87.8 to 95.6); cefuroxime (90.1%; 86.0 to 94.3) and cefixime (88.2%; 95% CI 83.7 - 92.6); whilst amoxicillin/clavulanic acid (82.8%; 77.5 to 88.0) and trimethoprim/
sulphamethoxazole (44.3%; CI 37.4 to 51.2) were the least efficacious agents.[6]
Recommendation: Ciprofloxacin, oral be retained for treatment of UTI. Fosfomycin, oral could be considered, but cost prohibits recommending this antimicrobial agent[7].
Level of Evidence: III Antimicrobial susceptibility study

Complicated cystitis: For pregnant women and adolescents
Amoxicillin/clavulanic acid 875/125 mg, oral: *deleted*
Nitrofurantoin, oral: *added*
Aligned with Section 6.4.5.1: Cystitis, in pregnancy in chapter 6: Obstetrics and gynaecology.
Level of Evidence: III Guidelines[8], Observational studies

8.5 PROSTATITIS

Acute bacterial prostatitis: In men > 35 years of age or if there is associated cystitis
Ciprofloxacin, oral: *duration of therapy not amended*
External comment was submitted to amend duration of therapy from “14 days” to “7 days”. No evidence was submitted and no evidence could be found to support this.
Recommendation: Duration of therapy of oral ciprofloxacin retained as 14 days, for treatment of cystitis. (See section 8.4: Urinary tract infection, above).

8.7 BENIGN PROSTATIC HYPERPLASIA (BPH)

Testosterone-5-alpha reductase inhibitors, oral: *not added*
External comment to consider these agents for inclusion to the PHC EML was not accepted.
Rationale: Management with 5-alpha reductase inhibitors not appropriate for primary level of care. NEMLC had not recommended this medicine for management of BPH at tertiary and quaternary level of care[9].

[6] Lewis DA, Gumede LY, van der Hoven LA, de Gita GN, de Kock EJ, de Lange T, Maseko V, Kekana V, Smuts FP, Perovic O. Antimicrobial susceptibility of organisms causing community-acquired urinary tract infections in Gauteng Province, South Africa. S Afr Med J. 2013 Mar 15;103(6):377-81. http://www.ncbi.nlm.nih.gov/pubmed/23725955
[7] SEP Database, 22 December 2017:Fosfomycin, oral, 3 g sachet = R 188.67
[8] Adult Hospital Level STGs and EML, 2015
[9] T&Q EML, December 2017

8.9 ENURESIS

Desmopressin: *not added*

External comment to consider this agent for inclusion to the PHC EML was not accepted. Management with desmopressin is provided for in the Paediatric Hospital Level STGs and EML, 2017, and the STG recommends that children with persistent enuresis be referred to secondary level for further management.

8.10 IMPOTENCE/ERECTILE DYSFUNCTION

Phosphodiesterase type 5 inhibitors, oral: *not added*

External comment to consider these agents for inclusion to the PHC EML was not accepted.

Level of Evidence: III Expert opinion

8.11 RENAL CALCULI

NSAIDs, oral: *not added*

Morphine, IV: *retained*

External comment was received motivating the use of NSAIDs rather than morphine, as the former was reported to be the safer option (no supporting evidence provided). However, the PHC Committee was of the opinion that a potent analgesic would be required in this clinical setting.

Level of Evidence: III Expert opinion

NEMLC MEETING DISCUSSION: 22 FEBRUARY 2018[10]

- **8.11 Renal calculi:** Morphine as an analgesic in this clinical setting was discussed.
  NEMLC Recommendation: The mode of administration of morphine be amended from IV to IM in this clinical setting at primary level of care for pragmatic purposes.
  Level of Evidence: III Expert opinion

[10] NEMLC minutes of the meeting, 22 February 2018