health
Department:
Health
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2030 NDP

SOUTH AFRICAN PRIMARY HEALTHCARE ESSENTIAL MEDICINES LIST
CHAPTER 9: ENDOCRINE 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 endocrine chapter

SECTION	MEDICINE	ADDED/DELETED/AMENDED/NOT ADDED/RETAINED
9.1.2 Type 1 diabetes mellitus, in adults	Targets for glycaemic control	Amended
	Neutral Protamine Hagedorn (NPH) insulin	Nomenclature amended
	HbA1C test	Not added as diagnostic test for diabetes mellitus
9.2.2 Type 2 diabetes mellitus, adults	Insulin, IM	Directions for use not amended (sulphonylureas be discontinued, prior to initiating insulin)
	Biphasic insulin, SC	Starting dose amended
9.3.1 Hypoglycaemia in diabetics	Glucagon, IM	Not added
- Unconscious patient: Adult	Dextrose, IV 50%	Deleted
	Dextrose, IV 10%	Added
- Unconscious patient: Child	Dextrose, IV 50%	Deleted
	Dextrose, IV 10%	Added
9.3.2Diabetic ketoacidosis (DKA) *- Children: If no shock or aftershock is corrected*	Sodium chloride 0.9%, IV	Directions for use amended
9.4.3 Diabetic nephropathy	Albumin: creatinine ratio cut-off (diagnose nephropathy)	Not amended (but described in mg/g & mg/mmol)
	ACE-inhibitor, oral	Directions for use amended
	ACE-inhibitor therapeutic class	Members of therapeutic class listed, but enalapril described in the STG as the example of class
9.5.2 Dyslipidaemia in diabetes	Aspirin, oral	Dose amended
	Simvastatin, oral	Dose not amended

9.1.2 TYPE 1 DIABETES MELLITUS, IN ADULTS

Targets for glycaemic control: *amended*

The targets for control in diabetes mellitus was aligned to the Adult Hospital Level STG,2015:

TARGETS FOR CONTROL
Glycaemic targets for control:

Patient type	Target HbA_{1c}	Target FPG*	Target PPG*
» Young, low risk » Newly diagnosed » No CVS disease	< 6.5%	4.0– 7.0 mmol/L	4.4– 7.8 mmol/L
» Majority of patients	< 7.0%	4.0– 7.0 mmol/L	5.0– 10.0 mmol/L
» Elderly » High risk » Hypoglycaemic unawareness » Poor short-term prognosis	< 7.5%	4.0– 7.0 mmol/L	< 12.0 mmol/L

***FPG: fasting plasma glucose; PPG: post prandial plasma glucose.**

Non-glycaemic targets:
» Body mass index ≤ 25 kg/m^2.
» BP ≤ 140/80 mmHg and ≥ 120/70 mmHg.

Neutral Protamine Hagedorn (NPH) insulin: *nomenclature amended*

Amended to World Health Organisation International Nonproprietary Name (INN), "Intermediate acting insulin".

HbA1C

HbA1C: *not added as diagnostic test for diabetes mellitus*

At the NEMLC meeting of 1 February 2018[1], the following Adult Hospital Level matter was tabled – the PHC STGs and EML was aligned to this recommendation.

Diagnosis

HbA1C: *not added for diagnosing diabetes mellitus*

(Refer to review: HbA1C for diagnosing diabetes mellitus, October 2017).

Recommendation: HbA1C not be recommended as a diagnostic test for diabetes mellitus.

Rationale: Evidence is inconclusive regarding the race/ethnic influence on HbA1C. The test has not been validated in the South African population to diagnose diabetes and is more expensive than the current standard finger prick glucose test.

Level of Evidence: III Human genetic studies, Prevalence study, Guidelines

Note: The PHC STGs and EML, 2018 recommends the following monitoring with HbA1c:

i*) Type 1 Diabetes mellitus, adults*:

Annually:

» HbA1c, one month before next hospital appointment.

i*) Type 2 Diabetes mellitus, adults*:

Annually:

» HbA1c, in patients who meet treatment goals (3–6 monthly in patients whose therapy has changed, until stable).

9.2.2 TYPE 2 DIABETES MELLITUS, ADULTS

Insulin therapy

Insulin, IM: *directions for use not amended (sulphonylureas be discontinued, prior to initiating insulin).*

The Adult Hospital Level STGs and EML, 2015 recommends that sulphonylureas (SUR) be discontinued, prior to initiation of insulin therapy. Most international guidelines leave it up to prescriber. The theoretical rationale for discontinuing SURs is that by the time insulin is initiated, the extensive beta cell depletion limits the efficacy of SURs. A semi-observational study (the study was a RCT that compared different insulin types – continuation or discontinuation of SURs was at the discretion of the treating physician) by Swinnen et al (2010)[2] showed that continuation versus discontinuation of SUR on initiating insulin showed similar efficacy, though more hypoglycaemia and weight gain was reported in the group continuing SURs.

Level of Evidence: III Observational study

Biphasic insulin, SC: *Starting dose amended*

Aligned with 2017 SEMDSA Guidelines, as follows.[3]

Insulin type	Starting dose	Increment
Add on therapy: • Intermediate to long-acting	10 units in the evening before bedtime, but not after 22h00.	If 10 units not effective: increase gradually to 20 units (2–4 units increase each week).
Substitution therapy: • Biphasic	Twice daily. Total daily dose:	4 units weekly. First increment is added to dose before breakfast.

[1] NEMLC minute of the meeting: 12 February 2018.

[2]Swinnen SG, Dain MP, Mauricio D, DeVries JH, Hoekstra JB, Holleman F. Continuation versus discontinuation of insulin secretagogues when initiating insulin in type 2 diabetes. Diabetes ObesMetab. 2010 Oct;12(10):923-5. http://www.ncbi.nlm.nih.gov/pubmed/20920046

[3]The Society for Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee.The 2017 SEMDSA Guideline for the Management of Type 2 Diabetes Guideline Committee. JEMDSA 2017; 21(1)(Supplement 1): S1-S196. http://www.jemdsa.co.za/index.php/JEMDSA/article/view/647/937

	~~15 units~~Start with 0.3 units/kg/day divided as follows: o $^2/_3$ of total daily dose, 30 minutes before breakfast. o $^1/_3$ of total daily dose, 30 minutes before supper.	Second increment is added to dose before supper.

Level of Evidence: III Guidelines

NEMLC meeting, 12 December 2017[4]:
NEMLC Recommendation: *Biphasic insulin dose:* An example be provided for the starting dose (0.3 units/kg/day) to minimise confusion and medication errors.

Following text was added to the STG:

Example of a dose calculation:
- For a 70 kg adult: 0.3 units x 70 kg = 21 units per day; divided as 14 units 30 minutes before breakfast and 7 units 30 minutes before breakfast.

9.3.1 HYPOGLYCAEMIA

Glucagon, IM: *not added*

In the previous PHC review (2014), it was noted that the incidence and prevalence of type 1 diabetes was low and thus the availability of glucagon at every primary healthcare facility nationwide was not warranted. In addition, fruitless expenditure due to inadequate refrigeration facilities or expiry of stock had been considered. The Committee did not feel that any of those factors were likely to have changed, so did not recommend investigating the issue again.

Level of Evidence: III Expert opinion

Unconscious patient: Child

Dextrose, 50% IV: *deleted*

Dextrose 10%, IV: *added*

As dextrose 10%, IV is available the guidance to compound a 10% solution from 50% dextrose was removed.

The text of the STG was updated as follows:

- Dextrose 10%, IV, 2–5 mL/kg.
  - ~~10% solution e.g. add 1 part 50% dextrose water to 4 parts water for injection to make 10% solution.~~

IV administration of dextrose in children with hypoglycaemia:
» Establish an IV line. Do not give excessive volumes of fluid: usually can keep line open with 2mL/kg/hour.
» Take a blood sample for emergency investigations and blood glucose.
» Check blood glucose.
  – **If low, i.e. < 2.5 mmol/L or if testing strips are not available, administer 2–5 mL/kg of 10% dextrose solution IV rapidly.**
  In the majority of cases an immediate clinical response can be expected.
» Recheck the blood glucose after infusion.
  – If still low, repeat 2 mL/kg of 10% dextrose solution.
» After recovery, maintain with 5–10% dextrose solution until blood glucose is stabilised.
» Feed the child as soon as conscious.

Unconscious patient: Adult

Dextrose, 50% IV:*deleted*

Dextrose 10%, IV: *added*

Aligned with the PHC emergencies and injuries chapter

Recommendation was amended from:

- ~~Dextrose 50%, IV, 50 mL immediately and reassess.~~
  - ~~If there is no clinical response, give a second 50% dextrose bolus.~~
  - ~~Followed with dextrose 10% solution.~~
  - ~~In the majority of cases an immediate clinical response can be expected.~~

To

- Dextrose 10%, solution, IV, 2–5 mL/kg.
  - Do not give unless hypoglycaemic or hypoglycaemia strongly suspected.
  - Do not give excessive volumes of fluid.
  - If hypoglycaemia is treated:
    - re-check blood glucose 10–15 minutes later;
    - if still low, give further bolus of dextrose 10%, IV, 2 mL/kg, and commence dextrose 5 or 10%, infusion, 3–5 mL/kg/hour to prevent

[4] NEMLC minutes of the meeting: 12 December 2017.

blood glucose dropping again.
Assess continuously until the patient shows signs of recovery.

Level of Evidence: III Disease oriented RCT[5], Expert opinion

9.3.2 DIABETIC KETOACIDOSIS (DKA) AND HYPEROSMOLAR HYPERGLYCAEMIC STATE (HHS)

As management for DKA and hyperosmolar hyperglycaemia at primary level of care are the same, the heading of this section was amended from "Diabetic ketoacidosis" to "Severe hyperglycaemia (diabetic ketoacidosis (DKA) &hyperosmolar hyperglycaemic state (HHS))".

Children

If no shock, or aftershock is corrected

Sodium chloride 0.9%, IV: *directions for use amended*

The weight-band dosing for the fluid rates of sodium chloride 0.9%, IV, in this clinical setting, was simplified for easier reading (aligned with the format in the rest of the book), as follows:

If no shock or aftershock is corrected

- Sodium chloride 0.9%, IV.

Fluid rates of sodium chloride 0.9%, IV (if no shock) in children awaiting transfer.	**Check regularly for shock or increasing dehydration**
Weight range kg	**Rate**(mL/hr) (2–10 kg: 6 mL/kg/hr) (>10-–20 kg: 5 mL/kg/hr) (>20–40 kg: 4 mL/kg/hr)
>4–6	25
>6–10	40
>10–15	60
>15–20	85
>20–30	100
>30–45	150
>45–80	200

9.4.3 DIABETIC NEPHROPATHY

Albumin: creatinine ratio: *cut-off to diagnose nephropathy not amended*

An external comment was received to align the albumin: creatinine ratio cut-off to diagnose diabetic nephropathy with the 2013 Canadian Guidelines[6], as > 2 mg/mmol.

The SEMDSA guidelines[7]are aligned with the Canadian guidelines (no justification provided); whilst the KDIGO CKD Guidelines (2013)[8]recommends 3 mg/mmol as the cut-off.

Recommendation: The current recommendation of > 3 mg/mmol for diagnosing diabetic nephropathy be retained.

Rationale: Aligned with the KDIGO CKD Guidelines (2013).

Level of Evidence: III Guidelines

NEMLC meeting, 12 Dec 2017[9]:

NEMLC Recommendation: The units for the albumin: creatinine ratio cut-off to diagnose nephropathy be aligned with the NHLS reports.

Text of the STG was amended as follows:

If ratio > 30 mg/g (3 mg/mmol), diagnose nephropathy.

ACE-inhibitor, oral: *directions for use amended*

[5] Moore C, Woollard M. Dextrose 10% or 50% in the treatment of hypoglycaemia out of hospital? A randomised controlled trial.Emerg Med J. 2005 Jul;22(7):512-5.https://www.ncbi.nlm.nih.gov/pubmed/15983093

[6]Canadian Diabetes Association Clinical Practice Guidelines Expert Committee.Canadian Diabetes Association 2013 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Can J Diabetes 2013;37(suppl 1):S1-S212. http://guidelines.diabetes.ca/executivesummary/ch29

[7]The Society for Endocrinology, Metabolism and Diabetes of South Africa Type 2 Diabetes Guidelines Expert Committee.The 2017 SEMDSA Guideline for the Management of Type 2 Diabetes Guideline Committee. JEMDSA 2017; 21(1)(Supplement 1): S1-S196.

[8] Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease.Kidney inter., Suppl. 2013; 3: 1–150. http://www.kdigo.org/clinical_practice_guidelines/pdf/CKD/KDIGO_2012_CKD_GL.pdf

[9] NEMLC minutes of the meeting: 12 December 2017.

The following was amended, aligned with the SAMF, 2014 and the Adult Hospital STGs and EML, 2015.

» Start treatment with an ACE-inhibitor and increase gradually to maximal dose if tolerated. ▪ ACE-inhibitor, e.g.: • Enalapril, oral, initiate with 5mg 12 hourly. o Increase to ~~20~~10 mg 12 hourly, as tolerated. o Monitor potassium, at baseline, within 1 month, and annually.

Level of Evidence: III Guidelines

ACE-inhibitor therapeutic class (but, enalapril described in the STG as the example of class):

Members of therapeutic class	Maximum daily dose
Enalapril, oral	20 mg
Captropril, oral	100 mg
Ramipril, oral	10 mg
Perindopril, oral	4 mg
Trandolapril, oral	2 mg
Lisinopril, oral	20 mg

Level of Evidence: I Systematic review[10], Guidelines[11]

9.5.2 DYSLIPIDAEMIA IN DIABETES

Aspirin, oral*: dose amended*

NEMLC meeting, 12 Dec 2017[12]:
9.5 Cardiovascular risk in diabetes
Aspirin: The recommendation for aspirin for secondary prevention of ischaemic events to be deleted from the diabetic chapter with a cross referral to the cardiovascular chapter: 4.1 Prevention of ischaemic heart disease and atherosclerosis, to ensure the guidance is read in the correct context. Furthermore, the preferred aspirin dose be changed from "100 mg" to "75 – 100 mg".
NEMLC recommendations:
- Aspirin for secondary prevention of ischaemic events be deleted from this STG, with a cross-reference to the cardiovascular chapter, section: 4.1 Prevention of ischaemic heart disease and atherosclerosis.
- Preferred aspirin dose be changed from "100 mg" to "75–100 mg", aligned with clinical evidence[13] and availability.

Simvastatin, oral: *dose not amended*
Simvastatin, oral, 10 mg daily retained in the STG for **primary** prevention of ischaemic events in diabetes mellitus type 2.

CONDITION(S) NOT RECCOMENDED FOR INCLUSION TO THE CHAPTER

GENDER DYSPHORIA

Testosterone cypionate, IM: *not added*
The PHC Committee was of the opinion that gender dysphoria should not be diagnosed at primary level of care, and would require down referral for management at PHC. The committee suggested that the application be considered at the Adult Hospital Level.

[10]Lv J, Perkovic V, Foote CV, Craig ME, Craig JC, Strippoli GF. Antihypertensive agents for preventing diabetic kidney disease. Cochrane Database Syst Rev. 2012 Dec 12;12:CD004136. https://www.ncbi.nlm.nih.gov/pubmed/23235603
[11] SAMF, 2016
[12] NEMLC minutes of the meeting: 12 December 2017.
[13] Adult Hospital Level CVS NEMLC report, 2 November 2017: Berger JS, Stebbins A, Granger CB, Ohman EM, Armstrong PW, Van de Werf F, White HD, Simes RJ, Harrington RA, Califf RM, Peterson ED. Initial aspirin dose and outcome among ST-elevation myocardial infarction patients treated with fibrinolytic therapy. Circulation. 2008 Jan 15;117(2):192-9. https://www.ncbi.nlm.nih.gov/pubmed/18086929