PHC Chapter 4: Cardiovascular Conditions
AH Chapter 3: Cardiovascular System

National Department of Health

Affordable Medicines Directorate
Essential Drugs Programme

Primary Healthcare Level Standard Treatment Guidelines – 2020-4 Review cycle
Adult Hospital Level Standard Treatment Guidelines – 2020-4 Review cycle

Evidence

Please access the National Essential Medicines List Committee (NEMLC) report for detailed evidence (including rationale, references and costings) informing decision-making on medicine addition, amendments and deletions:

NHI Website: https://www.health.gov.za/nhi-edp-stgs-eml
Knowledge Hub: www.knowledgehub.health.gov.za/e-library

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 STGs.

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PHC CH 4: Cardiovascular Conditions

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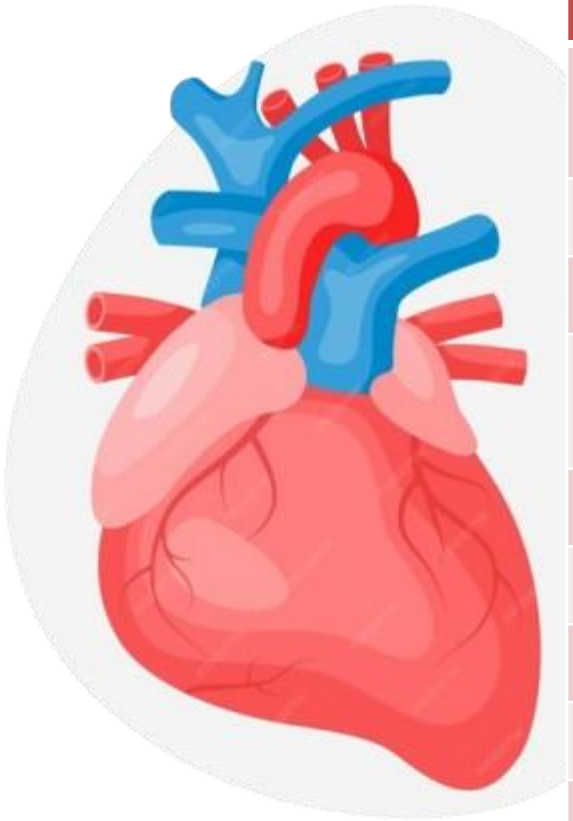
AH CH 3: Cardiovascular System

Presentation Outline



No.	Topic
1	Aspirin for Primary Prevention of Ischaemic Heart Disease
2	Cardiovascular Risk Assessment Tools
3	Oxygen Supplementation Caution
4	Day-time versus night-time dosing of antihypertensive medication
5	Enalapril Dosing in Hypertension
6	Indapamide for Hypertension
7	Glyceryl Trinitrate IV - AHL
8	Warfarin Management in Atrial Fibrillation - AHL
9	DOACs therapy in Atrial Fibrillation - AHL

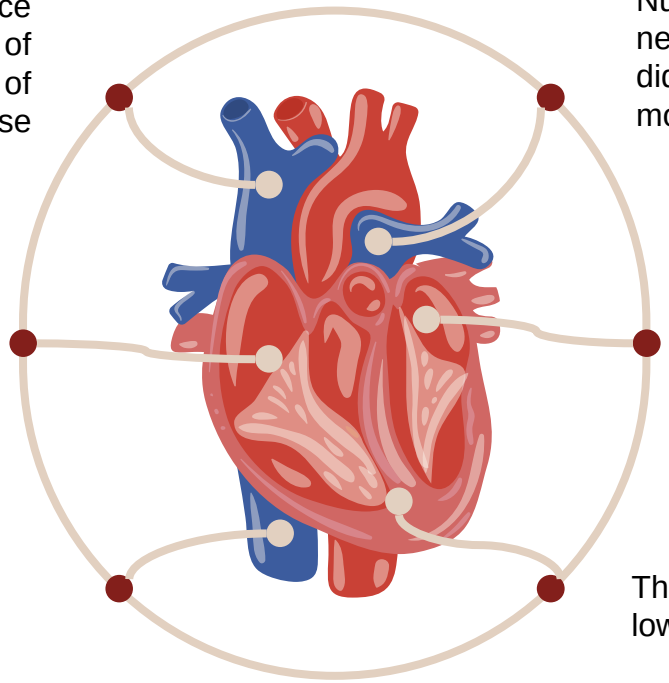
Aspirin for Primary Prevention of Ischaemic Heart disease

Evidence Summary: Evidence review of the use of aspirin for primary cardiovascular disease prevention.

There is a substantial body of evidence that collectively supports the use of aspirin for the secondary prevention of established cardiovascular disease

However, current data on the role of aspirin in primary prevention of cardiovascular disease is conflicting and controversial with potential benefits limited by an increased bleeding risk

The recently published systematic review of RCTs (n = 164 225) of aspirin in primary cardiovascular disease prevention found that aspirin for primary prevention prevents cardiovascular events, but increases risk of major bleeds



Number needed to treat (NNT) and Number needed to harm (NNH) are similar. Aspirin did not reduce all cause or cardiovascular mortality.

Aspirin for primary prevention reduces the risk of non-fatal ischaemic events but increases non-fatal bleeding events. This is observed in both high and low 10-year risk for cardiovascular events sub-groups as well as the diabetic subgroup.

This review has an AMSTAR rating of low to moderate quality

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National Department of Health: Affordable Medicines, EDP-Primary Healthcare and Adult Hospital level. Evidence Summary: Evidence review of the use of aspirin for primary cardiovascular disease prevention. Aspirin-for-primary-cardiovascular-disease-prevention-11-February-2022-final.pdf

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Aspirin for Primary Prevention of Ischaemic Heart disease

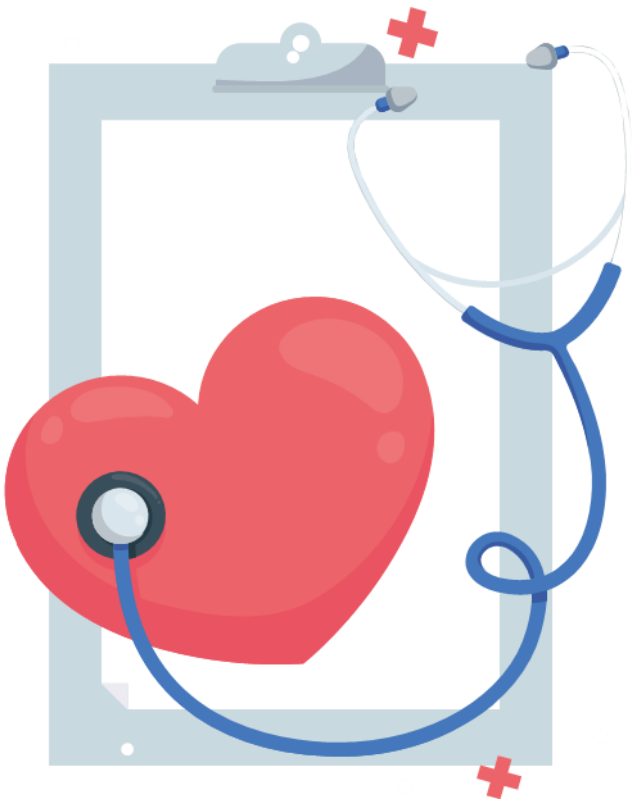
NEMLC Recommendation

NOT RECOMMENDED

NEMLC does not recommend the use of aspirin as primary prevention of IHD.

Rationale: Systematic review of RCTs (n = 164 225) found that the use of aspirin for primary cardiovascular disease prevention did not decrease all-cause cardiovascular mortality. Aspirin use decreased risk of cardiovascular events but increased major bleeding risk. The balance between the composite outcomes versus risk associated with aspirin favoured that aspirin not be used for primary prevention (including amongst diabetics, or patients at low or high risk). However, more importantly no mortality benefit was seen with aspirin.

Cardiovascular Risk Assessment Tools



An alternative non-laboratory based tool has been included in the newly created **Appendix III (*PHC)* & Appendix VII (*AHL*): Cardiovascular risk assessment**, which has been adapted with permission from the Knowledge Translation Unit and authors of the 2023 Adult Primary Care guideline.

This paper-based tool is an adaptation of the WHO paper-based risk calculator for cardiovascular disease management in primary care.

While NEMLC acknowledged the limitations of the WHO based tool, the Committee recommended that the paper-based tool be included for CV risk assessment as an interim replacement, until a tool that is more suitable for the local population is available.

The Framingham Risk model is used globally, and endorsed by the South African Lipid Guidelines.9 This tool has been transferred to the newly created Appendix III: Cardiovascular risk assessment which may be accessed on the NHI webpage.

Adopted with permission from the Knowledge Translation Unit and authors of the Adult Primary Care guideline (2023). This tool is based on the WHO cardiovascular disease non-laboratory-based Southern Sub-Saharan Africa. From: HEARTS technical package for cardiovascular disease management in primary healthcare risk based CVD management. World Health Organisation, Geneva, 2020.

D'Agostino RB, Sr., Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. Circulation. 2008;117(6):743-53.

Oxygen Supplementation Caution

Evidence Summary: The appropriate use of oxygen therapy for ST elevation myocardial infarction (STEMI): evidence from a contemporary systematic reviews and meta-analysis

External stakeholder comment indicated that the South African Society of Cardiovascular Intervention (SASCI) recommended 90% as a cut-off, for oxygen administration. The cut-off for oxygen administration was retained as 94% in the STG, as per the findings of the evidence summary below.

The most recent Systematic Review and Meta-analysis found that high oxygen supply in patients with acute STEMI may be associated with a significant 17% risk reduction of short-term mortality (until 30 days).

Despite this statistically significant difference in mortality, the trial sequential analysis showed that only 56.3% of the sample size required to assess the 17% risk reduction with a power 80% was reached, and the magnitude of the results were not large which precludes definite conclusions.

This consideration and the high risk of bias of the included trials led to successive downgrading in the GRADE analysis of the confidence in the pooled data

Oxygen Supplementation Caution

NEMLC Recommendation

NEMLC recommends that the current STG recommendation be retained for oxygen supplementation, **only if saturation <94%** with an additional caution not to administer oxygen if the patient is not hypoxic.

Rationale: Evidence suggests that acutely ill patients randomised to liberal oxygen therapy were more likely to die, without improving other patient outcomes. For pragmatic purposes the **current recommendation of <94% be retained.**

Day-time versus Night-time Dosing of Antihypertensive Medications

Pubmed search on the 9th January 2024, identified 3 recently published Systematic Reviews on the effect of night–time dosing of antihypertensive medication.

Maqsood MH et al. Timing of Antihypertensive Drug Therapy: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. 2023

Findings: 72 RCTs compared the effect of morning versus evening dosing of antihypertensive medication .The review authors conclude that while dosing of antihypertensive drugs significantly reduced ambulatory BP parameters and lowered cardiovascular events, this effect was mainly driven by trials involving the Hermida group. The authors further conclude that antihypertensive drugs should be taken at a time of the day that is convenient and optimizes adherence and minmises undesirable effects, unless there is a specific intention to lower night-time BP.

Maqsood MH et al. Timing of Antihypertensive Drug Therapy: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. Hypertension. 2023 Jul;80(7):1544-1554. doi: 10.1161/HYPERTENSIONAHA.122.20862. Epub 2023 May 22. PMID: 37212152.

Stergiou G et al. Bedtime dosing of antihypertensive medications: systematic review and consensus statement: International Society of Hypertension position paper endorsed by World Hypertension League and European Society of Hypertension. 2022

Findings: ABSTRACT ONLY. Preferred use of bedtime drug dosing of antihypertensive drugs should not be routinely recommended in clinical practice. Complete 24-h control of BP should be targeted using readily available, long-acting antihypertensive medications as monotherapy or combinations administered in a single morning dose. *The TIME study was published in 2022 and has been included in the SR by Maqsood MH et al. The BedMed due to be completed at the end of 2023 and BedMedFrail mid-2023 were yet to be published at the time of review.

Stergiou G et a;. Bedtime dosing of antihypertensive medications: systematic review and consensus statement: International Society of Hypertension position paper endorsed by World Hypertension League and European Society of Hypertension. J Hypertens. 2022 Oct 1;40(10):1847-1858. doi: 10.1097/HJH.0000000000003240. Epub 2022 Aug 12. PMID: 35983870

Ho CLB et al. The effect of taking blood pressure lowering medication at night on cardiovascular disease risk. A systematic review. 20213

Findings: Authors of this SR investigated the effect of taking antihypertensive treatment at night versus conventional morning treatment on the relative risk of major cardiovascular disease and all-cause mortality. Two RCTs were identified for inclusion in their review. According to the review authors, both studies reported a reduction of ~50% in major CVD events and all-cause mortality with nighttime dosing and a reduction of 60% in CVD mortality, however they cautioned against interpretation of these results in view of ongoing discussion on the validity of the trials

Ho CLB et al. The effect of taking blood pressure lowering medication at night on cardiovascular disease risk. A systematic review. J Hum Hypertens. 2021 Apr;35(4):308-314. doi: 10.1038/s41371-020-00469-1. Epub 2021 Jan 18. PMID: 33462391

Day-time versus Night-time Dosing of Antihypertensive Medications

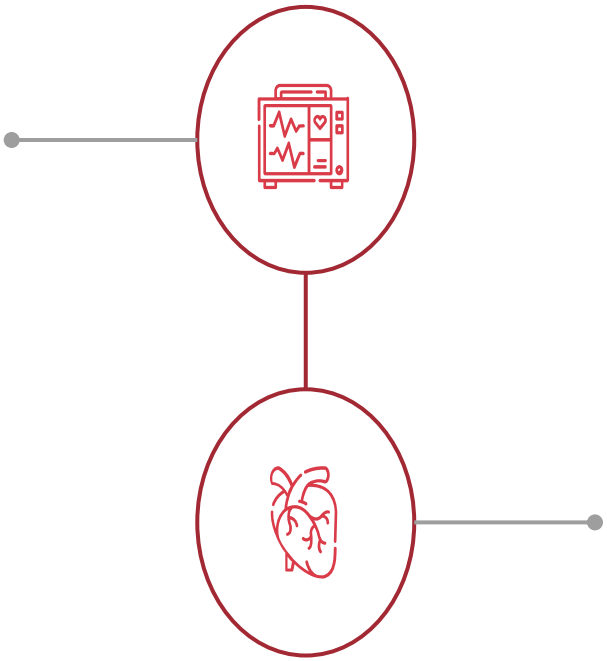
NEMLC Recommendation

NEMLC recommends that the STGs on hypertension in the PHC and AH CV chapters be amended from night time dosing to once daily dosing. The timing of the dose should be guided by the time of day that is most convenient for patients and that would optimize adherence and minimise side effects for individual patients.

Enalapril Dosing in Hypertension

Once daily versus twice daily administration of enalapril for the management of hypertension was previously reviewed by the PHC/AHL ERC during the 2017-2019 review cycle. A Pubmed search was undertaken to assess for any recent publications.

A review which included six studies was identified. Only one of the six studies included in the review was specific to enalapril - a randomized single-blind cross over study involving 25 patients.



The reviewers concluded that twice-daily dosing of ACE inhibitors may be as effective as once daily dosing which they acknowledge as supported by weak evidence. The authors acknowledge that current guidelines do not provide any recommendation for twice daily administration over once daily administration.

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Fischer K, Diec S (August 20, 2021) Once- Versus Twice-Daily Angiotensin-Converting Enzyme Inhibitors for Blood Pressure Control in Adult Patients With Hypertension. Cureus 13(8): e17331.
Girvin B, McDermott BJ, Johnston GD. A comparison of enalapril 20 mg once daily versus 10 mg twice daily in terms of blood pressure lowering and patient compliance. J Hypertens. 1999 Nov;17(11):1627-31. https://www.ncbi.nlm.nih.gov/pubmed/10608477

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Enalapril Dosing in Hypertension

NEMLC Recommendation

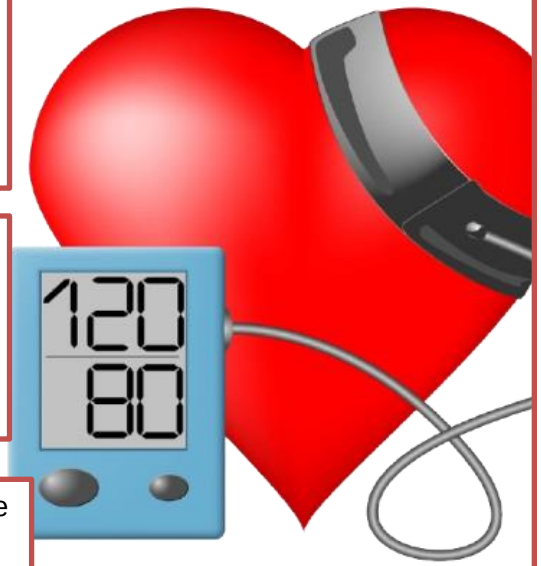
NEMLC recommends that the previous recommendation be retained i.e., *enalapril once daily for the management of hypertension. Available evidence found better compliance with once daily dosing, but no significant difference in blood pressure (also could not find evidence of superiority of the 12 hourly vs daily dosing of enalapril). Furthermore, enalapril 5 mg 12 hourly is more expensive than enalapril 10 mg daily (R6.00 vs R4.38, respectively for a 30 day treatment course*

Indapamide for Hypertension

Medicine Review: Indapamide as first-line therapy for uncomplicated primary hypertension compared to HCTZ

Hydrochlorothiazide (HCTZ) is currently the first-line pharmacological treatment for hypertension recommended in the STGs and EML for South Africa. Indapamide is not currently listed on the EML and is not on national tender

A review of systematic reviews and clinical practice guidelines that reported on or provided recommendations on first-line use of thiazide diuretics was conducted. Two relevant systematic reviews and three clinical practice guidelines were identified.



Findings from systematic reviews: There were no direct comparisons between the different diuretics regarding long-term clinical outcomes. Where head-to-head comparisons had been undertaken, they were usually based on blood pressure changes as the main outcome. Changes in blood pressure failed to explain the superiority of indapamide in reducing LVM.

Findings from clinical practice guidelines: The National Institute for Health and Care Excellence (NICE) 2011 guideline recommendation that use of thiazide-like diuretics (e.g. indapamide) are preferred over conventional thiazides (e.g. HCTZ) is based on lack of evidence supporting use of conventional thiazide diuretics, not comparative efficacy. The European Society of Cardiology and European Society of Hypertension (ESC/ESH) 2018 guideline doesn't state preference for either conventional thiazide or thiazide-like diuretics – instead it recommends two-drug combination therapy for the initial treatment of most people with hypertension, and thiazides are recommended as part of that combination therapy. The Hypertension Canada 2020 guideline recommended both thiazide and thiazide-like diuretics as monotherapy choices, with preference for longer-acting diuretics stated

The review found that the evidence supporting the use of indapamide over HCTZ is of low quality with uncertain impact on important clinical outcomes. In addition, indapamide is almost four times more expensive than HCTZ and a large patient population will be eligible to receive the treatment each year

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National Department of Health: Affordable Medicines, EDP-Primary Healthcare and Adult Hospital level. Medicine Review: Indapamide as first-line therapy for uncomplicated primary hypertension compared to HCTZ
Indapamide-versus-HCTZ-as-first-line-for-uncomplicated-primary-hypertension-v7.1-18-August-2022-final.pdf

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Indapamide for Hypertension

NEMLC Recommendation

NOT RECOMMENDED

NEMLC suggests that indapamide **not be recommended** for the first-line treatment of patients with uncomplicated hypertension.

Rationale: The clinical evidence supporting the use of indapamide over HCTZ is of low quality and uncertain. In addition, indapamide is more expensive than HCTZ and would have a significant impact on the pharmaceutical budget, while its additional clinical impact is uncertain. Indapamide may be considered for **inclusion in the therapeutic interchange** database as an alternative to HCTZ.

Glyceryl Trinitrate (GTN) IV - AHL

Guidance on the dilution and administration of GTN IV has been amended to accommodate for the different strengths of GTN IV formulations available which is now being procured through a Section 21 approval due to lack of a local supplier.

Due to the different pharmacokinetic profiles of GTN and Isosorbide Dinitrate (ISDN), the NEMLC do not regard these products as interchangeable for the relief of cardiac-related chest pain i.e. GTN has a quicker onset of action and termination of response. Furthermore, ISDN is not a suitable alternative to GTN for managing a hypertensive crisis.

Guidance on IV administrations has also been clarified as a step by step approach as tabulated in the STGs.

Glyceryl Trinitrate (GTN) IV - AHL

For ongoing chest pain, to control hypertension or treat pulmonary oedema:

- Glyceryl trinitrate, IV, 5–200 mcg/minute, titrated to response.
  - Guidance on preparation and administration included below.

Caution
Glyceryl trinitrate IV formulation must be diluted before infusion

STEP 1: Select the concentration as required for the individual patient

- For patients who are fluid congested or require higher doses for a clinical response, consider using a more concentrated solution e.g. 200 or 400 mcg/mL.

STEP 2: Select the volume of the diluent

- Patients who are likely to require treatment for a longer duration e.g. unstable angina prepare a larger volume e.g. 500mL.
- Compatible diluents include sodium chloride 0.9% or dextrose 5%.

STEP 3: Confirm the formulation of glyceryl trinitrate available and mix with diluent

- Confirm the strength of the GTN solution i.e. whether a 1mg/mL or 5mg/mL formulation is available.
- Depending on the formulation available, select the number of ampoules to be used based on the concentration and volume of the diluent as decided in Step 1 and 2 above.
- Ensure that the equivalent volume of diluent is removed from the bag before adding the total GTN volume e.g. if 100mLs of GTN is to be added, first remove 100mL of diluent from the bag before adding the GTN.

STEP 4: Set the flow rate for infusion

- Flush the PVC tube before administering to patient.
- Start with the lowest flow rate possible based on the concentration of the solution prepared.
- Increase by 5 mcg/minute every 5 minutes until response achieved or until the rate is 20 mcg/minute.
- If no response after 20 mcg/minute increase by 20 mcg/minute until response.
- Monitor blood pressure carefully.

E.g. To prepare a 200mcg/mL solution for a patient likely to require several hours of the GTN infusion:
Use 10 ampoules (100mL) of the 1mg/mL GTN formulation mixed with 400mL of diluent (100mL to be removed from a 500mL bag). Initiate the infusion at a flow rate 3mL/hr and titrate the infusion rate based on the patient's response.

STEP 1	STEP 2	STEP 3			
Concentration of dilution	Volume of diluent	Glyceryl trinitrate 1 mg/mL		Glyceryl trinitrate 5 mg/mL	
		Volume (Dose)	Number of 10mL ampoules	Volume (Dose)	Number of 10mL ampoules
100 mcg/mL	250 mL	25 mL (25 mg)	2.5	5 mL (25 mg)	0.5
200 mcg/mL		50 mL (50 mg)	5	10 mL (50 mg)	1
400 mcg/mL		100 mL (100 mg)	10	20 mL (100 mg)	2
100 mcg/mL	500 mL	50 mL (50 mg)	5	10 mL (50 mg)	1
200 mcg/mL		100 mL (100 mg)	10	20 mL (100 mg)	2
400 mcg/mL		200 mL (200 mg)	20	40 mL (200 mg)	4

STEP 4	Solution concentration (mcg/mL)	100 mcg/mL solution	200 mcg/mL solution	400 mcg/mL solution
	Dose (mcg/min)	Flow rate (microdrops/min = mL/hr)		
	5	3	–	–
	10	6	3	–
	15	9	–	–
	20	12	6	3
	30	18	9	–
	40	24	12	6
	60	36	18	9
	80	48	24	12
	100	60	30	15
	120	72	36	18
	160	96	48	24
	200	–	60	30

Table 3.3: Dilution of glyceryl trinitrate

Warfarin Management in Atrial Fibrillation- AHL

The Rosendaal method to calculate Time in Therapeutic range (TTR) has been included in Appendix II: Prescribing information for specific medicines. However, it has been reported that the Rosendaal method is effective if the gap between INR monitoring in stable patients, is not more than 56 days. Thus, INR monitoring in stable patients in the STG has been updated from "3-monthly" to "2-monthly"

Azar AJ, Cannegieter SC, Deckers JW, Briët E, van Bergen PF, Jonker JJ, Rosendaal FR. Optimal intensity of oral anticoagulant therapy after myocardial infarction. J Am Coll Cardiol. 1996 May;27(6):1349-55.
Rose AJ, Miller DR, Ozonoff A, Berlowitz DR, Ash AS, Zhao S, Reisman JI, Hylek EM. Gaps in monitoring during oral anticoagulation: insights into care transitions, monitoring barriers, and medication nonadherence. Chest. 2013 Mar;143(3):751-757

Warfarin Management in Atrial Fibrillation- AHL

Anticoagulate with warfarin:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to initiation dosing tables in Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to Maintenance dosing tables in Appendix II).
  - Every effort should be made to keep the time in therapeutic range (TTR) > ~~60%~~ 65%. If TTR ≤ ~~60%~~ 65% there is less benefit of warfarin therapy and a greater risk of stroke and haemorrhage.
  - See Appendix II for guidance on calculating TTR for management with warfarin.

Long-term therapy

Continue warfarin anticoagulation long-term, unless contra-indicated:

- Warfarin, oral, 5 mg daily.
  - Control with INR to therapeutic range:
    - INR between 2–3 and patient stable: monitor every ~~3~~ 2 months.
    - INR <1.5 or >3.5: monitor monthly.

Warfarin Management in Atrial Fibrillation- AHL

Time in therapeutic range (TTR)

The Rosendaal method is commonly used for monitoring and is validated to assess the time in therapeutic range (TTR). A TTR < 65% is associated with poorer outcomes and may signal a re-assessment of patient adherence and dosing.

Source: Rosendaal FR, Cannegieter SC, van der Meer FJ, Briët E. A method to determine the optimal intensity of oral anticoagulant therapy. Thromb Haemost. 1993 Mar 1;69(3):236-9. https://pubmed.ncbi.nlm.nih.gov/8470047/

Rosendaal calculation procedure (preferred method)

Example:

A patient has an INR reading of 2.4 on 1 October and a follow up INR measurement of 3.2 on 17 October.

If the patient's INR moves linearly from 2.4 to 3.2 throughout the 16-day interval, then we can estimate that the patient was within the INR therapeutic range (2 – 3) for approximately 75% of the time interval.

See calculation steps below:

Calculation steps:	Example:
1. Calculate the duration of the time interval between 2 INR values*	1 October to 17 October = 16 days
2. Calculate the amount of total INR shift in the time interval.	INR on 1 October: 2.4 INR on 17 October: 3.2 Total INR shift: 0.8
3. Calculate the amount of INR shift that is within the therapeutic range.	Upper INR threshold = 3.0 INR measurement in range = 2.4 Amount of INR shift within range: 3.0 - 2.4 = 0.6
4. Calculate the percent of total shift that is within therapeutic range. This is the %TTR for this specific time interval.	Amount of INR shift within range / Total INR shift = 0.6 /0.8 = 75%
5. Estimate the number of days in the interval that were within the therapeutic range	Duration of INR measurement interval X % TTR = 16 days X 75% = 12 days in therapeutic range
6. To calculate overall %TTR over multiple INR measurements, add total days in range for each time interval and divide by the total period of therapy.	A follow-up INR measurement on 30 October was 2.7. The %TTR for the interval of 17-30 October is 60% and days in therapeutic range is 8 days. The overall days in therapeutic range is 12 days + 8 days and the overall therapeutic period is 16 + 13 days. 20 days in therapeutic range / 29 days in treatment period = 69% cumulative TTR

Adapted from the *Rosendaal Method for % INR in range [Internet]. Using the ROSENDAAL method for calculating therapeutic time in range (TTR). INRpro.com; [cited 2022Nov29]. Available from: https://www.inrpro.com/rosendaal.asp.*

Note:

- The Rosendaal method for calculating TTR is not advised for intervals longer than 56 days/2 months between INR measurements.
- For step 3, if both INR measurements above or if both INR measurements are below the therapeutic range, time spent in therapeutic range is 0 and %TTR is also 0% for that time interval. E.g. first INR = 1.5 and second INR = 1.7
- For step 3, if one INR measurement is below therapeutic range and one is above the therapeutic range, then the INR shift within the therapeutic range will be 1. E.g. first INR = 1.5 and second INR = 3.2.
- For a TTR <65% adherence with warfarin therapy should be assessed and reinforced with the patient. Adjust the dose of warfarin only once it is established that poor adherence is not the cause of the sub-therapeutic TTR.

Direct Oral Anticoagulants (DOACs) Therapy in Atrial Fibrillation- AHL

Medicine Review: Evidence review of the clinical benefits and harms of Direct Oral Anticoagulants (DOACs) compared to warfarin for adult patients with chronic non-valvular atrial fibrillation (AF).

A rapid review of evidence regarding the use of DOACs versus warfarin for adult patients with chronic nonvalvular atrial fibrillation was conducted.

One systematic review with meta-analysis (was found Jia12 et al. which was deemed to be of critically low quality on the AMSTAR-2 rating), which included five randomized controlled trials (RCTs) that were mostly of good quality.

Compared to warfarin, "higher dose" DOACs resulted in a reduced risk of stroke and systemic embolism (relative risk [RR] = 0.80; 95% CI, 0.71-0.91; Number needed to treat to benefit [NNT] =149 [95% CI: 103 to 331]). Low-dose DOACs had similar efficacy in reducing the risk of stroke and systemic embolism compared to warfarin (RR = 1.03; 95% CI, 0.84-1.27). **Certainty of evidence: High**

DOACs reduced the risk of all-cause mortality, with a similar reduction noted whether a high dose (RR = 0.90; 95% CI, 0.85-0.95; NNT 177 [118 to 354]) or low dose DOAC regimen (RR = 0.89; 95% CI, 0.83-0.96; NNT 161 [95% CI: 104-442]) was used. **Certainty of evidence: High**

Compared to warfarin, DOACs reduce the risk for major bleeding (RR = 0.86; 95% CI: 0.74-0.99; NNT 119 [95% CI: 64-1660]). Lower dose DOAC regimens probably also result in a reduced risk for major bleeding (RR = 0.63, 95% CI: 0.38-1.04). **Certainty of evidence: High.**

The use of DOACs result in a lower risk of intracranial bleeding compared with warfarin use (RR = 0.48, [95% CI: 0.41-0.56]; NNT = 136 [95% CI: 120 to 161]). This reduction is more pronounced when a low dose regimen is used (RR = 0.31, [95% CI: 0.24-0.41]; NNT = 103 [95% CI: 93 to 120]). **Certainty of evidence: High**

The risk of gastrointestinal bleeding was significantly increased with the use of DOACs compared with warfarin (RR = 1.24 [95% CI: 1.10-1.39]; Number needed to harm = 224 [95% CI: 138 to 538]). This risk may be reduced with the use of low dose DOAC regimens (RR = 0.85, [95% CI: 0.72-1.00]). **Certainty of evidence: High**

Overall, the combined results of efficacy and safety support use of the DOACs as an alternative to warfarin for the long term prevention of stroke in patients with chronic atrial fibrillation.

Although numerous published cost-effectiveness analyses suggest that rivaroxaban is cost-effective in a long-term setting, there is still considerable uncertainty around the long-term outcomes and clinical benefits in a mixed population, real-world setting

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National Department of Health: Affordable Medicines, EDP-Adult Hospital level. Medicine Review: Evidence review of the clinical benefits and harms of Direct Oral Anticoagulants (DOACs) compared to warfarin for adult patients with chronic non-valvular atrial fibrillation (AF). Adult-Hospital-Chapter-3_Cardiovascular-System-with-supporting-NEMLC-report-appendix-reviews-2020-4-review-Version-1.0-1-November-2024-1.pdf

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Direct Oral Anticoagulants (DOACs) Therapy in Atrial Fibrillation- AHL

NEMLC Recommendation

NOT RECOMMENDED

NEMLC suggests that DOACs not be used for anticoagulation in atrial fibrillation.

Rationale: Direct oral anticoagulants (DOACs) have similar efficacy to warfarin in preventing ischaemic stroke and systemic embolism. They are associated with reduced mortality and lower rates of intracranial haemorrhage and major bleeding events. Despite these benefits, DOACs are not currently affordable. A rivaroxaban price reduction of at least 35% would be required for rivaroxaban to be considered as cost-effective using an ICER threshold of R100,000/QALY, while a price reduction of 75% would be required for cost-neutrality (Approximately R153.00 per patient per month).

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