





Pharmacist interprets the results and provides patient consultation

TARGET RANGES¹

Population	Target INR
Most patients on warfarin	2.0-3.0
Most patients on warfarin with mechanical mitral valves	2.5-3.5

For more information about INR targets for mechanical and bioprosthetic heart valves, refer to the [guideline](#) from Thrombosis Canada.

MANAGEMENT^{2*}

General Tips for Managing Out-of-Range INRs

- Try to determine the cause (*see tables on Out-of-Range INRs – Common Causes*). Questions to consider asking may include:
 - › Can you tell me what warfarin doses you've taken in the past 2 weeks?
 - › In the past week, have you missed any doses and if so, how many? How do you make sure you've taken all your doses, e.g., do you use a pill box, calendar, etc.?
 - › Have you recently started or stopped taking any medications (Rx and nonRx, e.g., antibiotics, acetaminophen) or supplements? Have there been any dose changes to any of your medications?
 - › How has your appetite been lately and are you eating regularly? Any recent changes to your diet?
 - › Do you drink alcohol and if so, how often and how much do you drink?
 - › How has your health been overall, i.e., any infections, fever, diarrhea, cold/flu, etc.?
- Consider therapy adjustments as necessary
 - › **One-time change:** to address a transient cause
 - › **Maintenance dose change:** for patients who have at least two consecutive out-of-range INRs in the same direction with no identifiable transient cause and who had stable, in-range INRs previously
 - › Both one-time and maintenance dose changes: as applicable

Out-of-Range INRs – Common Causes

High INRs [†]	Suggested Management [†]
DOSING – non-compliance or dosing errors (e.g., patient took a higher dose than prescribed)	<ul style="list-style-type: none"> • Review the actual doses of warfarin the patient has taken over the last several weeks • Simplify the regimen if possible (e.g., adjust the dosage to minimize the number of different tablets the patient needs to take) • Consider use of adherence aids (e.g., blister packs, warfarin dosing calendar)
DRUG INTERACTIONS (e.g., amoxicillin, macrolides, quinolones, metronidazole, TMP/SMX, fluconazole, amiodarone, some statins, fenofibrate, acetaminophen >1 g/day)	<ul style="list-style-type: none"> • Avoidance of drugs that interact with warfarin is generally not necessary • Temporary drug interactions: temporarily hold or decrease the dose of warfarin • Chronic drug interactions: decrease warfarin maintenance dose and measure INR more frequently until stable
MALNUTRITION (e.g., resulting in Vitamin K deficiency)	<ul style="list-style-type: none"> • Encourage a regular and consistent diet • Consider addition of meal replacement beverages as needed • Decrease warfarin maintenance dose and measure INR more frequently until stable
ALCOHOL CONSUMPTION	<ul style="list-style-type: none"> • Can continue usual warfarin maintenance dose if the INR increase is transient (i.e., caused by a one-time ingestion of a moderate to large amount of alcohol (>2 drinks))
HEALTH STATUS CHANGES (e.g., acute illness, fever, diarrhea, uncontrolled hyperthyroidism, CHF exacerbation; reduction in food intake)	<ul style="list-style-type: none"> • Decrease the warfarin dose temporarily and measure INR more frequently until the patient's health is stabilized

[†] Concomitant use of warfarin with antiplatelet agents (e.g., acetylsalicylic acid, clopidogrel, prasugrel, ticagrelor) and NSAIDs typically do not result in INR changes, however, the risk of bleeding is significantly increased. Therefore, the risks and benefits of concomitant use should be considered based on the indication for use, clinical necessity, and bleeding risk. Unless specifically indicated, concomitant use with warfarin should be avoided.

[†] Use as applicable. This is not a complete list and pharmacists should use professional judgement to determine the most appropriate management approach for each patient.

Low INRs	Suggested Management [†]
DOSING - missed doses, non-compliance, dosing errors (e.g., patient took a lower dose than prescribed)	<ul style="list-style-type: none"> Review the actual doses of warfarin taken over the last several weeks Simplify the regimen if possible (e.g., adjust the dosage to minimize the number of different tablets the patient needs to take) Consider use of adherence aids (e.g., blister packs, warfarin dosing calendar, reminder alarms)
UNDERDOSING	<ul style="list-style-type: none"> Aim to achieve an INR of 2.5 to decrease the chances of underdosing An INR of 1.5-2.0 carries a similar risk of bleeding as an INR of 2.0-3.0 but INRs <2.0 increase the risk of thrombosis
DRUG INTERACTIONS – Rx medications (e.g., phenytoin, carbamazepine, barbiturates, rifampin, azathioprine, trazodone); nonRx (e.g., green tea, ginseng, St. John's Wort)	<ul style="list-style-type: none"> Rx drug interactions: <ul style="list-style-type: none"> INR change usually observed within 2 weeks of drug initiation Incrementally increase warfarin maintenance dose until stable NonRx drug interactions: <ul style="list-style-type: none"> Avoid herbal supplements if possible Encourage consistency
LIFESTYLE CHANGES – dietary changes (e.g., increased intake in Vitamin K rich foods such as green leafy vegetables, soy, avocado, seaweed, meal replacement beverages that have Vitamin K); increased exercise	<ul style="list-style-type: none"> Patients do not need to eat less of foods rich in Vitamin K even though dietary intake of Vitamin K causes INR variability Encourage a regular and consistent lifestyle and diet Adjust warfarin if lifestyle and/or diet changes are long-term
[†] Use as applicable. This is not a complete list and pharmacists should use professional judgement to determine the most appropriate management approach for each patient.	

Single Out-of-Range INR

The specific approach to managing a single slightly out-of-range INR (e.g., INR 0.5 above or below target) in a patient who was previously in-range should take into consideration how much the value is out-of-range, the patient's past experience with out-of-range INRs and the patient's risk of thrombosis/stroke or bleeding. Two possible management options are:

Option	Repeat INR
Continue current maintenance dose	In 1-2 weeks
Make a one-time dosage change (increase or hold by ½ to 1 single dose) then resume current maintenance dose	

Example of a Maintenance Dosing Algorithm for Non-bleeding Patients on Warfarin (Assuming Target INR 2.0-3.0)^{*}

INR	Dosage Change of Warfarin [*]	Repeat INR
<2.0	Increase by 10-15% (Consider a 15% increase if INR ≤1.5 with no explanation)	Within 1 week
3.1-3.5	Decrease by 0-10%	Within 2 weeks
3.6-4.0	Hold 0-1 dose, decrease by 10-15%	Within 1 week
4.1-8.9 [#]	Hold 0-2 doses, decrease by 10-15%	In 2 days
>9.0 [#]	Hold 2 doses, decrease by 15-20%	Next day

^{*} This is to be used as a guide only and does not replace professional judgement. Other warfarin dosing algorithms are available.

^{*} Dose change percentage is based on the total weekly dose.

[#] For INRs >4.5 but <10 in the absence of clinically relevant bleeding, the usual recommendation is to temporarily hold the warfarin and not give Vitamin K. However, even in the absence of bleeding, if INR >10, depending on patient-specific factors such as bleeding risk factors, thrombosis risk if INR is over-corrected, and ability to repeat INR testing, Vitamin K may be given.

EXAMPLES OF ADDITIONAL SERVICES THAT MAY BE OFFERED

- Medication review/MedsCheck Annual
- Follow-up medication review/MedsCheck Follow-up
- Pharmaceutical Opinion
- Prescription adaptation/renewal
- Adherence packaging (e.g., dosette, blister packing)

(Refer to the [OPA Suggested Fee Guide for Uninsured Clinical and Professional Pharmacy Services](#) for more information as required)

Document and notify patient's primary care provider

Schedule follow up as required

(Refer to box on Target Populations for testing frequencies)

ABBREVIATIONS:

CHF: congestive heart failure; **NSAIDs:** non-steroidal anti-inflammatory drugs; **OHIP:** Ontario Health Insurance Plan; **POCT:** point-of-care test; **PT/INR:** prothrombin time/international normalized ratio; **Rx:** prescription; **TMP/SMX:** trimethoprim/sulfamethoxazole

DISCLAIMER:

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