1.14. Warfarin

For additional information regarding the management of oral anticoagulants, consult the following reference available online at: http://journal.publications.chestnet.org/data/Journals/CHEST/23443/112292.pdf

Pharmacokinetic Parameters

Table 1.14-1. Elimination Half-Lives of Vitamin K–Dependent Proteins

Factor	Half-Life
II	42–72 hr
VII	4–6 hr
IX	21–30 hr
X	27–48 hr
Protein C	8 hr
Protein S	60 hr

Drug–Drug Interactions

Table 1.14-2. Select Clinically Significant Warfarin Drug Interactions

Drugs/Drug Classes	Effect on INR	Mechanism
Alcohol (chronic use)	Decreased	Induction of warfarin metabolism
Carbamazepine	Decreased	Induction of warfarin metabolism
Cholestyramine	Decreased	Reduced absorption of warfarin
Thyroid hormones	Increased	Increased clotting factor catabolism
Alcohol (acute use)	Increased	Inhibition of warfarin metabolism
Amiodarone	Increased	Inhibition of warfarin metabolism
Aspirin	No effect	Increased bleeding risk
Clopidogrel/ticlopidine	No effect	Increased bleeding risk

Dosing Strategies

Table 1.14-3. Flexible Initiation Nomogram for Warfarin

Day	INR	5-mg Initiation Dose	10-mg Initiation Dose
1		5 mg	10 mg
2	< 1.5	5 mg	7.5 mg–10 mg
	1.5–1.9	2.5 mg	2.5 mg
	2.0–2.5	1.0– 2.5 mg	1.0–2.5 mg
	> 2.5	0	0
3	< 1.5	5–10 mg	5–10 mg
	1.5–1.9	2.5–5 mg	2.5–5 mg
	2.0–2.5	0–2.5 mg	0–2.5 mg
	2.6–3.0	0–2.5 mg	0–2.5 mg
	> 3.0	0	0
4	< 1.5	10 mg	10 mg
	1.5–1.9	5–7.5 mg	5–7.5 mg
	2.0–3.0	0–5 mg	0–5 mg
	> 3.0	0	0
5	< 1.5	10 mg	10 mg
	1.5–1.9	7.5–10 mg	7.5–10 mg
	2.0–3.0	0–5 mg	0–5 mg
	> 3.0	0	0
6	< 1.5	7.5–12.5 mg	7.5–12.5 mg
	1.5–1.9	5–10 mg	5–10 mg
	2.0–3.0	0–7.5 mg	0–7.5 mg
	> 3.0	0	0

INR: International normalized ratio.

Source: Reprinted with permission from Crowther MA, Harrison L, Hirsh J. Warfarin: less may be better. *Ann Intern Med*. 1997;127:332-333.

Table 1.14-4. Warfarin Dosing Adjustment Guidelines for INR Goal of 2–3

INR	Dosage Adjustment Guidelines
<1.5	Consider a booster dose of 1.5–2 times daily maintenance dose Consider resumption of prior maintenance dose if factor causing decreased INR is transient, e.g., missed warfarin dose(s) If dosage adjustment needed, increase maintenance dose by 10% to 20%
1.5–1.7	Consider a booster dose of 1.5–2 times daily maintenance dose Consider resumption of prior maintenance dose if factor causing decreased INR is considered, e.g., missed warfarin dose(s) If dosage adjustment needed, increase maintenance dose by 5% to 15%
1.8–1.9	No dosage adjustment may be necessary if the last two INRs were in range, if there is no clear explanation for the INR to be out of range, and if in the judgment of the clinician, the INR does not represent an increased risk of thromboembolism for the patient Consider a booster dose of 1.5–2 times daily maintenance dose Consider resumption of prior maintenance dose if factor causing decreased INR is transient, e.g., missed warfarin dose(s) If dosage adjustment needed, increase maintenance dose by 5% to 10%
2.0–3.0	Desired range
3.5–3.9	Consider holding one dose
> 4.0	Hold dosage until INR < upper limit of therapeutic range Consider use of mini dose (1.0–2.5 mg) oral vitamin K Consider resumption of prior maintenance dose if factor causing elevated INR is transient (e.g., acute alcohol ingestion) If dosage adjustment needed, decrease maintenance dose by 5% to 15%

INR: International normalized ratio.