

**Target Population:** Adult patients receiving anticoagulation therapy with the oral vitamin K antagonist, warfarin

**Full Guideline:** [Warfarin Management – Adult - Ambulatory](#)

### Guideline Overview

- Target INR and duration of therapy are based on indication for warfarin use- see [full guideline](#)
- [Risk factors which alter sensitivity](#) to warfarin
- [HAS-BLED Score](#)- prediction tool for risk of major bleeding with warfarin
- Warfarin dosing protocols for [initiation](#) and [maintenance](#)
- Warfarin [dosing pearls](#)
- [Laboratory monitoring](#) including [INR frequency](#)
- Common [signs and symptoms](#) of major bleeding/clotting
- Dose adjustments for [drug interactions](#)
- Factors that [increase](#) INR and bleeding risk
- Factors that [decrease](#) INR and increase clotting risk
- [Warfarin reversal](#)
- [References](#)

**Table 1:** [see guideline for INR goals and recommended duration of therapy by indication](#)

### Risk factors which alter sensitivity to warfarin

Table 2. Warfarin sensitivity factors

#### Increases sensitivity (usually require lower doses)

- Baseline (pre-warfarin) PT/INR (e.g., greater than 1.4)
- Advanced age (e.g., 60 years of age or older)<sup>1-10</sup>
- Underweight (e.g., BMI less than 18kg/m<sup>2</sup>)<sup>9,11,12</sup>
- Nutritional status (e.g., malnourished, low vitamin K intake/stores)
- Genetic factors (e.g., CYP2C9, VKORC1 phenotypes)
- Drug-drug interactions
- Hypoalbuminemia<sup>13,14</sup>
- Ethnicity (Asian)<sup>10,15,16</sup>
- Liver disease<sup>10,17</sup>
- Thyroid Disease (e.g., hyperthyroidism, Graves' disease)<sup>18-21</sup>
- Heart Failure<sup>22,23</sup>
- Febrile illness
- Prolonged vomiting and diarrhea
- Cannabinoids
- Alcohol

#### Decrease warfarin sensitivity (may require higher doses)

- Enteral feedings
- High-vitamin K intake
- Drug interactions
- Chewing tobacco

Table 3. HAS-BLED Score<sup>24</sup>

Factors	Points	Scoring
Hypertension (SBP >160 mmHg)	1	<b>Score = 0-1:</b> Low risk <b>Score = 2:</b> Moderate risk <b>Score ≥3:</b> High risk  <b>High bleed risk considerations:</b> <ul style="list-style-type: none"> <li>- Optimize blood pressure control</li> <li>- Check INRs frequently</li> <li>- Utilize anticoagulation clinic</li> <li>- Focus on fall prevention</li> <li>- Utilize direct oral anticoagulants</li> </ul>
Abnormal lab values <ul style="list-style-type: none"> <li>- Creatinine &gt;2.26 mg/dL</li> <li>- Bilirubin &gt;2x the upper limit of normal (ULN) <i>and</i> AST/ALT/AP &gt;3x ULN</li> </ul>	1	
Stroke history	1	
Bleeding history or predisposition	1	
Labile INRs: Time in Therapeutic Range <60%	1	
Elderly: > 65 years	1	
Drugs <ul style="list-style-type: none"> <li>- EtOH abuse</li> <li>- ASA or NSAID use</li> </ul>	1	

Table 4. Dosing for Warfarin Initiation (Week 1) with INR Goal 2-3<sup>25</sup>

Day Therapy	INR Value	Dose Adjustment
Day 1		5 mg daily (2.5 mg daily if high sensitivity to warfarin identified)
In 2-3 days after initiation	< 1.5 1.5-1.9 2.0-2.5  > 2.5	5 – 7.5 mg daily 2.5 - 5 mg daily 1 - 2.5 mg daily Hold and recheck INR next day
In additional 2-3 days after last INR check	< 1.5 1.5-1.9 2.0-3.0 > 3.0	7.5 – 10 mg daily 5 – 10 mg daily 2.5 – 5 mg daily Hold warfarin, recheck in 1-2 days
*If patient is started on 2.5 mg then target lower warfarin dose adjustments to avoid overshooting INR goal		

Table 5. Warfarin Maintenance Dosing Protocol with INR Goal 1.5-2.0<sup>25</sup>

INR less than 1.5	INR 1.5 – 2.0	INR 2.1 – 3.0	INR 3.1 – 3.9	INR 4.0-4.9	INR 5.0-8.9	INR greater than or equal to 9.0
Increase weekly dose 5%	No Change	Decrease weekly dose 5%	Half dose x 1 and Decrease weekly dose 10%	Hold 1 dose Decrease weekly dose by 10-20%	<b>Order required</b> Consider: Hold 2-3 doses, when able recheck INR before resuming warfarin Decrease weekly dose 10-20%; Check HCT or Hgb	Contact MD for urgent patient evaluation

Table 6. Warfarin Maintenance Dosing Protocol with INR Goal 2-3<sup>25</sup>

INR less than 1.5	INR 1.5 - 1.9	INR 2.0 - 3.0	INR 3.1- 3.9	INR 4.0-4.9	INR 5.0- 8.9	INR greater than or equal to 9.0
Extra Dose Increase weekly dose 10-20%	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Hold 1 dose Decrease weekly dose 10%	<b>Order required</b> Consider: Hold 2-3 doses, when able recheck INR before resuming warfarin Decrease weekly dose 10-20% Check HCT or Hgb	Contact MD for urgent patient evaluation

**Table 7. Warfarin Maintenance Dosing Protocol with INR Goal 2.5-3.5<sup>25</sup>**

INR less than 1.9	INR 1.9 - 2.4	INR 2.5 - 3.5	INR 3.6 - 4.5	INR 4.6-4.9	INR 5.0- 8.9	INR greater than or equal to 9.0
Extra Dose Increase weekly dose 10-20%	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Hold 1 dose Decrease weekly dose 10%	<b>Order required</b> Consider: Hold 1-2 doses, when able recheck INR before resuming warfarin Decrease weekly dose 10-20% Check HCT or Hgb	Contact MD for urgent patient evaluation

**Table 8. UW Health Dosing Pearls (UW Health GRADE very low quality evidence, C recommendation)**

INR range without a dosing table	Use same concept of adjusting the weekly dose by 5-10% based on the INR result
INR minimally out of range	If there is a transient reason for INR to be out of range (e.g. missed dose) or patient previously stable with unknown reason to be out of range, then may consider rechallenging the dose before making a weekly dose adjustment. Recheck the INR in 1-2 weeks.
Considerations for extra doses	An extra dose can be either an extra partial dose or extra full dose based on the INR and patient's known response to warfarin. The extra dose should not be included in the weekly dose adjustment
Considerations for held doses	A held dose should not be included in the weekly dose adjustment
Point of Care (POC) INR	If the INR is above 3.9, a repeat venipuncture is required to verify INR
INR < 2.0 AND mechanical valve with an INR goal of 2.5-3.5	Consider bridging with a low molecular weight heparin or as directed per the periprocedural guidelines
Variations in INR	Daily low dose vitamin K supplement should not be used to improve INR control

**Table 9. Laboratory Monitoring<sup>26,27</sup>**

Baseline		
Within the past 30 days	<ul style="list-style-type: none"> <li>• Baseline INR</li> <li>• Pregnancy test*</li> </ul>	*Pregnancy test is not needed if: <ol style="list-style-type: none"> <li>1. Are postmenopausal (12 months of amenorrhea in a woman &gt; 45 years old in the absence of other biological or physiological causes)</li> <li>2. Had a hysterectomy or bilateral salpingo-oophorectomy</li> <li>3. Have ovarian failure</li> <li>4. Had a bilateral tubal ligation or other surgical sterilization procedure</li> <li>5. Are known to be pregnant</li> <li>6. Have had a miscarriage or abortion in the last 7 days</li> <li>7. Have given birth within the past 4 weeks</li> </ol>
Within the past 90 days	<ul style="list-style-type: none"> <li>• Hemoglobin</li> <li>• Platelet count</li> </ul>	
Annually		
	<ul style="list-style-type: none"> <li>• Hemoglobin</li> <li>• Platelet count</li> </ul>	

Figure 1. Frequency of INR Monitoring after initiation of warfarin<sup>26-29</sup>

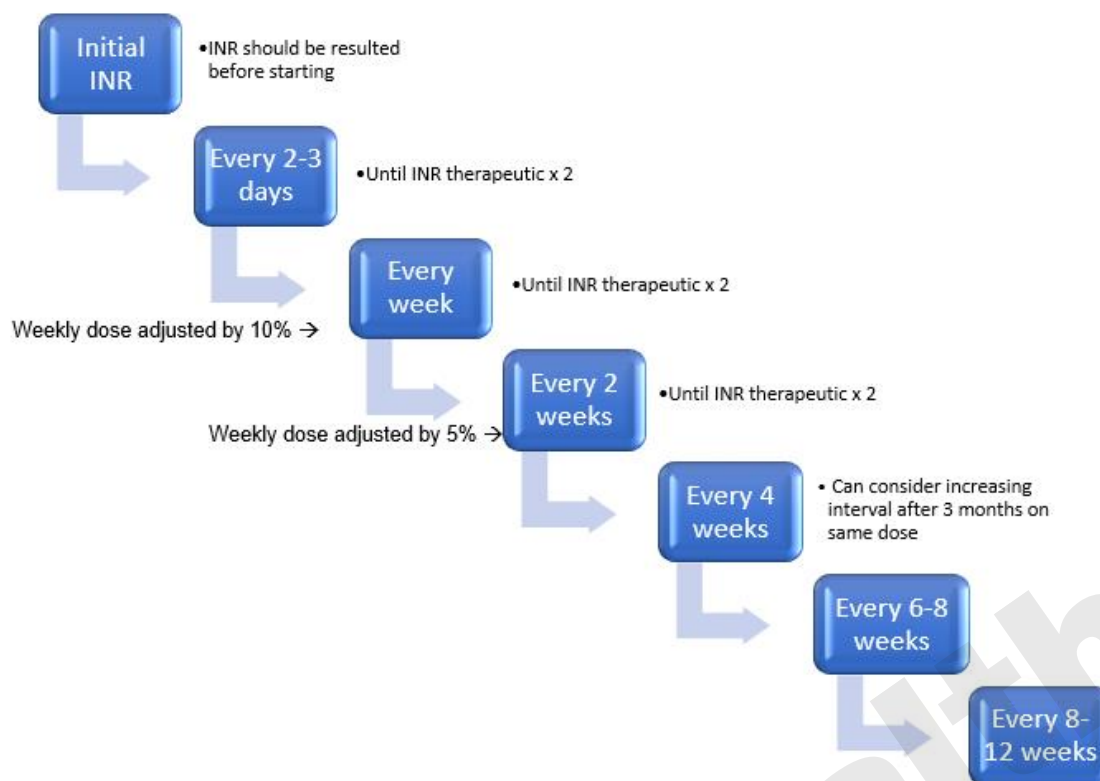


Table 10. Common Signs and Symptoms of Major Bleeding and Clotting<sup>30,31</sup>

Signs and Symptoms of Bleeding	Signs and Symptoms of Clotting
Blood in sputum	Chest or unilateral leg pain
Bloody emesis (bright red or coffee ground-like)	Unilateral lower extremity swelling
Blood in urine or stool (enough to color toilet water)	Warm, red or discolored skin of lower extremity
Bleeding that has not resolved or slowed within 10 minutes	Elevated heart rate (HR > 100 bpm)
	Shortness of breath
	Coughing or coughing up blood

Table 11. Dose Adjustment Recommendations for Common/Significant Warfarin-Drug Interactions<sup>26</sup>

Medication	INR check after starting	Adjustment
Amiodarone	Every 7 days	Target a 25-50% weekly dose reduction over 2-4 weeks
Rifampin	Every 7 days	Target a 50% weekly dose increase over 2 weeks
Fluconazole	2 – 3 days	Target a 30% weekly dose decrease
Metronidazole	2 – 3 days	Target a 30% weekly dose decrease
Sulfamethoxazole/ Trimethoprim	2 days	Target a 30% weekly dose decrease <b>Should reduce dose prior to starting medication to avoid critical INR elevation</b>

Table 12. Medications, Dietary Supplements, and Foods that INCREASE INR or bleeding risk<sup>10,26,27,32</sup>

Drug Class	Known Interaction	Probable Interaction	Possible Interaction	Unlikely Interaction
Anti-Infective	Ciprofloxacin Erythromycin <b>Fluconazole</b> Isoniazid <b>Metronidazole</b> Miconazole Miconazole Vaginal Suppository Moxifloxacin <b>Sulfamethoxazole</b> Voriconazole	Amoxicillin/clavulanate Azithromycin Clarithromycin Itraconazole Ketoconazole Levofloxacin Ritonavir Tetracycline	Amoxicillin Chloramphenicol Darunavir Daptomycin Etravirine Ivermectin Nitrofurantoin Norfloxacin Ofloxacin Saquinavir Telithromycin Terbinafine	Cefotetan Cefazolin Tigecycline
Cardiovascular	<b>Amiodarone*</b> Clofibrate Diltiazem Fenofibrate Propafenone Propranolol	Aspirin Fluvastatin Quinidine Ropinirole Simvastatin	Disopyramide Gemfibrozil Metolazone	
Analgesics, Anti-Inflammatory	Piroxicam	Acetaminophen Aspirin Celecoxib Tramadol	Indomethacin Propoxyphene Sulindac Tolmentin Topical Salicylates	Methylprednisolone Nabumetone
CNS Drugs	Alcohol Citalopram Entacapone Sertraline	Disulfiram Chloral hydrate Fluvoxamine Phenytoin	Felbamate	Diazepam Fluoxetine Quetiapine
GI Drugs and Food	Cimetidine Mango Omeprazole	Grapefruit	Orlistat	
Herbal Supplement	Fenugreek Feverfew Fish Oil Ginkgo Quiltinggao	Dandelion Danshen Don Quai Lycium PC-SPES Red or Sweet Clover	Capsicum <b>Forskolin</b> Garlic Ginger Turmeric	
Other	Anabolic Steroids Capecitabine Zileuton	Fluorouracil Gemcitabine Levamisole Paclitaxel Tamoxifen Tolterodine	Acarbose Cyclophosphamide Danazol Iphosphamide Trastuzumab	Etoposide Carboplatin Levonorgestrel

\*Indicates significant interaction

Table 13. Medications, Dietary Supplements, and Foods that DECREASE INR<sup>10,26,27,32</sup>

Drug Class	Known Interaction	Probable Interaction	Possible Interaction	Unlikely Interaction
Anti-Infective	Griseofulvin Nafcillin Ribavirin <b>Rifampin*</b>	Dicloxacillin Ritonovir Rifapentine	Terbinafine Nelfinavir Nevirapine	Cloxacillin Rifaximin Teicoplanin
Cardiovascular	Cholestyramine	Bosentan	Telmisartan	Furosemide
Analgesics, Anti-Inflammatory	Mesalamine	Azathioprine	Sulfasalazine	
CNS Drugs	Barbiturates Carbamazepine	Chlordiazepoxide		Propofol
GI Drugs and Food	High content vitamin K food Avocado	Soy milk Sucralfate	Sushi containing seaweed	
Herbal Supplement	Alfalfa	Ginseng Multivitamin St. John's Wort Parsley Chewing Tobacco	Co-Enzyme Q10 Yarrow Licorice	Green Tea
Other	Mercaptopurine	Chelation Therapy Influenza vaccine Raloxifene	Cyclosporine Etretinate Ubidecarenone	

\*Indicates significant interaction

[Click here for information on Warfarin Reversal](#)

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