Warfarin: Management of Elevated INR and Reversal

Elevated INR or Non-Life-Threatening Bleeding

**Warfarin Anticoagulation**

- **INR < 5**
  - Hold and/or decrease warfarin dose
  - No phytonadione needed
  - Recheck INR as clinically indicated.
  - For inpatients, consider recheck within 24-48 hrs.

- **INR ≥ 5 and ≤ 10 with NO Increased Bleeding Risk**
  - Hold the next 1 to 2 doses and consider warfarin dose adjustment
  - Consider holding additional dose(s) or restart warfarin with consideration to dose adjustment
  - Recheck INR as clinically indicated

- **INR ≥ 5 and ≤ 10 with Increased Bleeding Risk**
  - Hold warfarin
  - Does the patient have adequate gastrointestinal absorption or perfusion?
    - **NO**
      - Recheck INR within 24-48 hours unless clinical scenario indicates sooner follow-up.
      - If INR remains elevated with inadequate response to previous intervention, hold warfarin and may consider dose/re-dose of phytonadione by same route if indicated.
      - If adequate INR response, consider warfarin re-initiation.
      - For Obs/Admission criteria, see Appendix C
    - **YES**
      - Recheck INR within 24-48 hours
      - Based upon thrombosis vs. bleeding risk, consider phytonadione 1-2.5 mg ORALLY.

- **Supratherapeutic INR (≥ 3*)**
  - NO significant Bleeding AND NO Recent or Urgent Surgery / Invasive Procedure
  - If FFP given
    - Check INR within 1-2 h
  - Recheck for INR accuracy
  - Hold/discontinue warfarin therapy
  - Give phytonadione 2.5 to 5 mg PO or if the patient has inadequate gastrointestinal absorption or perfusion give by slow IV INFUSION over 30 minutes
  - Consider giving FFP for immediate effects.

- **INR > 10**
  - Re-check INR within 24 hours
  - If FFP given, see Appendix B.

*This guideline is applicable for the most common INR goal of 2-3. Therapeutic INR goals should be confirmed before reversal and INR adjusted according to warfarin indication. Examples of other INR goals are:
- High risk prosthetic valve 2.5-3.5
- Pulmonary hypertension 1.5-2.5

NOTE: Fresh Frozen Plasma (FFP) typically comes in volumes of 250-275 mL. Administer FFP 10-15 mL/kg and round to the nearest unit. For concerns of thrombosis in a patient if over-correction occurs, FFP units should be rounded down. In other cases of more severe bleeding, consider rounding the number of units up.

Based upon thrombosis vs. bleeding risk, consider phytonadione 1-2.5 mg by slow IV INFUSION over 30 min.
- May be repeated every 12 hrs.
- Do NOT give subcutaneously or intramuscularly due to erratic absorption

**Administer FFP**
- Typically comes in volumes of 250-275 mL
- Consider use of FFP**

*Recheck INR accuracy
Hold/discontinue warfarin therapy
Give phytonadione 2.5 to 5 mg PO or if the patient has inadequate gastrointestinal absorption or perfusion give by slow IV INFUSION over 30 minutes
Consider giving FFP for immediate effects.

See next page for “Serious or Life-Threatening Bleeding”

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Serious or Life-Threatening Bleeding

- Serious or life-threatening bleeding includes spontaneous intracerebral hemorrhage, gastrointestinal bleed requiring intervention, retroperitoneal hemorrhage, ruptured hollow viscus, emergent surgery.

- For further management and treatment goals of spontaneous ICH, see Management of Spontaneous Intracerebral Hemorrhage (ICH)/Intraparenchymal Hemorrhage (IPH) Guideline.

- For special populations such as LVADs, mechanical valves, or other patients at high risk for thromboembolic complications, consider consulting specialty areas / attendings.

- For patients at risk for thromboembolic complication or partial reversal (i.e. an INR ≤ 1.3 is not indicated) for a non-life threatening bleed consider giving flat dose of Kcentra® 500 units if INR ≤3 or 1000 units if INR >3

### Give phytonadione 10 mg by slow IV INFUSION over 30 min. (Do NOT give subcutaneously or intramuscular due to erratic absorption.)

**AND EITHER**

<table>
<thead>
<tr>
<th>Baseline INR</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4</td>
<td>25 units/kg</td>
</tr>
<tr>
<td>≥ 4</td>
<td>35 units/kg</td>
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</tbody>
</table>

Consider Kcentra® if INR needs reversed in <1 hour or concern for volume overload

- Recheck INR 15-30 minutes after Kcentra® administration
- If repeat INR ≥ 1.4 consider re-dosing Kcentra® with reduced dose.
  - Do not exceed a maximum cumulative dose of 5000 units or 50 units/kg in a 24-hour period

- Consider additional FFP for persistent bleeding.
- Phytonadione may be repeated every 12 hours.

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* Kcentra® is a factor IX concentrate that contains factors II, VII, IX, X, Protein C & S, Antithrombin III, human albumin, and heparin. Contraindicated in patients with heparin allergy. Dose is based on factor IX units. It is ordered / supplied by pharmacy. Baseline Labs should include chem 7, CBC, PT/INR, ionized calcium, arterial or venous blood gas.

** Kcentra® was not studied in patients who had a thromboembolic event, myocardial infarction, disseminated intravascular coagulation, cerebral vascular accident, transient ischemic attack, unstable angina pectoris, or severe peripheral vascular disease within the prior 3 months. Kcentra® may not be suitable in patients with thromboembolic events in the prior 3 months. PCC should only be administered to patients when the beneficial effects of use outweigh the serious risk of potential hypercoagulation. The use of factor products has been associated with thromboembolic complications including thrombosis and disseminated intravascular coagulation. Clinical surveillance for early signs of consumptive coagulopathy should be initiated with appropriate biological testing when administering PCC.
### Recommendations for Managing Warfarin Anticoagulation Therapy in Patients Requiring Invasive Procedures

#### Invasive Procedure or Urgent Surgery Needed

**Low Risk of Thromboembolism off of Anticoagulation**

- Hold warfarin dose 2 to 4 days prior to allow for procedure with an INR of 1.5 to 1.8 or less.

**Intermediate Risk of Thromboembolism off of Anticoagulation**

- Hold warfarin dose 2 to 4 days prior to allow for procedure with an INR of 1.5 to 1.8 or less.

**High Risk of Thromboembolism off of Anticoagulation**

- Hold warfarin dose 4-5 days prior to procedure.
- Begin therapy with therapeutic dose UFH or LMWH ~48 hours after last warfarin dose.

**Anticoagulation bridging not necessary.**

**Low Risk of Procedural Bleeding**

- Consider using therapeutic dose UFH or LMWH ~48 hours after last warfarin dose depending on patient's history.

**Intermediate Risk of Procedural Bleeding**

- Begin therapy with therapeutic dose UFH or LMWH ~48 hours after last warfarin dose.

**High Risk of Procedural Bleeding**

- Anticoagulation bridging not necessary.

**High Risk of Thromboembolism off of Anticoagulation**

- Hold warfarin dose 4-5 days prior to procedure.
- Phytonadione 2.5 mg PO or 1 mg by slow IV INFUSION over 30 min may be given 24 hr. prior to surgery if INR is not in desirable range.

**Intermediate Risk of Thromboembolism off of Anticoagulation**

- Consider using therapeutic dose UFH or LMWH ~48 hours after last warfarin dose depending on patient's history.

**Low Risk of Thromboembolism off of Anticoagulation**

- Hold warfarin dose 2 to 4 days prior to allow for procedure with an INR of 1.5 to 1.8 or less.

**Anticoagulation bridging not necessary.**

### Risk Stratification as an Indication for Anticoagulant Bridging Based Upon Thromboembolic Risk When NOT Fully Anticoagulated

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Intermediate Risk</th>
<th>High Risk</th>
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<tbody>
<tr>
<td>1 year risk of arterial embolism &gt; 10% or 1 month risk of VTE &gt; 10%</td>
<td>1 year risk of arterial embolism 5% to 10% or 1 month risk of VTE of 2% to 10%</td>
<td>1 year risk of arterial embolism &lt; 5% or 1 month risk of VTE &lt; 2%</td>
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**Anticoagulation Bridging Advised**

- Severe thrombophilia†
- Thromboembolic event within last 3 months
- Rheumatic atrial fibrillation
- Acute cardiac thromboembolism evidenced by echocardiogram
- Older mechanical valve
- Mechanical mitral valve
- Recently placed mechanical valve (< 3 months)
- Mechanical valve with recent (within 6 mo) stroke or TIA
- Afib with history of cardioembolism
- Afib CHADS₂ score of 5 or 6

**Anticoagulation Bridging Not Advised**

- Recurrent (>2) thromboembolic events
- Cerebrovascular disease with h/o multiple strokes/TIA's w/o risk factors for cardioembolism
- Afib CHADS₂ score of 3 or 4
- Mechanical bileaflet aortic valve and ≥ 1 of following: A Fib, prior stroke or TIA, HTN, DM, CHF, age >75 yr
- Venous thromboembolism >3 to 12 months ago
- Non-severe thrombophilia‡
- Venous thromboembolism with active cancer (treated within 6 mo or palliative)

**Anticoagulation Bridging as a case-by-case basis**

- Remote thromboembolic event >12 months ago and no other risk factors
- Intrinsic cerebrovascular disease w/o recurrent strokes/TIA's
- Afib CHADS₂ score of 0 or 2 (assume no prior stroke or TIA
- Mechanical bileaflet aortic valve
- Without A Fib and no other risk factors for stroke

### Emergency Surgery

- Give Phytonadione 5 to 10 mg PO or by slow IV INFUSION over 30 min. Do NOT give subcutaneously or intramuscularly due to erratic absorption

**AND EITHER**

- Give FFP (It is suggested that Phytonadione and FFP be administered together to avoid a rebound INR increase)
- Consider Prothrombin Complex Concentrate (PCC)[Kcentra®]. See Contraindications and Precautions** RISK (thromboembolism) vs. BENEFIT must be considered

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**If FFP/PCC given, check INR within 30 minutes. If repeat INR ≥ 1.4, consider additional FFP for persistent bleeding or re-dosing Kcentra® with reduced dose (Do not exceed a maximum cumulative dose of 5000 units or 50 units/kg in a 24-hour period**

**Phytonadione may be repeated every 12 hours, although consider the need for re-anticoagulation. Higher cumulative phytonadione doses induce warfarin resistance**

† deficiency protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities

‡ heterozygous factor V Leiden of prothrombin gene mutation

### Notes:

- For most common dental procedures/surgeries, no change in anticoagulation intensity is needed. Recent studies have reported that there was no significant difference in post-procedural bleeding at low or higher INR values. If bleeding complications are feared, epsilon aminocaproic acid mouthwash may be used without the interruption of anticoagulation.

### Risk Score

- 0-5 points: Low
- 6-10 points: Intermediate
- ≥ 11 points: High

### Calculations

- Baseline INR
- Therapeutic INR
- INR Trend
- INR Change

### Dosing

- UFH or LMWH
- Dosage adjustments
- Monitoring

### Complications

- Bleeding
- Thrombosis
- Anticoagulation Bridging

### Recommendations

- Anticoagulation Bridging Advised
- Anticoagulation Bridging Not Advised
- Case-by-case basis
References


Guideline Authors

• Erik Abel, PharmD, BCPS
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• Erin Reichert, PharmD, BCPS
• Colin Kaide, MD
• Virginia Mitchell, PharmD
• Tiffany Ortman, PharmD

Committee Approved: P&T Executive

Quality Measures

• Warfarin discontinued in all serious or life-threatening bleed cases
• Percent of patients who receive Kcentra®
• Baseline INR versus post-PCC INR
• Median time to repeat INR
• Mortality rate
  o Hospital mortality
  o 30-day mortality
• Mean hospital length of stay (days)

Guideline Approved


Disclaimer: Clinical practice guidelines and algorithms at The Ohio State University Wexner Medical Center (OSUWMC) are standards that are intended to provide general guidance to clinicians. Patient choice and clinician judgment must remain central to the selection of diagnostic tests and therapy. OSUWMC’s guidelines and algorithms are reviewed periodically for consistency with new evidence; however, new developments may not be represented.
Appendices

Appendix A – High Risk of Bleeding

- Elderly
- Heart Failure
- Cerebrovascular disease
- Hepatic or renal disease
- Diabetes
- Anemia

Appendix B

If FFP given:

a. Phytonadione and FFP should be administered together to avoid rebound INR increase
b. Recheck INR 1 hour after FFP administration if concern of bleeding or 6-12 hours and consider recheck of INR in 6-12 hours
c. If INR remains elevated 6 hours after dose, consider more FFP

Appendix C - Observation/Admission Criteria

1. Consider observation/admission if:
   a. Recent history of severe bleeding
   b. Fall risk
   c. Unknown cause of elevated INR (INR not elevated due to extra dose of warfarin or drug-interaction; patient may require further work up for infection, liver, or thyroid disease

2. For patients managed by OSUWMC Pharmacy Anticoagulation Clinic refer to pharmacist note for details and recommendations

3. If discharged, patient needs to contact Coumadin clinic provider to recheck INR within 24-48 hours