

# Anticoagulation for Venous Thromboembolism

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# Learning Objectives

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1. Incidence of Venous Thromboembolism
2. Introduction to Anticoagulants
3. Provoked vs Unprovoked VTE

# Learning Objectives

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4. Treatment Recommendations for VTE (2016 Chest Guidelines)

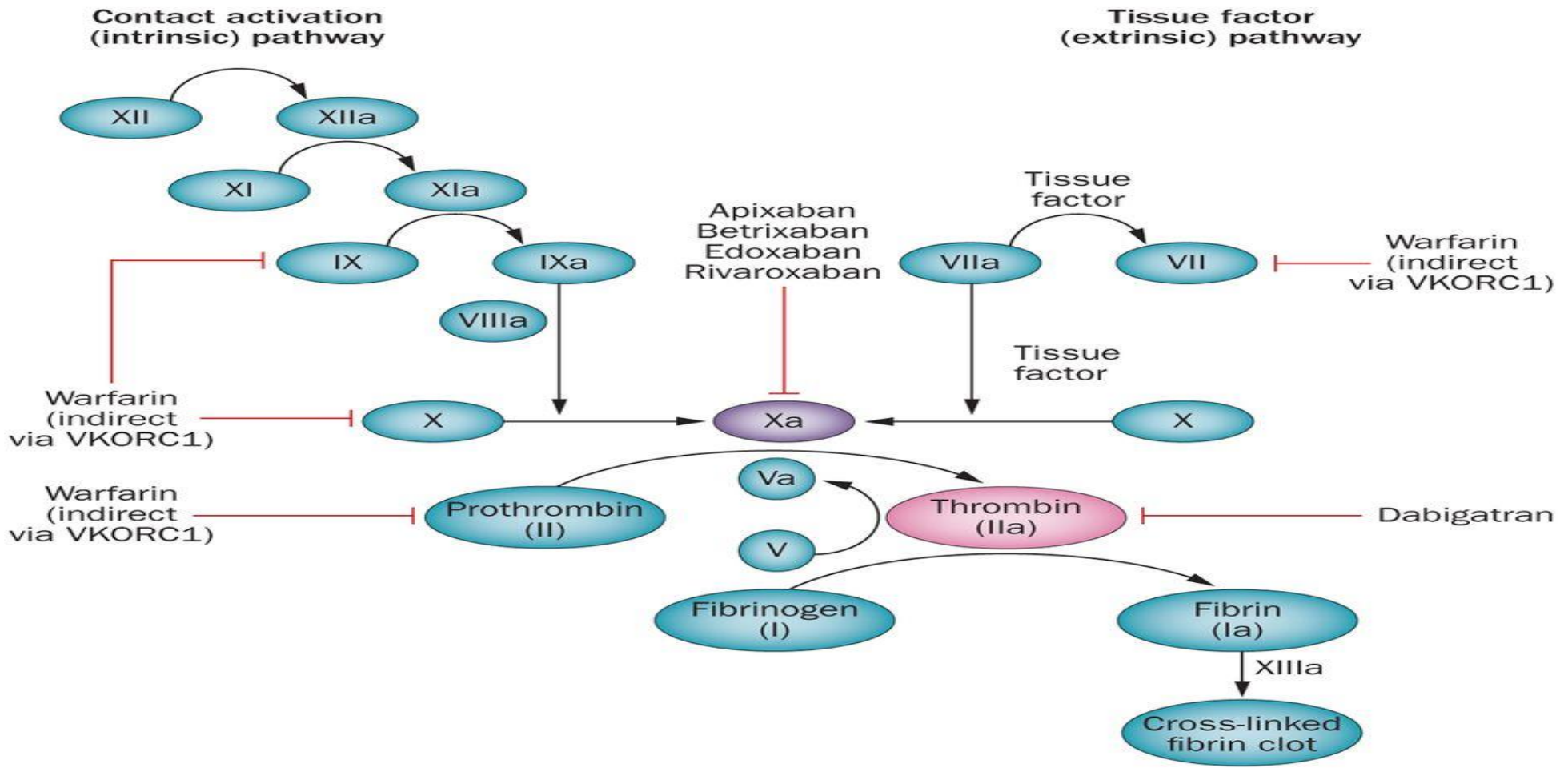
5. Dosing of anticoagulants and reversal agents



# Incidence of VTE in the US

-According the Centers for Disease Control, approximately 900,000 people are diagnosed with VTE every year

-Approximately 60,000-100,000 die of VTE annually



# Introduction to anticoagulants

# Warfarin

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-Vitamin K Antagonist

-Introduced in 1948 as a rat poison. Approved in 1954 for medical use.

-Anticoagulation for atrial fibrillation, valve replacement, treatment for VTE, left ventricular thrombus.

-VTE prophylaxis following orthopedic procedures

# Enoxaparin



- Potentiates antithrombin and irreversibly inactivates Xa
- Approved for use in 1993
- Anticoagulation for atrial fibrillation, valve replacement, treatment for VTE, left ventricular thrombus, unstable angina, STEMI, NSTEMI
- VTE prophylaxis following orthopedic procedures

# Dabigatran

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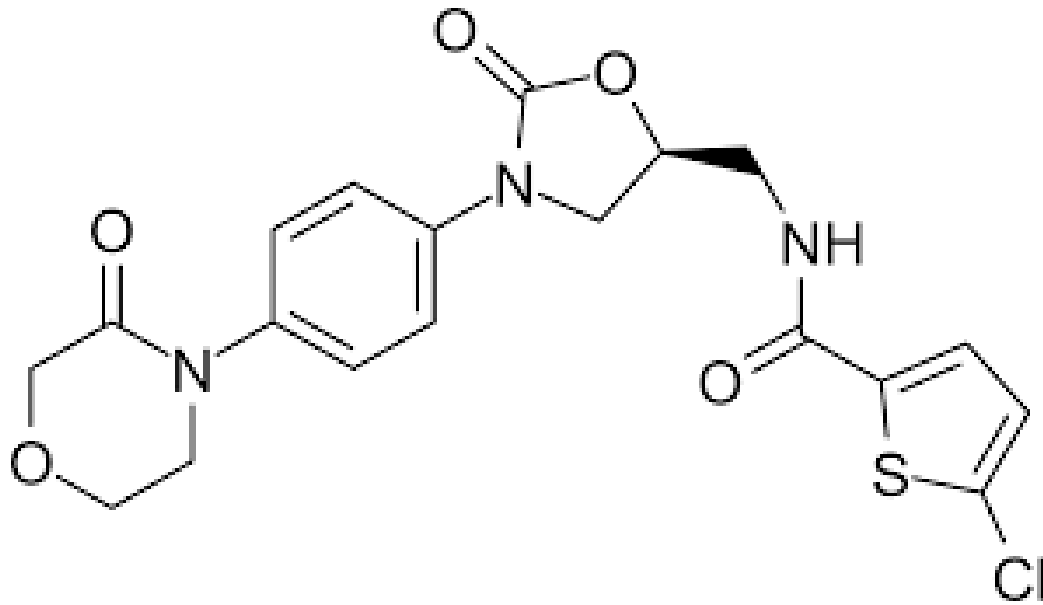


- Direct thrombin inhibitor
- Approved for use in 2010
- Anticoagulation for non-valvular atrial fibrillation, treatment for VTE
- VTE prophylaxis following orthopedic procedures



# Rivaroxaban

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-Factor Xa inhibitor

-Approved for use in 2011

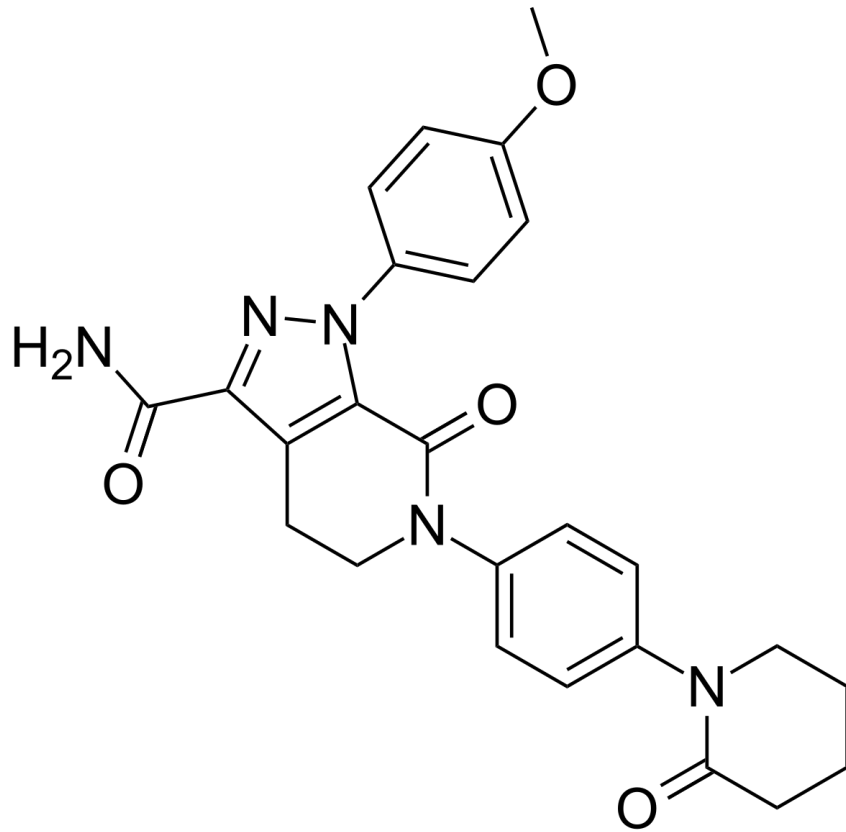
-Anticoagulation for non-valvular atrial fibrillation, treatment for VTE

-VTE prophylaxis following orthopedic procedures

-Also approved for cardiovascular risk reduction in 2018

# Introduction to anticoagulants (Apixaban)

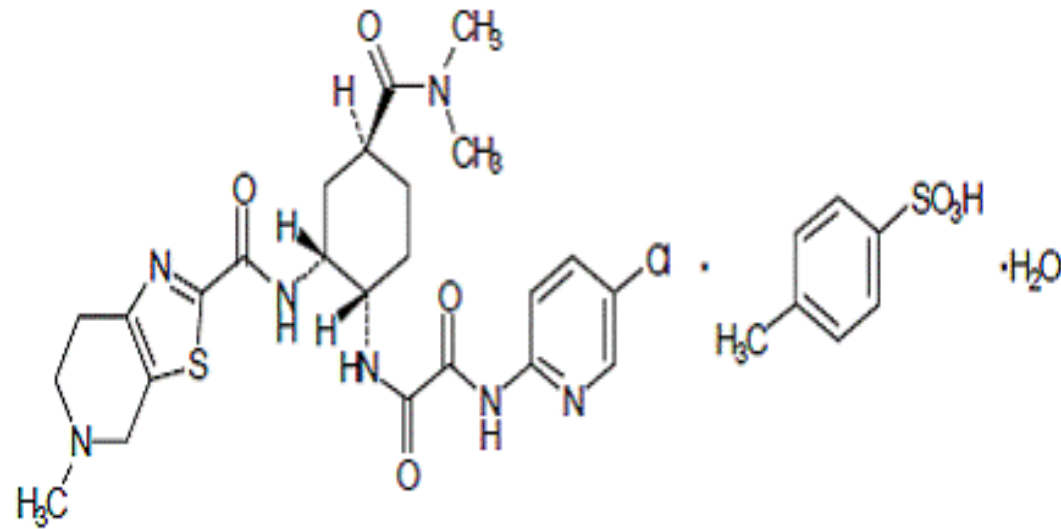
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- Factor Xa inhibitor
- Approved for use in 2014
- Anticoagulation for non-valvular atrial fibrillation, treatment for VTE
- VTE prophylaxis following orthopedic procedures

# Introduction to anticoagulants (Edoxaban)

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-Factor Xa inhibitor

-Approved for use in 2015

-Anticoagulation for non-valvular atrial fibrillation, treatment for VTE

# Provoked vs Unprovoked VTE

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Transient Major Risk Factors (during the 3 months prior to the diagnosis of VTE)

1. Major surgery > 30 minutes
2. Hospitalization or immobility > 3 days
3. Cesarean section
4. Long distance travel > 8 hours

Transient Minor Risk Factors (during the 2 months prior to the diagnosis of VTE)

1. Major surgery < 30 minutes
2. Hospitalization or immobility < 3 days
3. Estrogen therapy or pregnancy
4. Confined to bed out of hospital for at least 3 days with an acute illness
5. Leg injury associated with reduced mobility for 3 days

# Provoked vs Unprovoked VTE

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## Persistent Reversible Risks Factor

1. Curable malignancy
2. Inflammatory bowel disease that resolves
3. Other conditions with potentially curative treatment

## Persistent Irreversible Risk Factors

1. End-stage malignancy
2. Inherited thrombophilias
3. Chronic heart failure

# Treatment Recommendations

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1. In patients with DVT or PE and no cancer, recommendation is for dabigatran, rivaroxaban, apixaban or edoxaban over vitamin K antagonist therapy (Grade 2B).
2. For patients with DVT or PE and no cancer who are not treated with DOAC, recommendation is for VKA therapy over treatment with low-molecular weight heparin (Grade 2C).

# Treatment Recommendations

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3. In patients with “cancer-associated” DVT or PE, recommendation is for treatment with LMWH over VKA or DOAC therapy (Grade 2B-C).
4. Also, in patients with “cancer-associated” DVT or PE recommendation is for extended anticoagulation therapy (> 3 months) with no scheduled stop date regardless of bleeding risk (Grade 2C).

# Treatment Recommendations

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5. In patients with proximal DVT or PE “provoked” by nonsurgical transient risk factor recommendation is for treatment with anticoagulation for 3 months over treatment of shorter duration, longer duration (6, 12 or 24 months) or indefinite therapy (Grade 1B).
6. In patients with DVT or PE “provoked” by surgery, recommendation is for treatment with 3 months of anticoagulation over treatment of shorter duration, longer duration (6, 12 or 24 months) or indefinite therapy (Grade 1B).



# Bleeding Risk Factors

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1. Age > 65
2. Previous bleeding
3. Cancer
4. Renal failure
5. Liver failure
6. Thrombocytopenia
7. Previous stroke
8. Diabetes
9. Anemia
10. Antiplatelet therapy

# Bleeding Risk Factors

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- 11. Poor anticoagulant control
  - 12. Recent surgery
  - 13. Frequent falls
  - 14. Alcohol abuse
  - 15. NSAID use
- “Low Risk” – Zero risk factors  
(0.8% annual risk of bleeding)
- “Moderate Risk” – 1 risk factor  
(1.6% annual risk)
- “High Risk” – 2 or more risk factors  
(>6.5% annual risk)

# Treatment Recommendations

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7. In patients with “unprovoked” proximal DVT or PE and
  - “Low or moderate bleeding risk” recommendation is for extended anticoagulation with no scheduled stop date (Grade 2B).
  - “High bleeding risk” recommendation is for 3 months of anticoagulation therapy over extended therapy (Grade 1B)

# Treatment Recommendations

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8. In patients with an unprovoked DVT or PE who are stopping anticoagulation and do not have a contraindication to aspirin, aspirin is recommended to prevent recurrent VTE (Grade 2B).
9. In patients with acute DVT or PE who are treated with anticoagulants recommendation is against the use of an inferior vena cava filter (Grade 1B).

# Treatment Recommendations

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10. In patients with low risk PE and whose home circumstances are adequate, recommendation is for treatment at home or early discharge over standard discharge (after the first 5 days of treatment) (Grade 2B).

# Enoxaparin

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- I. Dosing for treatment of VTE
  - 1 mg/kg SQ twice daily
  - Alternative dosing 1.5mg/kg once daily
  - Discontinue if platelets <100k
  - For patients with CrCl < 30, dosing is 1mg/kg daily, no supplement for HD or PD

# Dabigatran

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- I. Dosing for treatment of VTE
  - 150mg PO BID
  - **For use in patients initially treated with parenteral anticoagulant for 5-10 days**
  - Use in patients with CrCl < 30 or on HD is not defined

# Rivaroxaban

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- I. Dosing for treatment of VTE
  - Initial dosing is 15mg PO BID for 21 days then 20mg daily
  - **Must be taken with food**
  - When transitioning from Warfarin to Rivaroxaban, Rivaroxaban can be initiated when INR is  $< 3$ .
  - Avoid use in patients with  $\text{CrCl} < 30$



# Apixaban

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- I. Dosing for treatment of VTE
  - Initial dosing is 10mg PO BID for 7 days then 5mg PO BID
  - When transitioning from Warfarin to Apixaban, Apixaban can be initiated when INR is  $< 2$ .
  - Avoid in patients with CrCl  $< 15$ .

# Edoxaban

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- I. Dosing for treatment of VTE
  - <60kg, 30mg daily
  - >60kg, 60mg daily
  - **For use in patients initially treated with parenteral anticoagulant for 5-10 days**
  - CrCl < 15 avoid use.

# Reversal Agents

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## I. Idarucizumab

- Approved in 2015 for reversal of Dabigatran
- Dose is 5mg IV x 1, can be repeated x 1
- Wholesale cost is \$3500 per dose

# Reversal Agents

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## I. Andexanet Alfa

- Approved in 2018 for reversal Factor Xa inhibitors
- Dose based on timing of most recent dose of Xa inhibitor
- Cost is \$25,000 to \$50,000 per dose

# References

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1. Antithrombotic Therapy for VTE Disease: CHEST Guideline and Expert Panel Report. Chest 2016;149:315-352.
2. Eliquis [package insert]. Princeton, NJ: Bristol-Myers Squibb; December 2012
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