Eliquis®
(apixaban) tablets 5mg 2.5mg

Dosing Guide
for All ELIQUIS Indications

Find out more at
hcp.eliquis.com
SELECTED IMPORTANT SAFETY INFORMATION

WARNING: (A) PREMATURE DISCONTINUATION OF ELIQUIS INCREASES THE RISK OF THROMBOTIC EVENTS, (B) SPINAL/EPIDURAL HEMATOMA

(A) Premature discontinuation of any oral anticoagulant, including ELIQUIS, increases the risk of thrombotic events. If anticoagulation with ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

(B) Epidural or spinal hematomas may occur in patients treated with ELIQUIS who are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:
- use of indwelling epidural catheters
- concomitant use of other drugs that affect hemostasis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
- a history of traumatic or repeated epidural or spinal punctures
- a history of spinal deformity or spinal surgery
- optimal timing between the administration of ELIQUIS and neuraxial procedures is not known

Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary.

Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated.

Approved for 6 indications

- to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (NVAF)
- for the treatment of deep vein thrombosis (DVT)
- for the treatment of pulmonary embolism (PE)
- to reduce the risk of recurrent DVT and PE following initial therapy
- for the prophylaxis of DVT, which may lead to PE, in patients who have undergone hip replacement surgery
- for the prophylaxis of DVT, which may lead to PE, in patients who have undergone knee replacement surgery
**Indication** | **Recommended dosing**
--- | ---
Reduction in the risk of stroke/systemic embolism in NVAF | 5 mg twice daily in most patients

**Dose adjustment for NVAF patients:** 2.5 mg twice daily is recommended for patients with at least 2 of the following characteristics:
- age ≥80 years
- body weight ≤60 kg
- serum creatinine ≥1.5 mg/dL

Treatment of DVT/PE | 10 mg twice daily for the first 7 days

▼ After 7 days, transition to ▼

5 mg twice daily

Reduction in the risk of recurrent DVT/PE following initial therapy | 2.5 mg twice daily after at least 6 months of treatment for DVT or PE

Prophylaxis of DVT, which may lead to PE, following hip or knee replacement surgery | 2.5 mg twice daily for 35 days starting 12 to 24 hours after hip replacement surgery

2.5 mg twice daily for 12 days starting 12 to 24 hours after knee replacement surgery

**CONTRAINDICATIONS**
- Active pathological bleeding
- Severe hypersensitivity reaction to ELIQUIS (e.g., anaphylactic reactions)

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
For patients with NVAF, Dosing for Reducing the Risk of Stroke & Systemic Embolism

5 mg taken orally twice daily recommended for most NVAF patients

**Recommended dose**

In 2 Phase III NVAF clinical trials, approximately 95% of ELIQUIS® (apixaban) patients received this dose.

**Dosage adjustment**

Patients with at least 2 of the following:

- **age** ≥80 years
- **body weight** ≤60 kg
- **serum creatinine** ≥1.5 mg/dl

PLEASE SEE PAGES 8-16 FOR ADDITIONAL IMPORTANT DOSING INFORMATION.

**SELECTED IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS**

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including ELIQUIS, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from ELIQUIS to warfarin in clinical trials in atrial fibrillation patients. If ELIQUIS is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
For patients with DVT/PE, DOSING FOR TREATING DVT/PE

10 mg taken orally twice daily for 7 days, followed by 5 mg taken orally twice daily, recommended for the treatment of DVT and PE

**Recommended dose**

<table>
<thead>
<tr>
<th>Day 1 to Day 7</th>
<th>Following Day 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg (two 5 mg tablets) twice daily</td>
<td>5 mg twice daily</td>
</tr>
</tbody>
</table>

An example of an ELIQUIS® (apixaban) prescription for a patient starting therapy for the treatment of DVT/PE

FOR: __________________________
ADDRESS: ______________________

RX

ELIQUIS 5 mg tablets
Take 2 tablets by mouth twice daily for 7 days
Followed by 1 tablet by mouth twice daily

First 30 days = 74 tablets
Subsequent prescriptions for a 30-day supply = 60 tablets (take one 5 mg tablet by mouth twice daily)

PLEASE SEE PAGES 8-16 FOR ADDITIONAL IMPORTANT DOSING INFORMATION.

**SELECTED IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS** (continued)

- **Bleeding Risk**: ELIQUIS increases the risk of bleeding and can cause serious, potentially fatal, bleeding.
  - Concomitant use of drugs affecting hemostasis increases the risk of bleeding, including aspirin and other antiplatelet agents, other anticoagulants, heparin, thrombolytic agents, SSRIs, SNRIs, and NSAIDs.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
For patients who have experienced a DVT/PE, REDUCING THE RISK OF RECURRENT DVT/PE FOLLOWING INITIAL THERAPY

2.5 mg taken orally twice daily recommended for the reduction in the risk of recurrent DVT/PE following initial therapy

Recommended dose

🎉 2.5 mg twice daily

Following ≥6 months of treatment for DVT or PE

Reduce dose by 50%: For patients receiving ELIQUIS® (apixaban) doses of 5 mg or 10 mg twice daily, when ELIQUIS is coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir).

*Clarithromycin*

Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

In patients already taking ELIQUIS at a dose of 2.5 mg twice daily: Avoid coadministration with combined P-gp and strong CYP3A4 inhibitors.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

- **Bleeding Risk** (continued)
  - Advise patients of signs and symptoms of blood loss and to report them immediately or go to an emergency room. Discontinue ELIQUIS in patients with active pathological hemorrhage.
  - There is no established way to reverse the anticoagulant effect of apixaban, which can be expected to persist for at least 24 hours after the last dose (i.e., about two half-lives). A specific antidote for ELIQUIS is not available.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
For patients who have undergone hip or knee replacement surgery, DOSING FOR PROPHYLAXIS OF DVT, WHICH MAY LEAD TO PE

2.5 mg taken orally twice daily recommended for hip or knee replacement surgery patients

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**Recommended dose**

- **2.5 mg twice daily**

  The initial dose should be taken 12 to 24 hours after hip or knee replacement surgery

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**In patients already taking ELIQUIS® (apixaban) at a dose of 2.5 mg twice daily:** Avoid coadministration with combined P-gp and strong CYP3A4 inhibitors.

- **Clarithromycin**

  Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

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**SELECTED IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS (continued)**

- **Spinal/Epidural Anesthesia or Puncture:** Patients treated with ELIQUIS undergoing spinal/epidural anesthesia or puncture may develop an epidural or spinal hematoma which can result in long-term or permanent paralysis.

  The risk of these events may be increased by the postoperative use of indwelling epidural catheters or the concomitant use of medicinal products affecting hemostasis. Indwelling epidural or intrathecal catheters should not be removed earlier than 24 hours after the last administration of ELIQUIS. The next dose of ELIQUIS should not be administered earlier than 5 hours after the removal of the catheter. The risk may also be increased by traumatic or repeated epidural or spinal puncture. If traumatic puncture occurs, delay the administration of ELIQUIS for 48 hours.

  Monitor patients frequently and if neurological compromise is noted, urgent diagnosis and treatment is necessary. Physicians should consider the potential benefit versus the risk of neuraxial intervention in ELIQUIS patients.

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Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
DOSING IN PATIENTS WITH RENAL IMPAIRMENT

ELIQUIS® (apixaban) elimination

Renal excretion accounts for about 27% of total clearance.

• ELIQUIS is eliminated in both urine and feces. Biliary and direct intestinal excretion contributes to elimination of ELIQUIS in the feces.

Dosing Considerations in NVAF Patients With Renal Impairment

No dose adjustment for renal impairment alone in patients with NVAF (see page 9 for additional dosage adjustment criteria).

Patients with end-stage renal disease (ESRD) on dialysis:

• Clinical efficacy and safety studies with ELIQUIS® (apixaban) did not enroll patients with ESRD on dialysis.

• In patients with ESRD maintained on intermittent hemodialysis, administration of ELIQUIS at the usually recommended dose will result in concentrations of apixaban and pharmacodynamic activity similar to those observed in the ARISTOTLE study.

• It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as were seen in ARISTOTLE.

SELECTED IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS (continued)

• Prosthetic Heart Valves: The safety and efficacy of ELIQUIS have not been studied in patients with prosthetic heart valves and is not recommended in these patients.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
Dosing Considerations in NVAF Patients With Renal Impairment

5 mg taken orally twice daily recommended for most NVAF patients

**Recommended dose**
In 2 Phase III NVAF clinical trials, approximately 95% of ELIQUIS® (apixaban) patients received this dose.

**Dosage adjustment**
Patients with at least 2 of the following:

- **age** ≥80 years
- **body weight** ≤60 kg
- **serum creatinine** ≥1.5 mg/dl

**SELECTED IMPORTANT SAFETY INFORMATION**

**WARNINGS AND PRECAUTIONS** (continued)

- **Acute PE in Hemodynamically Unstable Patients or Patients who Require Thrombolysis or Pulmonary Embolectomy**: Initiation of ELIQUIS is not recommended as an alternative to unfractionated heparin for the initial treatment of patients with PE who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
Dosing considerations in patients with renal impairment for all other ELIQUIS® (apixaban) indications

No dose adjustment is recommended for patients with renal impairment, including those with end-stage renal disease (ESRD) on dialysis, for the following indications:

- Prophylaxis of DVT, which may lead to PE, in patients who have undergone hip or knee replacement surgery
- Treatment of DVT
- Treatment of PE
- Reduction in the risk of recurrent DVT and PE following initial therapy

Clinical efficacy and safety studies with ELIQUIS did not enroll patients with ESRD on dialysis or patients with a CrCl <15 mL/min; therefore, dosing recommendations are based on pharmacokinetic and pharmacodynamic (anti-FXa activity) data in subjects with ESRD maintained on dialysis.

SELECTED IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS

- The most common and most serious adverse reactions reported with ELIQUIS were related to bleeding.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
### Dosing in patients with hepatic impairment

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>hepatic impairment (Child-Pugh class A)</td>
<td>hepatic impairment (Child-Pugh class B)</td>
<td>hepatic impairment (Child-Pugh class C)</td>
</tr>
<tr>
<td>No dose adjustment required</td>
<td>There is limited clinical experience with ELIQUIS® (apixaban) in patients with moderate hepatic impairment; dosing recommendation cannot be provided</td>
<td>ELIQUIS is not recommended</td>
</tr>
</tbody>
</table>

Adjust ELIQUIS dose for patients taking drugs that are combined P-gp and strong CYP3A4 inhibitors.

See Drug Interactions on page 15 for more information.

### SELECTED IMPORTANT SAFETY INFORMATION

#### TEMPORARY INTERRUPTION FOR SURGERY AND OTHER INTERVENTIONS

- ELIQUIS should be discontinued at least 48 hours prior to elective surgery or invasive procedures with a moderate or high risk of unacceptable or clinically significant bleeding. ELIQUIS should be discontinued at least 24 hours prior to elective surgery or invasive procedures with a low risk of bleeding or where the bleeding would be noncritical in location and easily controlled. Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
DOSING CONSIDERATIONS AND ADMINISTRATION OPTIONS

Additional dosing considerations

- Does not require routine monitoring using international normalized ratio (INR) or other tests of coagulation
- No known dietary restrictions
- Can be taken with or without food
- **Missed dose**: If a dose of ELIQUIS® (apixaban) is not taken at the scheduled time, the dose should be taken as soon as possible on the same day and twice-daily administration should be resumed. The dose should not be doubled to make up for a missed dose.

Temporary interruption for surgery and other interventions

<table>
<thead>
<tr>
<th>Bleeding risk with elective surgery or invasive procedures</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Moderate</strong> or <strong>high risk</strong> of unacceptable or clinically significant bleeding</td>
<td>Discontinue ELIQUIS at least <strong>48 hours</strong> prior</td>
</tr>
<tr>
<td><strong>Low risk</strong> or <strong>noncritical site</strong> and <strong>easily controlled</strong></td>
<td>Discontinue ELIQUIS at least <strong>24 hours</strong> prior</td>
</tr>
</tbody>
</table>

- Bridging anticoagulation during the 24 to 48 hours after stopping ELIQUIS and prior to the intervention is not generally required. ELIQUIS should be restarted after the surgical or other procedures as soon as adequate hemostasis has been established.

**SELECTED IMPORTANT SAFETY INFORMATION**

**DRUG INTERACTIONS**

- **Combined P-gp and Strong CYP3A4 Inhibitors**: Inhibitors of P-glycoprotein (P-gp) and cytochrome P450 3A4 (CYP3A4) increase exposure to apixaban and increase the risk of bleeding. For patients receiving ELIQUIS doses of 5 mg or 10 mg twice daily, reduce the dose of ELIQUIS by 50% when ELIQUIS is coadministered with drugs that are combined P-gp and strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, or ritonavir). In patients already taking 2.5 mg twice daily, avoid coadministration of ELIQUIS with combined P-gp and strong CYP3A4 inhibitors.

  **Clarithromycin**

  Although clarithromycin is a combined P-gp and strong CYP3A4 inhibitor, pharmacokinetic data suggest that no dose adjustment is necessary with concomitant administration with ELIQUIS.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
Switching from anticoagulants other than warfarin (oral or parenteral) to ELIQUIS

- Discontinue the anticoagulant other than warfarin and begin taking ELIQUIS at the usual time of the next dose of the anticoagulant other than warfarin

Switching from ELIQUIS to anticoagulants other than warfarin (oral or parenteral)

- Discontinue ELIQUIS and begin taking the new anticoagulant other than warfarin at the usual time of the next dose of ELIQUIS

Switching from ELIQUIS to warfarin

- ELIQUIS affects INR, so that initial INR measurements during transition to warfarin may not be useful for determining the appropriate dose of warfarin

- One approach is to discontinue ELIQUIS and begin both parenteral anticoagulant and warfarin at the time the next dose would have been taken, discontinuing the parenteral anticoagulant when INR reaches an acceptable range

Switching from warfarin to ELIQUIS

- Discontinue warfarin and start ELIQUIS when the INR is < 2.0

SELECTED IMPORTANT SAFETY INFORMATION

DRUG INTERACTIONS (continued)

- Combined P-gp and Strong CYP3A4 Inducers: Avoid concomitant use of ELIQUIS with combined P-gp and strong CYP3A4 inducers (e.g., rifampin, carbamazepine, phenytoin, St. John’s wort) because such drugs will decrease exposure to apixaban.
• For patients who are unable to swallow whole tablets, 5 mg and 2.5 mg ELIQUIS® (apixaban) tablets may be crushed and suspended in water, 5% dextrose in water (D5W), or apple juice, or mixed with applesauce and promptly administered orally.

• Alternatively, ELIQUIS tablets may be crushed and suspended in 60 mL of water or D5W and promptly delivered through a nasogastric tube.

• Crushed ELIQUIS tablets are stable in water, D5W, apple juice, and applesauce for up to 4 hours.

**SELECTED IMPORTANT SAFETY INFORMATION**

**DRUG INTERACTIONS** (continued)

• **Anticoagulants and Antiplatelet Agents:** Coadministration of antiplatelet agents, fibrinolytics, heparin, aspirin, and chronic NSAID use increases the risk of bleeding. APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo.
**DRUG INTERACTIONS**

<table>
<thead>
<tr>
<th>Combined P-gp and strong CYP3A4 inhibitors</th>
<th>Reduce dose by 50%: For patients receiving ELIQUIS® (apixaban) doses of 5 mg or 10 mg twice daily when coadministered with combined P-gp and strong CYP3A4 inhibitors</th>
</tr>
</thead>
</table>
| Ketoconazole                              | In patients already taking ELIQUIS at a dose of 2.5 mg twice daily:  
|                                           | • Avoid coadministration with combined P-gp and strong CYP3A4 inhibitors |
| Itraconazole                              | These drugs increase exposure to ELIQUIS and increase the risk of bleeding |
| Ritonavir                                 | PK data suggest that no dose adjustment is necessary |
| **Clarithromycin**                        | Avoid concomitant use. These drugs decrease exposure to ELIQUIS and increase the risk of stroke and other thromboembolic events. |
| **Combined P-gp and strong CYP3A4 inducers** |  
| Rifampin                                  |  
| Phenytoin                                 |  
| Carbamazepine                             |  
| St. John’s wort                           |  

PK=pharmacokinetic.  
These drug categories are examples described in the Full Prescribing Information, not an all-inclusive list.

### SELECTED IMPORTANT SAFETY INFORMATION

**PREGNANCY CATEGORY B**

- There are no adequate and well-controlled studies of ELIQUIS in pregnant women. Treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. ELIQUIS should be used during pregnancy only if the potential benefit outweighs the potential risk to the mother and fetus.

Please see additional Important Safety Information throughout. Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
**Drugs affecting hemostasis**

Coadministration with these drugs increases the risk of bleeding:
- Aspirin and other antiplatelet agents
- Other anticoagulants
- Heparin
- Thrombolytic agents
- Selective serotonin reuptake inhibitors (SSRIs)
- Serotonin norepinephrine reuptake inhibitors (SNRIs)
- Nonsteroidal anti-inflammatory drugs (NSAIDs), when used chronically
- Fibrinolytics

These drug categories are examples described in the Full Prescribing Information, not an all-inclusive list.

**Additional considerations**

- Apixaban is a substrate of both CYP3A4 and P-gp
- Famotidine, atenolol, prasugrel, and enoxaparin did not meaningfully alter the pharmacokinetics of ELIQUIS® (apixaban) in healthy subjects
- ELIQUIS did not meaningfully alter the pharmacokinetics of digoxin, naproxen, atenolol, prasugrel, or acetylsalicylic acid in healthy subjects
- APPRAISE-2, a placebo-controlled clinical trial of apixaban in high-risk post-acute coronary syndrome patients treated with aspirin or the combination of aspirin and clopidogrel, was terminated early due to a higher rate of bleeding with apixaban compared to placebo
- For diltiazem, no dose adjustment of ELIQUIS is required²
CONSIDERATIONS FOR REVERSING THE ANTIMICROBIAL EFFECT OF ELIQUIS® (apixaban)

A specific antidote for ELIQUIS is not available

- The apparent half-life of ELIQUIS is approximately 12 hours following oral administration
- The pharmacodynamic effect of ELIQUIS can be expected to persist for at least 24 hours after the last dose, i.e., for about 2 drug half-lives

<table>
<thead>
<tr>
<th>There is no established way to reverse bleeding in patients taking ELIQUIS</th>
<th>The use of procoagulant reversal agents may be considered but has not been evaluated in clinical studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hemodialysis does not appear to have a substantial impact on ELIQUIS exposure</td>
<td>- Prothrombin complex concentrate (PCC)</td>
</tr>
<tr>
<td>- Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of ELIQUIS</td>
<td>- Activated prothrombin complex concentrate</td>
</tr>
<tr>
<td>- There is no experience with antifibrinolytic agents (tranexamic acid, aminocaproic acid) in individuals receiving ELIQUIS</td>
<td>- Recombinant factor VIIa</td>
</tr>
<tr>
<td>- There is no experience with systemic hemostatics (desmopressin and aprotinin) in individuals receiving apixaban and they are not expected to be effective as a reversal agent</td>
<td>- When PCCs are used, monitoring for the anticoagulation effect of apixaban using a clotting test (PT, INR, or aPTT) or anti-factor Xa (FXa) activity is not useful and is not recommended</td>
</tr>
</tbody>
</table>

- Activated oral charcoal reduces absorption of ELIQUIS, thereby lowering ELIQUIS plasma concentration

aPTT = activated partial thromboplastin time; PT = Prothrombin time.

Please see full Prescribing Information including Boxed WARNINGS and Medication Guide or visit ELIQUIS.com.
Approved for 6 Indications

Find out more at:
hcp.eliquis.com


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