### ELIQUIS DOSAGE BY LEVEL OF RENAL IMPAIRMENT IN AF

<table>
<thead>
<tr>
<th>Creatinine clearance</th>
<th>Indication</th>
<th>Prevention of stroke and SE in AF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&gt;50-≤80 mL/min</td>
<td>5 mg BID</td>
</tr>
<tr>
<td></td>
<td>&gt;30 to ≤50 mL/min</td>
<td>Dose adjustment to 2.5 mg BID only if ≥2 of ABC criteria* (age ≥80 years, body weight ≤60 kg, creatinine level ≥133 µmol/L) are met</td>
</tr>
<tr>
<td>Moderate</td>
<td>≥25-≤30 mL/min</td>
<td>No dosing recommendation can be made as clinical data are very limited</td>
</tr>
<tr>
<td>Severe</td>
<td>≥15-≤24 mL/min</td>
<td>Not recommended</td>
</tr>
<tr>
<td></td>
<td>&lt;15 mL/min or undergoing dialysis</td>
<td></td>
</tr>
</tbody>
</table>

**OTHER CONSIDERATIONS**

- Use with caution in patients with elevated liver enzymes (ALT/AST >2 x ULN, or total bilirubin ≥1.5 x ULN)
- Use with caution in patients with mild or moderate hepatic impairment
- Not recommended in patients with severe hepatic impairment
- Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk

* These patients have been determined to be at higher risk of bleeding.
Clinical use:
Safety and efficacy not established in pediatric patients (<18 years); therefore, Health Canada has not authorized an indication for pediatric use.

Contraindications:
• Clinically significant active bleeding, including gastrointestinal bleeding
• Lesions or conditions at increased risk of clinically significant bleeding
• Hepatic disease associated with coagulopathy and clinically relevant bleeding risk
• Concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-glycoprotein
• Concomitant treatment with any other anticoagulant including unfractionated heparin, except at doses used to maintain a patent central venous or arterial catheter, low molecular weight heparins, such as enoxaparin and dalteparin, heparin derivatives, such as fondaparinux, and oral anticoagulants, such as warfarin, dabigatran, rivaroxaban, except under circumstances of switching therapy to or from apixaban

Most serious warnings and precautions:
• Bleeding: if severe, discontinue
• Peri-operative spinal/epidural anesthesia, lumbar puncture: increased risk of hematoma
• INR monitoring: not a valid measure to assess anticoagulant activity of ELIQUIS
• Premature discontinuation: increases risk of thrombotic events

Other relevant warnings and precautions:
• Caution when used with drugs that affect hemostasis
• Not recommended in patients with prosthetic heart valves or with hemodynamically significant rheumatic heart disease, especially mitral stenosis
• Avoid use with strong inducers of both CYP3A4 and P-gp
• Caution in patients with mild or moderate hepatic impairment (not recommended if severe) or elevated liver enzymes
• Caution in patients ≥75 years in the treatment of DVT and PE and prevention of recurrent DVT and PE
• Pre-operative/post-operative considerations
• Not recommended as an alternative to unfractionated heparin for the treatment of VTE in patients with pulmonary embolism who are hemodynamically unstable, or who may receive thrombolyis or pulmonary embolectomy
• Not recommended for patients with a history of thrombosis who are diagnosed with antiphospholipid syndrome (APS)
• Renal impairment: not recommended if creatinine clearance <15 mL/min or dialysis; dosing adjustments may be required; renal function should be monitored
• Not recommended in pregnant or nursing women
• Hip fracture surgery patients

For more information:
Please consult the Product Monograph at https://www.bms.com/assets/bms/ca/documents/productmonograph/ELIQUIS_EN_PM.pdf or https://www.pfizer.ca/pm/en/eliquis.pdf for important information relating to adverse reactions, drug interactions, and dosing information which have not been discussed in this piece.
The Product Monograph is also available by calling 1-866-463-6267.

References: 1. IQVIA, Compuscript, June 2020. 2. ELIQUIS Product Monograph. Pfizer Canada ULC and Bristol-Myers Squibb Canada Co.
**ELIQUIS: DOSAGE RECOMMENDATIONS**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Dosing Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevention of stroke and systemic embolism in AF</strong></td>
<td>5 mg BID</td>
</tr>
<tr>
<td><strong>Treatment of acute DVT or PE</strong></td>
<td>10 mg BID for the first 7 days</td>
</tr>
<tr>
<td><strong>Continued prevention of recurrent DVT or PE</strong></td>
<td>2.5 mg BID</td>
</tr>
<tr>
<td><strong>Prevention of VTE in:</strong></td>
<td></td>
</tr>
<tr>
<td>– elective knee replacement surgery</td>
<td>2.5 mg BID for 10 to 14 days</td>
</tr>
<tr>
<td>– elective hip replacement surgery</td>
<td>2.5 mg BID for 32 to 38 days</td>
</tr>
</tbody>
</table>

Please consult the Product Monograph for complete dosage and administration instructions. ELIQUIS is indicated for the prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective knee or hip replacement surgery; the prevention of stroke and systemic embolism in patients with atrial fibrillation (AF); the treatment of venous thromboembolic events (deep vein thrombosis [DVT], pulmonary embolism [PE]) and for the prevention of recurrent DVT and PE.

As for any non-vitamin K antagonist oral anticoagulant (NOAC) drug, before initiating ELIQUIS, ensure that the patient understands and is prepared to accept adherence to NOAC therapy, as directed. ELIQUIS should be taken regularly, as prescribed, to ensure optimal effectiveness. All temporary discontinuations should be avoided, unless medically indicated.

NOAC = non-vitamin K antagonist oral anticoagulant

* Comparative clinical significance unknown.
† Patients fulfilling ≥2 of the following criteria: age ≥80 years, body weight ≤60 kg, or serum creatinine ≥133 µmol/L. These patients have been determined to be at higher risk of bleeding.
‡ The duration of therapy should be individualised after careful assessment of the treatment benefit against the risk of bleeding. Short duration of therapy (at least 3 months) should be based on transient risk factors (e.g., recent surgery, trauma, immobilisation) and extended duration should be based on permanent risk factors or idiopathic DVT or PE.
§ Following a minimum of 6 months of treatment for DVT or PE.
RECOMMENDED DOSING FOR THE PREVENTION OF STROKE AND SYSTEMIC EMBOLISM IN PATIENTS WITH ATRIAL FIBRILLATION

Switching from LMWH to ELIQUIS

1. Discontinue LMWH
2. Start ELIQUIS at the next scheduled dose

Switching from warfarin or other VKA therapy to ELIQUIS

1. Discontinue warfarin or other VKA therapy
2. When the international normalized ratio (INR) is <2.0, start ELIQUIS

≥2 CRITERIA

- Age ≥80 years
- Body weight ≤60 kg
- Creatinine ≥133 µmol/L (serum)

Dosage adjustment to 2.5 mg BID is only required in patients who have ≥2 of the “ABC” criteria†

VKA = vitamin K antagonist;
LMWH = low molecular weight heparin

* Please consult the Product Monograph for complete dosage and administration instructions.
† These patients have been determined to be at higher risk of bleeding.
RECOMMENDED DOSING FOR THE TREATMENT OF VENOUS THROMBOEMBOLIC EVENTS (DVT AND PE) AND PREVENTION OF RECURRENT DVT AND PE

TREATMENT OF ACUTE DVT OR PE

- **10 mg BID**
  - **MORNING**: 5 mg
  - **NIGHT**: 5 mg
  - **7 days**

- **5 mg BID**
  - **MORNING**: 5 mg
  - **NIGHT**: 5 mg
  - **6 months†**

CONTINUED PREVENTION OF RECURRENT DVT AND PE

- **2.5 mg BID**
  - **MORNING**: 5 mg
  - **NIGHT**: 5 mg
  - **6 months and beyond‡**

* Please consult the Product Monograph for complete dosage and administration instructions.
† The duration of therapy should be individualised after careful assessment of the treatment benefit against the risk of bleeding. Short duration of therapy (at least 3 months) should be based on transient risk factors (e.g., recent surgery, trauma, immobilisation) and extended duration should be based on permanent risk factors or idiopathic DVT or PE.‡ Following a minimum of 6 months of treatment for DVT or PE.
**ELIQUIS DOSAGE BY LEVEL OF RENAL IMPAIRMENT IN VTE**

<table>
<thead>
<tr>
<th>Creatinine clearance</th>
<th>Prevention of VTE after elective knee or hip replacement surgery</th>
<th>Treatment of acute DVT or PE</th>
<th>Continued prevention of recurrent DVT or PE†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal &gt;80 mL/min</td>
<td>2.5 mg BID</td>
<td>10 mg BID for 7 days, followed by 5 mg BID</td>
<td>2.5 mg BID</td>
</tr>
<tr>
<td>Mild &gt;50 to ≤80 mL/min</td>
<td>2.5 mg BID*</td>
<td>10 mg BID for 7 days, followed by 5 mg BID†</td>
<td>2.5 mg BID†</td>
</tr>
<tr>
<td>Moderate ≥30 to ≤50 mL/min</td>
<td>2.5 mg BID*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe ≤15 mL/min or undergoing dialysis</td>
<td>2.5 mg BID*</td>
<td>Not recommended</td>
<td></td>
</tr>
</tbody>
</table>

* These patients have been determined to be at higher risk of bleeding.
† Must be used with caution due to potentially higher bleeding risks.
‡ After a minimum of 6 months of treatment for DVT or PE.