**Simple Protection for More Patients**

### Xarelto®

#### Accurate Dosing Matters

| Prevention of Stroke and Systemic Embolism in adults with non-valvular Atrial Fibrillation with one or more risk factors<sup>a</sup> | Patients with CrCl > 49 mL/min with food<br>20 mg OD<br>OR<br>15 mg OD<br>Patients with CrCl 15 to 49 mL/min* with food | **Xarelto®**<br>**Bayer**<br>**150 Years**<br>**Science For A Better Life**

| Treatment of DVT and PE...<br>... and Extended Treatment for prevention of recurrent DVT and PE in adults | Patients with CrCl > 15 mL/min* with food<br>15 mg OD<br>Patients with CrCl 15 to 49 mL/min* with food<br>15 mg OD<br>AFTER 3 WEEKS TRANSITION TO<br>20 mg OD<br>Patients with CrCl > 15 mL/min* with food | **Xarelto®**<br>**Bayer**<br>**150 Years**<br>**Science For A Better Life**

| Prevention of VTE in adults undergoing elective hip or knee replacement surgery | Patients with CrCl > 15 mL/min*<br>10 mg OD<br>The initial dose should be taken 6 to 10 hours after surgery once haemostasis has been established | **Xarelto®**<br>**Bayer**<br>**150 Years**<br>**Science For A Better Life**

| Secondary Prevention of ACS in Combination with Standard Antiplatelet Therapy<sup>b</sup> in adults with elevated cardiac biomarkers<sup>c</sup> | Patients with CrCl > 15 mL/min*<br>2.5 mg BID<br>The initial dose should be taken after stabilisation of the ACS event | **Xarelto®**<br>**Bayer**<br>**150 Years**<br>**Science For A Better Life**

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<sup>a</sup> such as congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, prior stroke or transient ischaemic attack

<sup>b</sup> Acetylsalicylic acid (ASA) alone or ASA in combination with clopidogrel or ticlopidine

<sup>c</sup> Troponin-I/T; creatine kinase-muscle and brain isoenzyme (CK-MB)

*Not indicated in patients with CrCl < 15 ml/min; use with caution in patients with CrCl 15-29 ml/min
Xarelto®: The First Oral, Direct Factor Xa Inhibitor

Overcoming the Limitations of Current Standards of Care⁵,⁶,⁷

♦ Oral administration¹

♦ No dose adjustment with regard to age or body weight¹,²,³

♦ No need for routine coagulation monitoring⁴,¹

♦ No known dietary restrictions¹

♦ Low risk of drug-drug interactions¹

♦ Fast onset of anticoagulation⁴

This data applies to the Xarelto® 10 mg dose. Similar results are expected at higher doses.

OD=once daily

¹ INR values should not be used as they are not a dependable measure of the anticoagulant activity of Xarelto®

² Risk factors include: congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, and prior stroke or transient ischaemic attack

³ Use with caution when concomitantly receiving other medicinal products which increase Xarelto® plasma concentrations
Non-Valvular Atrial Fibrillation

Prevention of Stroke and Systemic Embolism in Adults with Non-valvular AF with One or More Risk Factors

20 mg OD

One 20 mg tablet, once daily with food

For Renally Impaired Patients

15 mg OD

One 15 mg tablet, once daily with food for renally impaired patients

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Recommended Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-49 mL/min</td>
<td>15 mg once daily</td>
</tr>
<tr>
<td>15-29 mL/min</td>
<td>15 mg once daily, use with caution</td>
</tr>
<tr>
<td>&lt;15 mL/min</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

Important Notes

- Xarelto® provides protection from day one, and should be continued long term provided the benefit of prevention of stroke and systemic embolism outweighs the risk of bleeding
- Xarelto® is not recommended for patients with prosthetic heart valves
Deep Vein Thrombosis and Pulmonary Embolism
Treatment of DVT and PE and Prevention of Recurrent DVT and PE in Adults

First 3 weeks after initiation of Xarelto®:
one 15 mg tablet, twice daily with food

After 3 weeks
One 20 mg tablet, once daily with food

For Renally Impaired Patients

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
<th>Recommended Dosage Weeks 1-3</th>
<th>Recommended Dosage After 3 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-49 mL/min</td>
<td>15 mg twice dailya</td>
<td>20 mg once dailya</td>
</tr>
<tr>
<td>15-29 mL/min</td>
<td>15 mg twice daily, use with caution</td>
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</tr>
<tr>
<td>&lt;15 mL/min</td>
<td>Not recommended</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

♦ A reduction of the dose from 20 mg once daily to 15 mg once daily in renally impaired patients should be considered if the patient’s assessed risk for bleeding outweighs the risk for recurrent DVT and PE

Important Notes
♦ The duration of therapy should be individualised after careful assessment of the treatment benefit against bleeding risk
♦ Xarelto® is not recommended as an alternative to UFH in patients with PE who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy
After **hip replacement surgery**

One 10 mg tablet, once daily with or without food for 5 weeks

10 mg OD

After **knee replacement surgery**

One 10 mg tablet, once daily with or without food for 2 weeks

10 mg OD

**For Renally Impaired Patients**

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<tr>
<td>30-49 mL/min</td>
<td>10 mg once daily&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>15-29 mL/min</td>
<td>10 mg once daily, use with caution</td>
</tr>
<tr>
<td>&lt;15 mL/min</td>
<td>Not recommended</td>
</tr>
</tbody>
</table>

**Important Notes**

- No preoperative anticoagulation necessary
- Initiate Xarelto® 6-10 hours after surgery, provided that haemostasis has been established
- Do NOT start earlier than 6 hours after surgery in order not to interfere with haemostasis

UFH=unfractionated heparin

<sup>a</sup> Use with caution when concomitantly receiving other medicinal products which increase Xarelto® plasma concentrations
Acute Coronary Syndrome
Secondary Prevention of ACS in Adults with Elevated Cardiac Biomarkers\(^a\) in Combination with Standard Antiplatelet Therapy\(^b\)

One 2.5 mg tablet, twice daily in combination with standard antiplatelet therapy\(^b\) with or without food\(^1\)

Initiate Xarelto® 2.5 mg BID as soon as possible after stabilisation of the ACS event
- At the earliest, 24 hours after admission to hospital
- When parenteral anticoagulation therapy would normally be discontinued

Therapy with Xarelto® 2.5 mg BID is recommended for 12 months. Extension of treatment beyond 12 months should be done on an individual patient basis\(^d\).

For Renally Impaired Patients\(^1\)

<table>
<thead>
<tr>
<th>Creatinine Clearance</th>
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</thead>
<tbody>
<tr>
<td>30-49 mL/min</td>
<td>2.5 mg twice daily(^c)</td>
</tr>
<tr>
<td>15-29 mL/min</td>
<td>2.5 mg twice daily, use with caution</td>
</tr>
<tr>
<td>&lt;15 mL/min</td>
<td>Not recommended</td>
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</tbody>
</table>

Important Notes\(^1\)
- Initiate Xarelto® 2.5 mg BID as soon as possible after stabilisation of the ACS event
  - At the earliest, 24 hours after admission to hospital
  - When parenteral anticoagulation therapy would normally be discontinued
- Therapy with Xarelto® 2.5 mg BID is recommended for 12 months. Extension of treatment beyond 12 months should be done on an individual patient basis\(^d\).

ACS=acute coronary syndrome
ASA=acetylsalicylic acid; BID=twice daily; GI=gastrointestinal; ICH=intracranial haemorrhage; TIA=transient ischaemic attack
\(^a\) Troponin-I/T; creatine kinase-muscle and brain isoenzyme (CK-MB)
\(^b\) ASA alone or in combination with clopidogrel or ticlopidine
\(^c\) Use with caution when concomitantly receiving other medicinal products which increase Xarelto® plasma concentrations
\(^d\) Experience up to 24 months is limited
Patient Selection Matters

**Appropriate patients for Xarelto® 2.5 mg BID in combination with standard antiplatelet therapy**¹,²

- Adult patients after an acute coronary syndrome with elevated cardiac biomarkers³

**Exclude patients with¹**

- History of stroke or TIA
- Current or recent condition at significant risk of major bleeding (eg: GI bleeding, ICH)
- Creatinine clearance <15 mL/min
- Concomitant anticoagulation

**Use with caution in patients with¹**

- Expected increased bleeding risk, eg:
  - Creatinine clearance 15-29 mL/min
  - Other risk factors.
  - Refer to full SmPC before prescribing

The use of Xarelto® 2.5 mg BID in combination with standard antiplatelet therapy in patients at known increased risk for bleeding should be balanced against the benefit in terms of prevention of atherothrombotic events.¹
Switching Patients from LMWH to Xarelto®

Switching patients treated for DVT or PE or prevention of recurrent DVT and PE

Dosing for Patients on Anticoagulation Therapy for the First 3 weeks

♦ Xarelto® should be started 0 to 2 hours before the
time of the next scheduled administration of LMWH

♦ Continue the twice-daily regimen of Xarelto®
until patients have received a total of 3 weeks of
anticoagulant therapy, then switch to the once-daily
regimen of Xarelto® according to the label

<table>
<thead>
<tr>
<th>LMWH (sc)</th>
<th>XARELTO®</th>
</tr>
</thead>
<tbody>
<tr>
<td>STOP LMWH</td>
<td>SWITCH TO XARELTO® 0 TO 2 HOURS BEFORE THE NEXT SCHEDULED ADMINISTRATION OF LMWH</td>
</tr>
<tr>
<td>0-2 h</td>
<td>CONTINUE XARELTO®</td>
</tr>
<tr>
<td></td>
<td>AFTER 21 DAYS</td>
</tr>
<tr>
<td>One 15 mg tablet twice daily</td>
<td>No routine coagulation monitoring required.*</td>
</tr>
</tbody>
</table>
| One 20 mg tablet once daily

Dosing for Patients on Anticoagulation Therapy After 3 weeks

♦ Xarelto® should be started 0 to 2 hours before the
time of the next scheduled administration of
LMWH

<table>
<thead>
<tr>
<th>LMWH (sc)</th>
<th>XARELTO®</th>
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<tbody>
<tr>
<td>STOP LMWH</td>
<td>SWITCH TO XARELTO® 0 TO 2 HOURS BEFORE THE NEXT SCHEDULED ADMINISTRATION OF LMWH</td>
</tr>
<tr>
<td>0-2 h</td>
<td>CONTINUE XARELTO®</td>
</tr>
<tr>
<td></td>
<td>One 20 mg tablet, once daily</td>
</tr>
<tr>
<td></td>
<td>No routine coagulation monitoring required.*</td>
</tr>
</tbody>
</table>
Switching patients following elective hip or knee replacement surgery¹

- Xarelto® should be started 0 to 2 hours before the time of the next scheduled administration of LMWH
- After knee replacement surgery one 10 mg tablet once daily for 2 weeks
- After hip replacement surgery one 10 mg tablet once daily for 5 weeks

<table>
<thead>
<tr>
<th>SURGERY</th>
<th>LMWH (sc)</th>
<th>XARELTO®</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STOP LMWH</td>
<td>CONTINUE XARELTO®</td>
</tr>
<tr>
<td></td>
<td>SWITCH TO XARELTO® 0 TO 2 HOURS BEFORE THE NEXT SCHEDULED ADMINISTRATION OF LMWH</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0-2 h</td>
<td>One 10 mg tablet, once daily</td>
</tr>
</tbody>
</table>

No routine coagulation monitoring required.²

LMWH=low-molecular-weight heparin; sc=subcutaneous
⁴ INR values should not be used as they are not a dependable measure of the anticoagulant activity of Xarelto®
⁵ For dosing for renally impaired patients, see page 4
Switching Patients from VKA to Xarelto®

Switching patients with non-valvular AF treated for prevention of stroke and systemic embolism¹
♦ Treatment with VKAs should be stopped
♦ To assess the residual effect of VKAs, closely monitor the INR
♦ Xarelto® therapy should be initiated when the INR is ≤3.0

Switching patients treated for DVT or PE or treated to prevent the recurrence of DVT and PE¹
♦ Treatment with VKAs should be stopped
♦ To assess the residual effect of VKAs, closely monitor the INR
♦ Xarelto® therapy should be initiated when the INR is ≤2.5

VKA=vitamin K antagonist

See dosing recommendations for required daily dose.
**Xarelto® Characteristics**

Xarelto® is a fast-acting, novel oral anticoagulant that provides protection for your patients.

<table>
<thead>
<tr>
<th>Administration</th>
<th>Oral¹</th>
</tr>
</thead>
</table>
| **Bioavailability**    | ~80-100%¹:  
                          | 2.5 mg and 10 mg independent of food intake¹  
                          | 15 mg and 20 mg when taken with food¹ |
| **Half-life**          | 5-9 h in young adults¹  
                          | 11-13 h in elderly patients¹ |
| **Time to peak plasma concentration** | 2-4 hours¹ |
| **Renal excretion as unchanged drug** | ~33%¹ |
Xarelto®: Responsible Use Matters

Like all anticoagulants, Xarelto® may increase the risk of bleeding

Patients potentially at higher risk of bleeding

♦ Patients with decreased renal function
♦ Elderly patients
♦ Patients concomitantly receiving certain other drugs affecting haemostasis (such as NSAIDs, ASA, platelet aggregation inhibitors) or increasing Xarelto® plasma concentrations (concomitant inhibitors of CYP3A4 and P-gp)
♦ Patients with other risk factors for bleeding

Xarelto® is not recommended for use

♦ In patients below 18 years of age
♦ In patients with creatinine clearance <15 mL/min
♦ In patients receiving concomitant systemic treatment with strong inhibitors of both CYP3A4 and P-gp such as azole-antimycotics (ketoconazole, itraconazole, voriconazole and posaconazole) or HIV protease inhibitors (eg, ritonavir)
♦ In patients undergoing hip fracture surgery
♦ For patients with prosthetic heart valves
♦ As an alternative to UFH in patients with PE who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy

Given the limited clinical data available with dronedarone, co-administration with Xarelto® should be avoided

NSAIDs=nonsteroidal anti-inflammatory drugs
Xarelto® is contraindicated in case of:

♦ Hypersensitivity to the active substance or to any of the excipients
♦ Active clinically significant bleeding
♦ Lesion or condition at significant risk of major bleeding such as current or recent GI ulceration, presence of malignant neoplasms at high risk of bleeding, recent brain or spinal injury, recent brain, spinal or ophthalmic surgery, recent intracranial haemorrhage, known or suspected oesophageal varices, arteriovenous malformations, vascular aneurysms, or major intraspinal or intracerebral vascular abnormalities
♦ Concomitant treatment with any other anticoagulant agent parenteral or oral, except under the circumstances of switching therapy to or from Xarelto® or when UFH is given at doses necessary to maintain a patent central venous or arterial catheter
♦ Hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C
♦ Pregnancy and breast feeding

Xarelto® 2.5 mg BID is also contraindicated in case of:
♦ Prior stroke or TIA
**Xarelto® 2.5 mg film-coated tablets**

(Refer to full SmPC before prescribing.)

**Composition:** Active ingredient: 2.5 mg rivaroxaban. Excipients: Microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, hypromellose, sodium laurilsulfate, magnesium stearate, macrogol 3350, titanium dioxide (E171), iron oxide yellow (E172).

**Indication:** Prevention of atherothrombotic events in adult patients after an acute coronary syndrome (ACS) with elevated cardiac biomarkers, co-administered with acetylsalicylic acid (ASA) alone or with ASA plus clopidogrel or ticlopidine.

**Contraindications:** Hypersensitivity to the active substance or any of the excipients; clinically significant active bleeding; lesion or condition at significant risk of major bleeding; concomitant treatment with any other anticoagulant agent except under the circumstances of switching therapy to or from rivaroxaban or when unfractionated heparin is given at doses necessary to maintain a patent central venous or arterial catheter; concomitant treatment of ACS with antiplatelet therapy in patients with a prior stroke or a transient ischaemic attack (TIA); hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy and breast feeding.

**Warnings and Precautions:** Treatment in combination with other antiplatelet agents than ASA and clopidogrel/ticlopidine has not been studied and is not recommended. Clinical surveillance in line with anticoagulation practice is recommended throughout treatment. Xarelto® should be discontinued if severe haemorrhage occurs. Not recommended: in patients with severe renal impairment (creatinine clearance <15 ml/min); in patients receiving concomitant systemic treatment with strong concurrent CYP3A4- and P-gp-inhibitors, i.e. azole-antimycotics or HIV protease inhibitors; in patients with increased bleeding risk; due to lack of data: in patients below 18 years of age; in patients concomitantly treated with dronedarone. Use with caution: in conditions with increased risk of haemorrhage; in patients with severe renal impairment (creatinine clearance 15 - 29 ml/min) or with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; in patients treated concomitantly with medicinal products affecting haemostasis or with strong CYP3A4 inducers; in patients > 75 years of age or with low body weight. Patients on treatment with Xarelto® and ASA or Xarelto® and ASA plus clopidogrel/ticlopidine should only receive concomitant treatment with NSAIDs if the benefit outweighs the bleeding risk. In patients at risk of ulcerative gastrointestinal disease prophylactic treatment may be considered. Although treatment with rivaroxaban does not require routine monitoring of exposure, rivaroxaban levels measured with a calibrated quantitative anti-Factor Xa assay may be useful in exceptional situations. Xarelto® film-coated tablets contain lactose. **Undesirable effects:** Common: anaemia, dizziness, headache, eye haemorrhage, hypotension, haematoma, epistaxis, haemoptysis, gingival bleeding, gastrointestinal tract haemorrhage, gastrointestinal and abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting, pruritus, rash, ecchymosis, cutaneous and subcutaneous haemorrhage, pain in extremity, urogenital tract haemorrhage, pain in extremity, urogenital tract haemorrhage, renal impairment, fever, peripheral oedema, decreased general strength and energy, increase in transaminases, post-procedural haemorrhage, contusion, wound secretion. Uncommon: thrombocytemia, allergic reaction, dermatitis allergic, cerebral and intracranial haemorrhage, syncope, tachycardia, dry mouth, hepatic function abnormal, urticaria, haemarthrosis, feeling unwell, increases in: bilirubin, blood alkaline phosphatase, LDH, lipase, amylase, GGT. Rare: jaundice, muscle haemorrhage, localised oedema, bilirubin conjugated increased, vascular pseudoaneurysm (uncommon in prevention therapy in ACS following percutaneous intervention). Frequency not known: compartment syndrome or (acute) renal failure secondary to a bleeding. **Classification for supply:** Medicinal product subject to medical prescription. **Marketing Authorisation Holder:** Bayer Pharma AG, D-13342 Berlin, Germany Further information available from: medinfo@bayerhealthcare.com **Version:** EU/1
Xarelto® 10 mg film-coated tablets

(Refer to full SmPC before prescribing.)

**Composition:** Active ingredient: 10 mg rivaroxaban. Excipients: Microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, hypromellose, sodium laurilsulfate, magnesium stearate, macrogol 3350, titanium dioxide (E171), iron oxide red (E172).

**Indication:** Prevention of venous thromboembolism (VTE) in adult patients undergoing elective hip or knee replacement surgery. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients; active clinically significant bleeding; lesion or condition considered as significant risk for major bleeding; concomitant treatment with any other anticoagulants except under the circumstances of switching therapy to or from rivaroxaban or when unfractionated heparin is given at doses necessary to maintain an open central venous or arterial catheter; hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy and breast feeding. **Warnings and Precautions:** Increasing age may increase haemorrhagic risk. **Not recommended:** in patients with severe renal impairment (creatinine clearance <15 ml/min); in patients receiving concomitant systemic treatment with strong concurrent CYP3A4- and P-gp-inhibitors, i.e. azole-antimycotics or HIV protease inhibitors; due to lack of data: in patients below 18 years of age, in patients undergoing hip fracture surgery, in patients concomitantly treated with dronedarone. Use with caution: in patients with increased bleeding risk; in patients with severe renal impairment (creatinine clearance 15 - 29 ml/min) or with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; in patients treated concomitantly with medicinal products affecting coagulation or with strong CYP3A4 inducers; when neuraxial anaesthesia or spinal/epidural puncture is employed. In patients at risk of ulcerative gastrointestinal disease prophylactic treatment may be considered. There is no need for monitoring of coagulation parameters during treatment with rivaroxaban in clinical routine, if clinically indicated rivaroxaban levels can be measured by calibrated quantitative anti-Factor Xa tests. Xarelto contains lactose. **Undesirable effects:** Common: anaemia, dizziness, headache, syncope, eye haemorrhage, tachycardia, hypotension, haematoma, epistaxis, gastrointestinal tract haemorrhage, gastrointestinal and abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting, pruritus, rash, ecchymosis, pain in extremity, urogenital tract haemorrhage, fever, peripheral oedema, decreased general strength and energy, increase in transaminases, post-procedural haemorrhage, contusion, wound secretion. Uncommon: thrombocythemia, allergic reaction, dermatitis allergic, cerebral and intracranial haemorrhage, haemoptysis, dry mouth, hepatic function abnormal, urticaria, cutaneous and subcutaneous haemorrhage, haemarthrosis, renal impairment, feeling unwell, localised oedema. increases in: bilirubin, blood alkaline phosphatase, LDH, lipase, amylase, GGT. Rare: jaundice, muscle haemorrhage, bilirubin conjugated increased. **Frequency not known:** pseudoaneurysm following percutaneous intervention, compartment syndrome or (acute) renal failure secondary to a bleeding. **Classification for supply:** Medicinal product subject to medical prescription. **Marketing Authorisation Holder:** Bayer Pharma AG, D-13342 Berlin, Germany. Further information available from: medinfo@bayerhealthcare.com

**References:**
7. Clexane® [summary of product characteristics]: Guildford, Surrey, United Kingdom: Sanofi-Aventis; December 2011.
Xarelto® 15 mg / 20 mg film-coated tablets
(Remember to review SmPC before prescribing.)

**Composition:** Active ingredient: 15 mg / 20 mg rivaroxaban. Excipients: Microcrystalline cellulose, croscarmellose sodium, lactose monohydrate, hypromellose, sodium laurilsulfate, magnesium stearate, macrogol 3350, titanium dioxide (E171), iron oxide red (E172).

**Indication:** Prevention of stroke and systemic embolism in adult patients with non-valvular atrial fibrillation with one or more risk factors, such as congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischaemic attack. Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), and prevention of recurrent DVT and PE in adults.

**Contraindications:** Hypersensitivity to the active substance or any of the excipients; clinically significant active bleeding; lesion or condition at significant risk of major bleeding; concomitant treatment with any other anticoagulant agent except under the circumstances of switching therapy to or from rivaroxaban or when unfractionated heparin is given at doses necessary to maintain a patent central venous or arterial catheter; hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child Pugh B and C; pregnancy and breast feeding.

**Warnings and Precautions:** Clinical surveillance in line with anticoagulation practice is recommended throughout treatment. Xarelto® should be discontinued if severe haemorrhage occurs. Not recommended: in patients with severe renal impairment (creatinine clearance <15 ml/min); in patients receiving concomitant systemic treatment with strong concurrent CYP3A4- and P-gp-inhibitors, i.e. azole-antimycotics or HIV protease inhibitors; in patients with increased bleeding risk; due to lack of data: in patients below 18 years of age, in patients with prosthetic heart valves, in patients with PE who are haemodynamically unstable or may receive thrombolysis or pulmonary embolectomy; in patients concomitantly treated with dronedarone.

**Use with caution:** in conditions with increased risk of haemorrhage; in patients with severe renal impairment (creatinine clearance 15 - 29 ml/min) or with renal impairment concomitantly receiving other medicinal products which increase rivaroxaban plasma concentrations; in patients treated concomitantly with medicinal products affecting haemostasis or with strong CYP3A4 inducers. In patients at risk of ulcerative gastrointestinal disease prophylactic treatment may be considered. Although treatment with rivaroxaban does not require routine monitoring of exposure, rivaroxaban levels measured with a calibrated quantitative anti-Factor Xa assay may be useful in exceptional situations. Specific dose recommendations apply for patients with moderate to severe renal impairment and in case of DVT/PE-patients only if the patient’s assessed risk for bleeding outweighs the risk for recurrent DVT and PE. Xarelto® contains lactose.

**Undesirable effects:**

- **Common:** anaemia, dizziness, headache, eye haemorrhage, hypotension, haematoma, epistaxis, haemoptysis, gingival bleeding, gastrointestinal tract haemorrhage, gastrointestinal and abdominal pains, dyspepsia, nausea, constipation, diarrhoea, vomiting, pruritus, rash, ecchymosis, cutaneous and subcutaneous haemorrhage, pain in extremity, urogenital tract haemorrhage, renal impairment, fever, peripheral oedema, decreased general strength and energy, increase in transaminases, post-procedural haemorrhage, contusion, wound secretion.
- **Uncommon:** thrombocythemia, allergic reaction, dermatitis allergic, cerebral and intracranial haemorrhage, syncope, tachycardia, dry mouth, hepatic function abnormal, urticaria, haemarthrosis, feeling unwell, increases in: bilirubin, blood alkaline phosphatase, LDH, lipase, amylase, GGT. Rare: jaundice, muscle haemorrhage, localised oedema, bilirubin conjugated increased, vascular pseudoaneurysm (uncommon in prevention therapy in ACS following percutaneous intervention). Frequency not known: compartment syndrome or (acute) renal failure secondary to a bleeding.

**Classification for supply:** Medicinal product subject to medical prescription. Marketing Authorisation Holder: Bayer Pharma AG, D-13342 Berlin, Germany Further information available from: medinfo@bayerhealthcare.com Version: EU/3.1

Please see the full Summary of Product Characteristics and Prescriber Guide for further information and provide your patient with the Patient Alert Card upon prescribing Xarelto®.