Xarelto®
rivaroxaban
tablets & oral suspension

CONDITION-SPECIFIC DOSING

Includes adult and pediatric dosing information

Adult indications

CAD:
To reduce the risk of major CV events*
PAD:
To reduce the risk of major thrombotic vascular events†

2.5 mg

Tablets shown not actual size.

Twice daily with once-daily aspirin (75 mg to 100 mg)
No dose adjustment needed based on CrCl

NVAF:
Reduce stroke risk‡

20 mg

In patients with CrCl >50 mL/min
Once daily with the evening meal

15 mg

Tablets shown not actual size.

MODERATE TO SEVERE RENAL IMPAIRMENT DOSE

In patients with CrCl ≤50 mL/min
Once daily with the evening meal

RENAL DOSING CONSIDERATIONS

- **Nonvalvular atrial fibrillation:** Periodically assess renal function as clinically indicated (ie, more frequently in situations in which renal function may decline) and adjust therapy accordingly. Consider dose adjustment or discontinuation of XARELTO in patients who develop acute renal failure while on XARELTO
- **CAD and/or PAD:** For patients with CrCl <15 mL/min, no data are available, and limited data are available for patients with a CrCl of 15 to 30 mL/min. Clinical efficacy and safety studies with XARELTO did not enroll patients with ESRD on dialysis
- See section 8.6 of the Prescribing Information for additional information

*Major CV events were a composite of CV death, MI, and stroke.
†Reduction of a composite of MI, ischemic stroke, acute limb ischemia, and major amputation of a vascular etiology.
‡Calculate CrCl based on actual weight.
CrCl = creatinine clearance; CV = cardiovascular; ESRD = end-stage renal disease; MI = myocardial infarction; NVAF = nonvalvular atrial fibrillation; PAD = peripheral artery disease.

AVAILABLE STRENGTHS


2.5 mg


10 mg


15 mg


20 mg

Colors directly match product packaging. Tablets shown not actual size.

IMPORTANT SAFETY INFORMATION

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

A. Premature discontinuation of XARELTO® increases the risk of thrombotic events

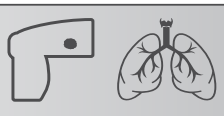
Premature discontinuation of any oral anticoagulant, including XARELTO®, increases the risk of thrombotic events. If anticoagulation with XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.

Please read Important Safety Information on the following pages and full Prescribing Information, including Boxed WARNINGS for XARELTO.

Adult indications

For all DVT/PE/VTE dosing below, avoid use in patients with CrCl <15 mL/min

DVT/PE:
Treatment of DVT or PE*†



15 mg
For the first 21 days
Twice daily with food, at approximately the same time each day

20 mg
Starting at day 22
Once daily with food, at approximately the same time each day for remaining treatment

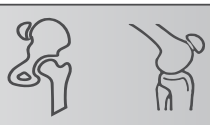
Tablets shown not actual size.

DVT/PE:
Reduction in the risk of recurrence of DVT and/or PE*†

10 mg
After ≥6 months of standard anticoagulant treatment in patients at continued risk of DVT/PE
Once daily with or without food

Tablets shown not actual size.

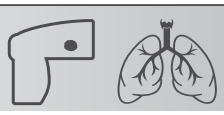
DVT PROPHYLAXIS:
Following hip or knee replacement surgery*†‡



10 mg
Hip replacement surgery: For 35 days
Once daily with or without food
Knee replacement surgery: For 12 days
Once daily with or without food

Tablets shown not actual size.

VTE PROPHYLAXIS:
Acutely ill medical patient*§



10 mg
For total duration of 31 to 39 days
Once daily with or without food

Tablets shown not actual size.

*Calculate CrCl based on actual weight.
†Patients with CrCl <30 mL/min were not studied, but administration of XARELTO is expected to result in serum concentrations of rivaroxaban similar to those in patients with moderate renal impairment (CrCl 30 to <50 mL/min).
‡The initial dose should be taken 6 to 10 hours after surgery provided that hemostasis has been established.
§XARELTO is recommended for acutely ill medical patients who are not at high risk for bleeding.

CrCl = creatinine clearance; DVT = deep vein thrombosis; PE = pulmonary embolism; VTE = venous thromboembolism.

IMPORTANT SAFETY INFORMATION (cont'd)

B. Spinal/epidural hematoma

Epidural or spinal hematomas have occurred in patients treated with XARELTO® 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 non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants, *see* Drug Interactions**
- **A history of traumatic or repeated epidural or spinal punctures**
- **A history of spinal deformity or spinal surgery**
- **Optimal timing between the administration of XARELTO® 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 for thromboprophylaxis.

BLEED RISK

XARELTO (rivaroxaban) increases the risk of bleeding, including in any organ, and can cause serious or fatal bleeding. In clinical trials, the most common adverse reactions with XARELTO were bleeding complications. XARELTO is contraindicated in patients with active pathological bleeding.

- In deciding whether to prescribe XARELTO to patients at increased risk of bleeding, the risk of thrombotic events should be weighed against the risk of bleeding

Concomitant use of drugs affecting hemostasis increases the risk of bleeding. These include:	
Examples of drugs affecting hemostasis	Aspirin, $P2Y_{12}$ platelet inhibitors, dual antiplatelet therapy, other antithrombotic agents, fibrinolytic therapy, NSAIDs, SSRIs, and SNRIs

Concomitant use of drugs that are known combined P-gp and strong CYP3A inhibitors increases rivaroxaban exposure and may increase bleeding risk, and therefore should be avoided. These include:	
Examples of drugs that are combined P-gp and strong CYP3A inhibitors	Ketoconazole and ritonavir

MANAGING BLEEDING IN XARELTO PATIENTS

BLEED MANAGEMENT‖

Promptly evaluate any signs and symptoms of blood loss and consider the need for blood replacement

Discontinue XARELTO in patients with active pathological hemorrhage

A specific agent to reverse the anti-factor Xa activity of XARELTO is not available

Use of procoagulant reversal agents—such as PCCs, activated prothrombin complex concentrate, or rFVIIa—may be considered but has not been evaluated in clinical efficacy and safety studies

Monitoring for the anticoagulation effect of XARELTO using a clotting test (PT, INR, or aPTT) or anti-factor Xa activity is not recommended

‖**This is not intended to replace clinical judgment or determine individual patient care.**

CONSIDERATIONS

- The terminal elimination half-life of XARELTO is 5 to 9 hours in healthy subjects aged 20 to 45 years and 11 to 13 hours in elderly subjects aged 60 to 76 years
- XARELTO is not dialyzable due to high plasma protein binding
- Protamine sulfate and vitamin K are not expected to affect the anticoagulant activity of XARELTO

aPTT = activated partial thromboplastin time; INR = international normalized ratio; NSAID = nonsteroidal anti-inflammatory drug; PCC = prothrombin complex concentrate; PT = prothrombin time; rFVIIa = recombinant factor VIIa; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

INDICATIONS

XARELTO® (rivaroxaban) is indicated to reduce the risk of stroke and systemic embolism in adult patients with nonvalvular atrial fibrillation (AF).

There are limited data on the relative effectiveness of XARELTO® and warfarin in reducing the risk of stroke and systemic embolism when warfarin therapy is well controlled.

XARELTO® is indicated for the treatment of deep vein thrombosis (DVT). XARELTO® is indicated for the treatment of pulmonary embolism (PE). XARELTO® is indicated for the reduction in the risk of recurrence of DVT and/or PE in adult patients at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at least 6 months.

XARELTO® is indicated for the prophylaxis of DVT, which may lead to PE in adult patients undergoing knee or hip replacement surgery.

Please read Important Safety Information on the following pages and full Prescribing Information, including Boxed WARNINGS for XARELTO.

Adult indications

SWITCHING TO AND FROM XARELTO (rivaroxaban)

SWITCHING TO XARELTO	
From warfarin	Stop warfarin and start XARELTO when INR is <3.0 in adults to avoid periods of inadequate anticoagulation
From unfractionated heparin	Stop the infusion and start XARELTO at the same time
From other anticoagulants	Start XARELTO 0 to 2 hours prior to the next scheduled evening administration of the other anticoagulant and omit administration of the other anticoagulant
SWITCHING FROM XARELTO	
To warfarin	No clinical trial data are available to guide converting patients from XARELTO to warfarin. XARELTO affects INR, so INR measurements made during coadministration with warfarin may not be useful for determining the appropriate dose of warfarin. One approach is to discontinue XARELTO and begin both a parenteral anticoagulant and warfarin at the time the next dose of XARELTO would have been taken
To other anticoagulants*	Stop XARELTO and start other anticoagulant when the next dose of XARELTO would have been given

*Oral or parenteral rapid-onset anticoagulants.

INR = international normalized ratio.

TEMPORARY DISCONTINUATION FOR SURGERY AND OTHER PROCEDURES

If XARELTO must be discontinued for a procedure, follow these guidelines:

Before procedure:

- Stop XARELTO at least 24 hours before the procedure
- In deciding whether a procedure should be delayed until 24 hours after the last dose of XARELTO, the increased risk of bleeding should be weighed against the urgency of intervention

After procedure:

- Restart XARELTO as soon as adequate hemostasis is established
- If oral medication cannot be taken during or after surgical procedures, consider a parenteral anticoagulant

Half-life of XARELTO	Healthy subjects aged 20 to 45 years	5 to 9 hours
	Elderly subjects aged 60 to 76 years	11 to 13 hours

DISTINCT PHARMACOLOGIC PROFILE

RAPID ONSET OF ACTION

- XARELTO (rivaroxaban) reaches maximum plasma concentrations and inhibits Factor Xa at 2 to 4 hours after the medication is taken[†,††]

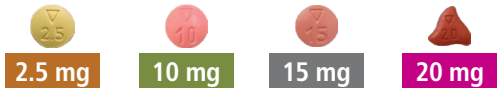
[†]Phase 1 randomized, single-blinded, placebo-controlled, dose-escalation study in 108 healthy white males, aged 19 to 45 years. Single doses of rivaroxaban 1.25-, 5-, 10-, 15-, 20-, 30-, 40-, 60-, or 80-mg tablets were tested.

BIOAVAILABILITY

- The 2.5-mg and 10-mg doses of XARELTO have nearly complete bioavailability and are not affected by food. XARELTO 2.5-mg and 10-mg tablets can be taken with or without food
- A 20-mg dose of XARELTO has nearly complete bioavailability when taken with food. XARELTO 15-mg and 20-mg tablets should be taken with food as directed

The clinical significance of this pharmacokinetic information has not been established

FOOD CONSIDERATIONS



Tablets shown not actual size.

	2.5 mg	10 mg	15 mg	20 mg
Take with food			✓‡	✓‡
Take with or without food	✓	✓		

‡For NVAF, take once daily with evening meal.

XARELTO HAS CONVENIENT ORAL DOSING VIA CRUSHABLE ADMINISTRATION

ORAL ADMINISTRATION OF CRUSHED XARELTO TABLETS

Crush XARELTO tablet	Mix with applesauce	Administer orally immediately	Follow 15-mg and 20-mg doses immediately with food (not required for 2.5-mg and 10-mg doses)

ADMINISTRATION OF XARELTO VIA NG OR GASTRIC FEEDING TUBE

Confirm tube placement	Suspend crushed XARELTO tablet in 50 mL of water	Administer immediately Avoid administration distal to stomach	Follow 15-mg and 20-mg doses immediately by enteral feeding (not required for 2.5-mg and 10-mg doses)

NG = nasogastric.

INDICATIONS (cont'd)

XARELTO® is indicated for the prophylaxis of venous thromboembolism (VTE) and VTE-related death during hospitalization and post hospital discharge in adult patients admitted for an acute medical illness who are at risk for thromboembolic complications due to moderate or severe restricted mobility and other risk factors for VTE, and not at high risk of bleeding.

XARELTO®, in combination with aspirin, is indicated to reduce the risk of major cardiovascular events (cardiovascular death, myocardial infarction, and stroke) in adult patients with coronary artery disease (CAD).

XARELTO®, in combination with aspirin, is indicated to reduce the risk of major thrombotic vascular events (myocardial infarction, ischemic stroke, acute limb ischemia, and major amputation of a vascular etiology) in adult patients with peripheral artery disease (PAD), including patients who have recently undergone a lower extremity revascularization procedure due to symptomatic PAD.

Please read Important Safety Information on the following pages and full Prescribing Information, including Boxed WARNINGS for XARELTO.

IMPORTANT SAFETY INFORMATION (cont'd)

CONTRAINDICATIONS

- Active pathological bleeding
- Severe hypersensitivity reaction to XARELTO® (eg, anaphylactic reactions)

WARNINGS AND PRECAUTIONS

- **Increased Risk of Thrombotic Events after Premature Discontinuation:** Premature discontinuation of any oral anticoagulant, including XARELTO®, in the absence of adequate alternative anticoagulation increases the risk of thrombotic events. An increased rate of stroke was observed during the transition from XARELTO® to warfarin in clinical trials in atrial fibrillation patients. If XARELTO® is discontinued for a reason other than pathological bleeding or completion of a course of therapy, consider coverage with another anticoagulant.
- **Risk of Bleeding:** XARELTO® increases the risk of bleeding, including in any organ, and can cause serious or fatal bleeding. Promptly evaluate any signs or symptoms of blood loss and consider the need for blood replacement. Discontinue in patients with active pathological hemorrhage.

Adult indications

RECOMMENDED IN MULTIPLE TREATMENT GUIDELINES

CAD and/or PAD

- **2024 ACC/AHA/Multisociety Guideline** for the management of lower extremity PAD[2]
- **2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline** for the management of patients with CCD[3]*
- **2021 ESC/EACTS Guidelines** for the Management of Valvular Heart Disease[4]

VTE

- **2025 NCCN Guidelines** for Management of VTE in Patients with Cancer[5]
- **2019 ESC Guidelines** for Diagnosis and Management of Acute PE[6]
- **2018 ISTH Guidelines** for Acute Treatment of VTE in Patients with Cancer[7]
- **2016 ACCP Guidelines** for Antithrombotic Therapy for VTE Disease[8]
- **2012 ACCP Guidelines** for the Prevention of VTE in Orthopedic Surgery Patients[9]

NVAF

- **2023 ACC/AHA/ACCP/HRS Guideline Recommendations**[10]
- **2023 ACC/AHA/ACCP/HRS Guideline** for the diagnosis and management of AF[10]
- **2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guidelines** for the Management of Patients with Atrial Fibrillation[11]
- **2021 AHA/ASA Guidelines** for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack[12]
- **2014 AAN Guidelines** for the Prevention of Stroke in Nonvalvular Atrial Fibrillation[13]
- **2013 ACCF/AHA Guidelines** for the Management of Heart Failure (Anticoagulation Recommendations for AF)[14]

*CCD is defined as a group of conditions that includes CAD, IHD diagnosed only by diagnostic testing, and chronic angina syndromes.

AAN = American Academy of Neurology; ACC = American College of Cardiology; ACCF = American College of Cardiology Foundation; ACCP = American College of Chest Physicians; AHA = American Heart Association; ASA = American Stroke Association; ASPC = American Society for Preventive Cardiology; EACTS = European Association for Cardio-Thoracic Surgery; ESC = European Society of Cardiology; HRS = Heart Rhythm Society; ISTH = International Society on Thrombosis and Haemostasis; NCCN = National Comprehensive Cancer Network®; NLA = National Lipid Association; PCNA = Preventive Cardiovascular Nurses Association.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

- A specific agent to reverse the anti-factor Xa activity of rivaroxaban is not available. Because of high plasma protein binding, rivaroxaban is not dialyzable.
- Concomitant use of other drugs that impair hemostasis increases risk of bleeding. These include aspirin, $P2Y_{12}$ platelet inhibitors, dual antiplatelet therapy, other antithrombotic agents, fibrinolytic therapy, NSAIDs, selective serotonin reuptake inhibitors (SSRIs), and serotonin norepinephrine reuptake inhibitors (SNRIs).
- Risk of Hemorrhage in Acutely Ill Medical Patients at High Risk of Bleeding: Acutely ill medical patients with the following conditions are at increased risk of bleeding with the use of XARELTO® for primary VTE prophylaxis: history of bronchiectasis, pulmonary cavitation, or pulmonary hemorrhage; active cancer (ie, undergoing acute, in-hospital cancer treatment); active gastroduodenal ulcer or history of bleeding in the three months prior to treatment; or dual antiplatelet therapy. XARELTO® is not for use for primary VTE prophylaxis in these hospitalized, acutely ill medical patients at high risk of bleeding.

- **Spinal/Epidural Anesthesia or Puncture:** When neuraxial anesthesia (spinal/epidural anesthesia) or spinal puncture is employed, patients treated with anticoagulant agents for prevention of thromboembolic complications are at risk of developing an epidural or spinal hematoma, which can result in long-term or permanent paralysis. To reduce the potential risk of bleeding associated with concurrent use of XARELTO® and epidural or spinal anesthesia/analgesia or spinal puncture, consider the pharmacokinetic profile of XARELTO®.

Please read Important Safety Information on the following pages and full Prescribing Information, including Boxed WARNINGS for XARELTO.

XARELTO WITHME TRIAL OFFER: FREE 30-DAY TRIAL SUPPLY FOR ELIGIBLE PATIENTS

Eligible patients receive a free 30-day trial supply of XARELTO (rivaroxaban) with a valid signed 30-day prescription for any XARELTO dose other than 10-mg tablet or 1-mg/mL oral suspension. The XARELTO withMe Trial Offer can be used with the XARELTO Starter Pack. The XARELTO withMe Trial Offer helps you and your patient determine if XARELTO is right for them. At the conclusion of the program, you and your patient decide whether to continue treatment. Terms expire at the end of each calendar year and may change. One (1) use is allowed per lifetime.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

Placement or removal of an epidural catheter or lumbar puncture is best performed when the anticoagulant effect of XARELTO® is low; however, the exact timing to reach a sufficiently low anticoagulant effect in each patient is not known. An indwelling epidural or intrathecal catheter should not be removed before at least 2 half-lives have elapsed (ie, 18 hours in young patients aged 20 to 45 years and 26 hours in elderly patients aged 60 to 76 years), after the last administration of XARELTO®. The next dose should not be administered earlier than 6 hours after the removal of the catheter. If traumatic puncture occurs, delay the administration of XARELTO® for 24 hours. Monitor frequently to detect signs or symptoms of neurological impairment, such as midline back pain, sensory and motor deficits (numbness, tingling, or weakness in lower limbs), or bowel and/or bladder dysfunction. Instruct patients to immediately report any of the above signs or symptoms. If signs or symptoms of spinal hematoma are suspected, initiate urgent diagnosis and treatment including consideration for spinal cord decompression even though such treatment may not prevent or reverse neurological sequelae.

- **Use in Patients with Renal Impairment:**
  - **Nonvalvular Atrial Fibrillation:** Periodically assess renal function as clinically indicated (ie, more frequently in situations in which renal function may decline) and adjust therapy accordingly. Consider dose adjustment or discontinuation in patients who develop acute renal failure while on XARELTO®. Clinical efficacy and safety studies with XARELTO® did not enroll patients with CrCl <30 mL/min or end-stage renal disease (ESRD) on dialysis.
  - **Treatment of Deep Vein Thrombosis (DVT), Pulmonary Embolism (PE), and Reduction in the Risk of Recurrence of DVT and of PE:** In patients with CrCl <30 mL/min, rivaroxaban exposure and pharmacodynamic effects are increased compared to patients with normal renal function. There are limited clinical data in patients with CrCl 15 to <30 mL/min; therefore, observe closely and promptly evaluate any signs or symptoms of blood loss in these patients. There are no clinical data in patients with CrCl <15 mL/min (including patients on dialysis); therefore, avoid the use of XARELTO® in these patients. Discontinue XARELTO® in patients who develop acute renal failure while on treatment.
  - **Prophylaxis of Deep Vein Thrombosis Following Hip or Knee Replacement Surgery:** In patients with CrCl <30 mL/min, rivaroxaban exposure and pharmacodynamic effects are increased compared to patients with normal renal function. There are limited clinical data in patients with CrCl 15 to <30 mL/min; therefore, observe closely and promptly evaluate signs or symptoms of blood loss in these patients. There are no clinical data in patients with CrCl <15 mL/min (including patients on dialysis); therefore, avoid the use of XARELTO® in these patients. Discontinue XARELTO® in patients who develop acute renal failure while on treatment.
  - **Prophylaxis of Venous Thromboembolism in Acutely Ill Medical Patients at Risk for Thromboembolic Complications Not at High Risk of Bleeding:** In patients with CrCl <30 mL/min, rivaroxaban exposure and pharmacodynamic effects are increased compared to patients with normal renal function. There are limited clinical data in patients with CrCl 15 to <30 mL/min; therefore, observe closely and promptly evaluate any signs or symptoms of blood loss in these patients. There are no clinical data in patients with CrCl <15 mL/min (including patients on dialysis); therefore, avoid the use of XARELTO® in these patients. Discontinue XARELTO® in patients who develop acute renal failure while on treatment.
  - **Reduction of Risk of Major Cardiovascular Events in Patients with CAD and Reduction of Risk of Major Thrombotic Vascular Events in Patients with PAD, Including Patients after Recent Lower Extremity Revascularization Due to Symptomatic PAD:** For patients with CrCl <15 mL/min, no data are available, and limited data are available for patients with a CrCl of 15 to 30 mL/min. In patients with CrCl <30 mL/min, a dose of 2.5 mg XARELTO® twice daily is expected to give an exposure similar to that in patients with moderate renal impairment (CrCl 30 to <50 mL/min), whose efficacy and safety outcomes were similar to those with preserved renal function. Clinical efficacy and safety studies with XARELTO® did not enroll patients with end-stage renal disease (ESRD) on dialysis.

Pediatric indications

Pediatric VTE and post-Fontan care are complex.[15,16]

Helping protect against thrombosis doesn't have to be.

Recommended dosage in pediatric patients from birth to <18 years of age for treatment of VTE and reduction in the risk of recurrent VTE after at least 5 days of initial parenteral anticoagulant treatment.*†

1 mg XARELTO = 1 mL suspension

3x daily with oral suspension only‡§

Body weight	Dosage	Total dose
2.6 kg to 2.9 kg	0.8 mg	2.4 mg
3 kg to 3.9 kg	0.9 mg	2.7 mg
4 kg to 4.9 kg	1.4 mg	4.2 mg
5 kg to 6.9 kg	1.6 mg	4.8 mg
7 kg to 7.9 kg	1.8 mg	5.4 mg
8 kg to 8.9 kg	2.4 mg	7.2 mg
9 kg to 9.9 kg	2.8 mg	8.4 mg
10 kg to 11.9 kg	3 mg	9 mg

Twice daily with oral suspension only‡§

Body weight	Dosage	Total dose
12 to 29.9 kg	5 mg	10 mg

Once daily with oral suspension or tablets‡§

Body weight	Dosage	Total dose
30 to 49.9 kg	15 mg	15 mg
≥50 kg	20 mg	20 mg

*Initiate XARELTO treatment following at least 5 days of initial parenteral anticoagulation therapy.

†Patients <6 months of age should meet the following criteria: at birth were at least 37 weeks of gestation, have had at least 10 days of oral feeding, and weigh ≥2.6 kg at the time of dosing.

‡Once a day: approximately 24 hours apart; 2 times a day: approximately 12 hours apart; 3 times a day: approximately 8 hours apart.

§All doses should be taken with feeding or with food since exposures match that of 20-mg daily dose in adults.

To increase absorption, all doses should be taken with feeding or with food

Monitor the child's weight and review the dose regularly, especially for children below 12 kg. This is to ensure a therapeutic dose is maintained.

INDICATIONS

XARELTO® is indicated for the treatment of venous thromboembolism (VTE) and reduction in the risk of recurrent VTE in pediatric patients from birth to less than 18 years after at least 5 days of initial parenteral anticoagulant treatment.

XARELTO® is indicated for thromboprophylaxis in pediatric patients aged 2 years and older with congenital heart disease who have undergone the Fontan procedure.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

- **Pediatric Patients:** There are limited clinical data in pediatric patients 1 year or older with moderate or severe renal impairment (eGFR <50 mL/min/1.73 m^2); therefore, avoid use of XARELTO® in these patients.

  There are no clinical data in pediatric patients younger than 1 year with serum creatinine results above 97.5th percentile; therefore, avoid the use of XARELTO® in these patients.

Please read Important Safety Information on the following pages and full Prescribing Information, including Boxed WARNINGS for XARELTO.

Dosing of XARELTO (rivaroxaban) was not studied and therefore dosing cannot be reliably determined in the following patient populations. Its use is therefore not recommended in children less than 6 months of age with any of the following:

- Less than 37 weeks of gestation at birth
- Less than 10 days of oral feeding
- Body weight of less than 2.6 kg

All pediatric patients (except <2 years old with catheter-related thrombosis): Therapy with XARELTO should be continued for at least 3 months in children with thrombosis. Treatment can be extended up to 12 months when clinically necessary. The benefit of continued therapy beyond 3 months should be assessed on an individual basis, taking into account the risk for recurrent thrombosis versus the potential risk of bleeding.

Pediatric patients <2 years old with catheter-related thrombosis: Therapy with XARELTO should be continued for at least 1 month in children less than 2 years old with catheter-related thrombosis. Treatment can be extended up to 3 months when clinically necessary. The benefit of continued therapy beyond 1 month should be assessed on an individual basis, taking into account the risk for recurrent thrombosis versus the potential risk of bleeding.

Recommended dosage in pediatric patients aged 2 years and older with CHD for thromboprophylaxis after the Fontan procedure

1 mg XARELTO = 1 mL suspension

Twice daily with oral suspension only‖¶

Body weight	Dosage	Total dose
7 kg to 7.9 kg	1.1 mg	2.2 mg
8 kg to 9.9 kg	1.6 mg	3.2 mg
10 kg to 11.9 kg	1.7 mg	3.4 mg
12 kg to 19.9 kg	2 mg	4 mg
20 kg to 29.9 kg	2.5 mg	5 mg

Once daily with oral suspension only‖¶

Body weight	Dosage	Total dose
30 to 49.9 kg	7.5 mg	7.5 mg

Once daily with oral suspension or tablets‖¶

Body weight	Dosage	Total dose
≥50 kg	10 mg	10 mg

‖Once a day: approximately 24 hours apart; 2 times a day: approximately 12 hours apart.

¶All doses can be taken with or without food since exposures match that of 10-mg daily dose in adults.

CHD = congenital heart disease.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

- **Use in Patients with Hepatic Impairment:** No clinical data are available for adult patients with severe hepatic impairment. Avoid use in patients with moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment or with any hepatic disease associated with coagulopathy, since drug exposure and bleeding risk may be increased. No clinical data are available in pediatric patients with hepatic impairment.
- **Use with P-gp and Strong CYP3A Inhibitors or Inducers:** Avoid concomitant use of XARELTO® with known combined P-gp and strong CYP3A inhibitors or inducers.
- **Risk of Pregnancy-Related Hemorrhage:** In pregnant women, XARELTO® should be used only if the potential benefit justifies the potential risk to the mother and fetus. XARELTO® dosing in pregnancy has not been studied. The anticoagulant effect of XARELTO® cannot be monitored with standard laboratory testing. Promptly evaluate signs or symptoms suggesting blood loss (eg, a drop in hemoglobin and/or hematocrit, hypotension, or fetal distress).
- **Patients with Prosthetic Heart Valves:** Use of XARELTO® is not recommended in patients who have had transcatheter aortic valve replacement (TAVR), based on the results of the GALILEO study, which reported higher rates of death and bleeding in patients randomized to XARELTO® compared to those randomized to an antiplatelet regimen. Safety and efficacy of XARELTO® have not been studied in patients with other prosthetic heart valves or other valve procedures. Use of XARELTO® is not recommended in patients with prosthetic heart valves.

Pediatric indications

ADMINISTRATION

- **Food effect:** For the treatment of VTE in children, the XARELTO (rivaroxaban) dose should be taken with food to increase absorption. For thromboprophylaxis after Fontan procedure, the dose can be taken with or without food.
- **Vomit or spit up:** If the patient vomits or spits up the dose within 30 minutes after receiving the dose, a new dose should be given. However, if the patient vomits more than 30 minutes after the dose is taken, the dose should not be re-administered and the next dose should be taken as scheduled. If the patient vomits or spits up the dose repeatedly, the caregiver should contact the child's doctor right away.
- **Tablets:** XARELTO tablet must not be split in an attempt to provide a fraction of a tablet dose. For children unable to swallow 10-mg, 15-mg, or 20-mg whole tablets, XARELTO oral suspension should be used. XARELTO 2.5-mg tablets are not recommended for use in pediatric patients.

CONSIDERATIONS

- The half-life of rivaroxaban in plasma of pediatric patients treated for VTE decreased with decreasing age
- Mean half-life values were 4.2 hours in adolescents, 3 hours in children 2 to 12 years of age, 1.9 hours in children 0.5 to <2 years of age, and 1.6 hours in children <0.5 years of age
- An exploratory analysis in pediatric patients treated for VTE did not reveal relevant differences in rivaroxaban exposure based on gender

SWITCHING TO AND FROM XARELTO

- **SWITCHING TO XARELTO**

  From warfarin: Stop warfarin and start XARELTO when INR is <2.5 in pediatric patients to avoid periods of inadequate anticoagulation.

  From other anticoagulants: Start XARELTO 0 to 2 hours prior to the next scheduled administration of the drug (e.g., LMWH or non-warfarin oral anticoagulant) and omit administration of the other anticoagulant. For UFH being administered by continuous infusion, stop the infusion and start XARELTO at the same time.

- **SWITCHING FROM XARELTO**

  To warfarin: To ensure adequate anticoagulation during the transition from XARELTO to warfarin, continue XARELTO for at least 2 days after the first dose of warfarin. After 2 days of co-administration, an INR should be obtained prior to the next scheduled dose of XARELTO. Co-administration of XARELTO and warfarin is advised to continue until the INR is ≥2.0. Once XARELTO is discontinued, INR testing may be done reliably 24 hours after the last dose.

  To anticoagulants other than warfarin: For pediatric patients currently taking XARELTO and transitioning to an anticoagulant with rapid onset, discontinue XARELTO and give the first dose of the other anticoagulant (oral or parenteral) at the time that the next XARELTO dose would have been taken.

LMWH = low-molecular-weight heparin; UFH = unfractionated heparin.

IMPORTANT SAFETY INFORMATION (cont'd)
WARNINGS AND PRECAUTIONS (cont'd)

- **Acute PE in Hemodynamically Unstable Patients/Patients Who Require Thrombolysis or Pulmonary Embolectomy:** Initiation of XARELTO® is not recommended acutely as an alternative to unfractionated heparin in patients with pulmonary embolism who present with hemodynamic instability or who may receive thrombolysis or pulmonary embolectomy.
- **Increased Risk of Thrombosis in Patients with Antiphospholipid Syndrome:** Direct-acting oral anticoagulants (DOACs), including XARELTO®, are not recommended for use in patients with triple-positive antiphospholipid syndrome (APS). For patients with APS (especially those who are triple positive [positive for lupus anticoagulant, anticardiolipin, and anti-beta 2-glycoprotein I antibodies]), treatment with DOACs has been associated with increased rates of recurrent thrombotic events compared with vitamin K antagonist therapy.

DRUG INTERACTIONS

- Combined P-gp and strong CYP3A inhibitors increase exposure to rivaroxaban and may increase risk of bleeding.
- Combined P-gp and strong CYP3A inducers decrease exposure to rivaroxaban and may increase risk of thromboembolic events.

Please read Important Safety Information on the following pages and full Prescribing Information, including Boxed WARNINGS for XARELTO.

USE IN RENAL IMPAIRMENT

- **Patients ≥1 year of age:**

  Mild renal impairment (eGFR: 50 to ≤80 mL/min/1.73 m^2): no dose adjustment is required

  Moderate or severe renal impairment (eGFR: <50 mL/min/1.73 m^2): avoid use, as limited clinical data are available

eGFR can be done using the updated Schwartz formula, eGFR (Schwartz) = (0.413 x height in cm)/SCr in mg/dL, if SCr is measured by an enzymatic creatinine method that has been calibrated to be traceable to IDMS.

If SCr is measured with routine methods that have not been recalibrated to be traceable to IDMS (eg, the traditional Jaffé reaction), the eGFR should be obtained from the original Schwartz formula: eGFR (mL/min/1.73 m^2) = k * height (cm)/SCr (mg/dL), where k is proportionality constant:

k = 0.55 in children 1 year to 13 years

k = 0.55 in girls >13 and <18 years

k = 0.70 in boys >13 and <18 years

- **Patients <1 year of age:**

  Determine renal function using serum creatinine. Avoid use of XARELTO (rivaroxaban) in pediatric patients younger than 1 year with serum creatinine results above 97.5th percentile, as no clinical data are available

Reference values of serum creatinine in pediatric patients <1 year of age

Age week	97.5th percentile of creatinine (mg/dL)	97.5th percentile of creatinine (µmol/L)
Week 2	0.52	46
Week 3	0.46	41
Week 4	0.42	37
Month 2	0.37	33
Month 3	0.34	30
Month 4-6	0.34	30
Month 7-9	0.34	30
Month 10-12	0.36	32

eGFR = estimated glomerular filtration rate; IDMS = isotope dilution mass spectrometry; SCr = serum creatinine.

IMPORTANT SAFETY INFORMATION (cont'd)
DRUG INTERACTIONS (cont'd)

- XARELTO® should not be used in patients with CrCl 15 to <80 mL/min who are receiving concomitant combined P-gp and moderate CYP3A inhibitors (eg, erythromycin) unless the potential benefit justifies the potential risk.
- Coadministration of enoxaparin, warfarin, aspirin, clopidogrel, and chronic NSAID use may increase risk of bleeding.
- Avoid concurrent use of XARELTO® with other anticoagulants due to increased bleeding risk, unless benefit outweighs risk. Promptly evaluate signs or symptoms of blood loss if patients are treated concomitantly with aspirin, other platelet aggregation inhibitors, or NSAIDs.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** The limited available data on XARELTO® in pregnant women are insufficient to inform a drug-associated risk of adverse developmental outcomes. Use XARELTO® with caution in pregnant patients because of the potential for pregnancy-related hemorrhage and/or emergent delivery. The anticoagulant effect of XARELTO® cannot be reliably monitored with standard laboratory testing. Consider the benefits and risks of XARELTO® for the mother and possible risks to the fetus when prescribing to a pregnant woman.
  - Fetal/Neonatal adverse reactions: Based on the pharmacologic activity of Factor Xa inhibitors and the potential to cross the placenta, bleeding may occur at any site in the fetus and/or neonate.
  - Labor or delivery: The risk of bleeding should be balanced with the risk of thrombotic events when considering use in this setting.
  - There are no adequate or well-controlled studies of XARELTO® in pregnant women, and dosing for pregnant women has not been established. Post-marketing experience is currently insufficient to determine a rivaroxaban-associated risk for major birth defects or miscarriage.

Pediatric indications

ADMINISTRATION OPTIONS

ADMINISTRATION

- **Oral suspension:** For children unable to swallow 10-mg, 15-mg, or 20-mg whole tablets, XARELTO (rivaroxaban) oral suspension should be used. XARELTO 2.5-mg tablets are not recommended for use in pediatric patients.
- **Administration of XARELTO oral suspension via NG tube or gastric feeding tube:** XARELTO oral suspension may be given through NG or gastric feeding tube. After the administration, flush the feeding tube with water.

  For the treatment or reduction in risk of recurrent VTE in pediatric patients, the dose should then be immediately followed by enteral feeding to increase absorption.

  For thromboprophylaxis in pediatric patients with CHD who have undergone the Fontan procedure, the dose is not required to be followed by enteral feeding.

  An in vitro compatibility study indicated that XARELTO oral suspension can be used with PVC, polyurethane, or silicone NG tubing.

CHD = congenital heart disease; PVC = polyvinyl chloride.

MISSED DOSE

IF XARELTO IS TAKEN ONCE A DAY

The patient should take the missed dose as soon as possible once it is noticed, but only on the same day. If this is not possible, the patient should skip the dose and continue with the next dose as prescribed. The patient should not take 2 doses to make up for a missed dose. On the following day, the patient should continue with their regular regimen.

IF XARELTO IS TAKEN TWICE A DAY

The patient should take the missed morning dose as soon as possible once it is noticed. A missed morning dose may be taken together with the evening dose. A missed evening dose can only be taken in the same evening. On the following day, the patient should continue with their regular regimen.

IF XARELTO IS TAKEN THREE TIMES A DAY

The patient should skip the missed dose and go back to the regular dosing schedule at the usual time without compensating for the missed dose. On the following day, the patient should continue with their regular regimen.

PREPARATION INSTRUCTIONS FOR PHARMACY OF XARELTO FOR ORAL SUSPENSION

Tap the bottle until all granules flow freely	Add 150 mL of purified water	Shake for 60 seconds	Check that all granules are wetted and the suspension is uniform

Push the adapter into bottleneck and recap bottle. Write the "Discard after" date on the bottle and carton.	The suspension must be used within 60 days. Dispense in the original bottle. Dispense the bottle upright with the syringes provided in the original carton.

Store reconstituted suspension at room temperature between 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). Do not freeze.

Alert the patient or caregiver to read the Medication Guide and Instructions for Use. It is recommended the pharmacist counsel the caregiver on proper use.

IMPORTANT SAFETY INFORMATION (cont'd)
USE IN SPECIFIC POPULATIONS (cont'd)

- **Lactation:** Rivaroxaban has been detected in human milk. There are insufficient data to determine the effects of rivaroxaban on the breastfed child or on milk production. Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for XARELTO® and any potential adverse effects on the breastfed infant from XARELTO® or from the underlying maternal condition.

Please read Important Safety Information on the following page and full Prescribing Information, including Boxed WARNINGS for XARELTO.

IMPORTANT SAFETY INFORMATION (cont'd)
USE IN SPECIFIC POPULATIONS (cont'd)

- **Females and Males of Reproductive Potential:** Females of reproductive potential requiring anticoagulation should discuss pregnancy planning with their physician. The risk of clinically significant uterine bleeding, potentially requiring gynecological surgical interventions, identified with oral anticoagulants, including XARELTO®, should be assessed in females of reproductive potential and those with abnormal uterine bleeding.
- **Pediatric Use:** XARELTO® was not studied and therefore dosing cannot be reliably determined or recommended in children less than 6 months who were less than 37 weeks of gestation at birth, had less than 10 days of oral feeding, or had a body weight of less than 2.6 kg.

  Clinical studies that evaluated safety, efficacy, and pharmacokinetic/pharmacodynamic data support the use of XARELTO® 10-mg, 15-mg, and 20-mg tablets in pediatric patients. For the XARELTO® 2.5-mg tablets, there are no safety, efficacy, and pharmacokinetic/pharmacodynamic data to support the use in pediatric patients. Therefore, XARELTO® 2.5-mg tablets are not recommended for use in pediatric patients.

  Although not all adverse reactions identified in the adult population have been observed in clinical trials of children and adolescent patients, the same warnings and precautions for adults should be considered for children and adolescents.
- **Geriatric Use:** In clinical trials the efficacy of XARELTO® in the elderly (65 years or older) was similar to that seen in patients younger than 65 years. Both thrombotic and bleeding event rates were higher in these older patients.

OVERDOSAGE

- Overdose of XARELTO® may lead to hemorrhage. Discontinue XARELTO® and initiate appropriate therapy if bleeding complications associated with overdosage occur. A specific agent to reverse the anti-factor Xa activity of rivaroxaban is not available.

ADVERSE REACTIONS

- Most common adverse reactions in adult patients with XARELTO® were bleeding complications.
- Most common adverse reactions in pediatric patients were bleeding, cough, vomiting, and gastroenteritis.

Please read full Prescribing Information, including Boxed WARNINGS for XARELTO®.

cp-62551v14

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Once a decision has been made to prescribe XARELTO

J&J withMe

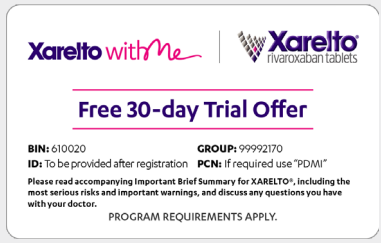
Xarelto® rivaroxaban tablets & oral suspension

Starting and staying on a medication can feel overwhelming for your patients. Johnson & Johnson has resources to help you support your patients.

If you have any questions or need support, call 888-XARELTO (888-927-3586), Monday–Friday, 8:00 AM–8:00 PM ET.

XARELTO withMe Trial Offer

Free 30-day trial supply for eligible patients



Eligible patients receive a free 30-day trial supply of XARELTO with a valid signed 30-day prescription for any XARELTO dose other than 10-mg tablet or 1-mg/mL oral suspension. The XARELTO withMe Trial Offer can be used with the XARELTO Starter Pack.

The XARELTO withMe Trial Offer helps you and your patient determine if XARELTO is right for them. At the conclusion of the program, you and your patient decide whether to continue treatment. Terms expire at the end of each calendar year and may change. One (1) use is allowed per lifetime.

The patient support and resources provided by XARELTO withMe are not intended to provide medical advice, replace a treatment plan from the patient's doctor or nurse, provide case management services, or serve as a reason to prescribe XARELTO.

Please read full Prescribing Information, including Boxed WARNINGS for XARELTO.

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