ANTICOAGULATION PRESCRIBING TIPS

Medicines Management Programme

These prescribing tips are intended to assist prescribers, and advise on the appropriate dosing, when a direct oral anticoagulant (DOAC) is selected for treatment. Dosing recommendations are based on the *Summary of Product Characteristics (SmPC)* for each product (available on www.hpra.ie).

Licensed and reimbursed indications for DOACs

Not all DOACs are licensed for use in all indications, with dose and frequency of administration varying depending on the indication.

Refer to individual dosing page as per indication:

- Stroke prevention in adults with non-valvular atrial fibrillation (NVAF) (page 2)*
- Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) (page 3)
- Prophylaxis of thromboembolism in adult patients after elective total knee replacement (TKR) or total hip replacement (THR) surgery (page 4)
- Prevention of atherothrombotic events in adult patients with coronary artery disease (CAD) or symptomatic peripheral artery disease (PAD) at high risk of ischaemic events (with aspirin) (page 5) - an online reimbursement application system is in place for rivaroxaban 2.5mg film-coated tablets for this indication.

*The Medicines Management Programme consider **WARFARIN** or **APIXABAN** to be the agents of choice for most patients with **NVAF.**[1]

- **WARFARIN** is an appropriate first-line treatment option for stroke prevention in **NVAF** when time in therapeutic range **(TTR) > 70%.**
- **APIXABAN** is the preferred DOAC for stroke prevention in **NVAF**.

The following points should be considered when prescribing a DOAC:

1. Initiation and follow-up: Ensure **correct dose and frequency of administration of the individual DOAC** is chosen at initiation and reviewed at all subsequent appointments based on: licensed indication, age, renal function, weight, concomitant medicines etc.[2-5] Renal function should be assessed regularly and dose adjusted or therapy reviewed as appropriate (at least 6 monthly and more frequently if renal impairment or risk factors for impaired renal function). Refer to SmPCs for further details.
2. For initiation of treatment for DVT/PE: ensure initiation dose and dose adjustment is prescribed clearly. Review the requirement to continue treatment after 3 and/or 6 months.
3. For stroke prevention with NVAF in Primary Care refer to the ICGP reference guide: "Practical use of Direct Oral Anticoagulants (DOACs) in Atrial Fibrillation in General Practice (2020)" (available on www.icgp.ie).[6]
4. Significant drug interactions may occur with DOAC therapy and the most common of these are highlighted in this prescribing aid.[2-5]
5. When used for stroke prevention in adults with NVAF, treatment of DVT and PE and prophylaxis of thromboembolism in adults after elective TKR or THR surgery, poor compliance/missed doses with a DOAC carries a risk of thrombotic events due to the short half-life of these agents.[2-5]

Safe use of DOACs

ENSURE THE CORRECT DOAC, DOSE AND FREQUENCY IS PRESCRIBED FOR THE CORRECT INDICATION

There are four DOACs available with multiple indications and differing doses and frequencies. Care must be taken when prescribing, transcribing, dispensing and administering all DOACs to ensure the dose and frequency are correct for the indication and for the individual patient being treated.

REPORTING OF SUSPECTED ADVERSE REACTIONS

The reporting of suspected adverse drug reactions after the authorisation of a medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse drug reactions to the Health Products Regulatory Authority (HPRA).

Abbreviations: CAD: Coronary artery disease; DOAC: Direct oral anticoagulant; DVT: Deep vein thrombosis; HPRA: Health Products Regulatory Authority; ICGP: Irish College of General Practitioners; NVAF: Non-valvular atrial fibrillation; PAD: Peripheral artery disease; PE: Pulmonary embolism; SmPC: Summary of Product Characteristics; THR: Total hip replacement; TKR: Total knee replacement; TTR: Time in therapeutic range

References:

1. Medicines Management Programme 2019. Oral anticoagulants for stroke prevention in non-valvular atrial fibrillation. Available on www.hse.ie/yourmedicines
2. Pradaxa® (Dabigatran) hard capsules. Summary of Product Characteristics. Last revised 25/07/2022. Accessed on www.ema.Europa.eu on 22/08/2022.
3. Xarelto® (Rivaroxaban) film-coated tablets. Summary of Product Characteristics. Last revised 13/12/2021. Accessed on www.ema.Europa.eu on 22/08/2022.
4. Eliquis® (Apixaban) film-coated tablets. Summary of Product Characteristics. Last revised 04/04/2022. Accessed on www.ema.Europa.eu on 22/08/2022.
5. Lixiana ® (Edoxaban) film-coated tablets. Summary of Product Characteristics. Last revised 23/04/2021. Accessed on www.ema.Europa.eu on 22/08/2022.
6. Irish College of General Practitioners Quick Reference Guide (ICGP QRG). Practical use of Direct Oral Anticoagulants (DOACs) in Atrial Fibrillation in General Practice. Dublin: ICGP; February 2020. [Available from www.icgp.ie]

Version 3.0 MMP August 2022
Available on www.hse.ie/yourmedicines
Contact mmp@hse.ie for more details

STROKE PREVENTION IN ADULTS WITH NON-VALVULAR ATRIAL FIBRILLATION (NVAF)

Individual Summary of Product Characteristics (SmPCs) are available on www.hpra.ie

GENERAL INFORMATION — **Creatinine Clearance (CrCl) should be measured using Cockroft-Gault equation (SI units) : CrCl = (140 – Age (yrs)) x Weight (kg) x constant [1.23 for males & 1.04 for females] / Serum Creatinine (μmol/L)**

APIXABAN

Adjust dose for AGE, BODY WEIGHT, RENAL FUNCTION, and consider INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard dose	5mg twice daily (BD)
Where at least two of the following characteristics are present: serum creatinine ≥ 133 μmol/L, age ≥ 80 yrs, or weight ≤ 60 kg	2.5mg BD
CrCl 15-29 ml/min (regardless of age or weight)	2.5mg BD – **CAUTION**
NOT RECOMMENDED in CrCl < 15 ml/min or in patients undergoing dialysis	

Interactions : this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): strong **inhibitors** of CYP3A4 and P-gp, such as azole-antimycotics (e.g. ketoconazole, itraconazole, posaconazole, voriconazole) and HIV protease inhibitors (e.g. ritonavir) - check SmPC for more details
CAUTION (risk of reduced efficacy): strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk. Not recommended in severe hepatic impairment.*

APIXABAN is the MMP preferred DOAC for stroke prevention in **NVAF** and may be considered 1st line treatment, particularly if there are tolerability issues and/or labile international normalised ratios (INRs) with warfarin.

DABIGATRAN

Adjust dose for AGE, RENAL FUNCTION, GORD, and INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard dose	150mg twice daily (BD)
Between 75-80 years **or** CrCl 30-50 ml/min **or** GORD/Gastritis/Oesophagitis **or** Other patients at increased risk of bleeding	150mg BD or 110mg BD based on individual assessment of thrombotic risk and bleeding risk
≥ 80 years **or** concomitant verapamil (take verapamil at the same time as dabigatran)	110mg BD
CONTRAINDICATED in CrCl < 30 ml/min	

Interactions : this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
CONTRAINDICATED: P-gp **inhibitors -** ciclosporin, dronedarone, glecaprevir/pibrentasvir, itraconazole, ketoconazole
AVOID CONCURRENT USE: P-gp **inhibitor** - tacrolimus
AVOID CONCURRENT USE (reduced efficacy): P-gp **inducers** (e.g. carbamazepine, phenytoin, rifampicin, St. John's Wort)
CAUTION (increased bleeding risk): P-gp **inhibitors** - amiodarone, clarithromycin, posaconazole, quinidine, ticagrelor**,** verapamil (see dosing section, important to take verapamil and dabigatran at the same time)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Not recommended in hepatic impairment and contraindicated in hepatic impairment *or liver disease that is expected to have any impact on survival.*

Important information: DO NOT OPEN OR CRUSH CAPSULES
Blister Pack: Store in the ORIGINAL PACKAGE in order to protect from moisture - not suitable for Monitored Dosage Systems

EDOXABAN

Adjust dose for RENAL FUNCTION, BODY WEIGHT and consider INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard dose	60mg once daily
CrCl 15-50 ml/min **or** low body weight (≤ 60 kg) **or** concomitant ciclosporin, dronedarone, erythromycin or ketoconazole (P-gp-inhibitors) (based on clinical data)	30mg once daily
According to clinical data no dose adjustment is needed if concomitant use with amiodarone, quinidine or verapamil (P-gp-inhibitors)	
NOT RECOMMENDED in CrCl < 15 ml/min or in patients undergoing dialysis	

Interactions: this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
CAUTION: co-administration of aspirin in elderly patients. The concomitant chronic use of high dose aspirin (>300mg) is not recommended, doses higher than 100mg should only be performed under medical supervision
CAUTION (increased bleeding risk): P-gp **inhibitors** – see dosing guidance opposite for dose reduction recommendations
CAUTION (risk of reduced efficacy): P-gp **inducers** (e.g. phenytoin, carbamazepine, phenobarbital, St. John's Wort)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents, SSRIs/SNRIs
Caution in mild to moderate hepatic impairment, not recommended in severe hepatic impairment and contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*

NOTE: Edoxaban is predominately absorbed in the upper gastrointestinal tract. Therefore medicines or disease conditions that increase gastric emptying and gut motility may reduce edoxaban dissolution and absorption.
Important information: Clinical trials showed a trend towards decreasing efficacy with INCREASING creatinine clearance - careful evaluation of patients with NVAF and high creatinine clearance is recommended prior to use.

RIVAROXABAN

Adjust dose for RENAL FUNCTION and consider INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard Dose	20mg once daily
CrCl 30-49 ml/min	15mg once daily (caution with concomitant medications which increase rivaroxaban plasma concentration)
CrCl 15-29 ml/min **(EXTREME CAUTION)**	15mg once daily – **EXTREME CAUTION**
NOT RECOMMENDED in CrCl < 15 ml/min	

Interactions : this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): Strong **inhibitor**s of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors)
AVOID CONCURRENT USE: dronedarone – limited clinical data
AVOID CONCURRENT USE (risk of reduced efficacy): Strong **inducers** of CYP3A4 (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION: moderate to strong **inhibitors** of CYP3A4 and/or P-gp (e.g. clarithromycin, erythromycin, fluconazole) in patients with renal impairment
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*

Important information: 15mg and 20mg tablets should be taken WITH FOOD

DEEP VEIN THROMBOSIS (DVT) AND PULMONARY EMBOLISM (PE)

Individual Summary of Product Characteristics (SmPCs) are available on www.hpra.ie

GENERAL INFORMATION | **Creatinine Clearance (CrCl) should be measured using Cockroft-Gault equation (SI units): CrCl = (140 – Age (yrs)) x Weight (kg) x constant [1.23 for males & 1.04 for females] / Serum Creatinine ($\mu mol/L$)**

Discharge prescription (after first diagnosis) should **clearly state** intended **DURATION OF TREATMENT**. If **rivaroxaban** , state how many further days of twice daily (BD) dosing (i.e. 21 days minus number of days doses have already given in hospital) before reducing to once daily and if **apixaban**, how many further days of 10mg BD before reducing to 5mg BD

APIXABAN

Remain aware of possible risks with increased AGE, low BODY WEIGHT, RENAL FUNCTION, and consider INTERACTIONS

DOSING: Treatment of DVT/PE

Standard Dose	10mg twice daily (BD) for 7 days then reduce to 5mg BD for at least 3 months
CrCl 15-29 ml/min	No dose adjustment recommended, use with CAUTION
NOT RECOMMENDED in CrCl < 15 ml/min or in patients undergoing dialysis	
Prevention of recurrent DVT/PE	2.5mg BD. Dose should be started following completion of 6 months treatment with apixaban 5mg twice daily or another anticoagulant. The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk for bleeding.

Interactions : this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): strong **inhibitors** of CYP3A4 and P-gp, such as azole-antimycotics (e.g. ketoconazole, itraconazole, posaconazole, voriconazole) and HIV protease inhibitors (e.g. ritonavir) - check SmPC for more details
AVOID CONCURRENT USE (Treatment of DVT/PE) (risk of reduced efficacy): strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St John's Wort)
CAUTION (Prevention of recurrent DVT/PE) (risk of reduced efficacy): strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*
Not recommended in severe hepatic impairment.

DABIGATRAN

Adjust dose for AGE, RENAL FUNCTION, GORD, and INTERACTIONS

DOSING : Treatment of DVT/PE and prevention of recurrent DVT/PE

Standard Dose: Initial treatment with at least 5 days of **parenteral anticoagulant.** Then **150mg dabigatran twice daily (BD)** for at least 3 months (longer durations determined according to risk factors)

Between 75-80 years **or** CrCl 30-50 ml/min **or** GORD/Gastritis/Oesophagitis **or** Other patients at increased risk of bleeding	150mg BD or 110mg BD based on individual assessment of thrombotic risk and bleeding risk
≥ 80 years **or** Concomitant verapamil (take verapamil at the same time as dabigatran)	110mg BD **NOTE**: For DVT/PE the recommendation for the use of 110mg BD is based on pharmacokinetic and pharmacodynamic analyses and **has not been studied in this clinical setting**.

CONTRAINDICATED in CrCl < 30 ml/min

Interactions : this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
CONTRAINDICATED: P-gp **inhibitors** - ciclosporin, dronedarone, glecaprevir/pibrentasvir, itraconazole, ketoconazole
AVOID CONCURRENT USE: P-gp **inhibitor** - tacrolimus
AVOID CONCURRENT USE (reduced efficacy): P-gp **inducers** (e.g. carbamazepine, phenytoin, rifampicin, St. John's Wort)
CAUTION (increased bleeding risk): P-gp **inhibitors** - amiodarone, clarithromycin, posaconazole, quinidine, ticagrelor**,** verapamil (see dosing section, important to take verapamil and dabigatran at the same time)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Not recommended in hepatic impairment and contraindicated in hepatic impairment *or liver disease that is expected to have any impact on survival.*

Important information: DO NOT OPEN OR CRUSH CAPSULE
Blister Pack : Store in the ORIGINAL PACKAGE in order to protect from moisture - not suitable for Monitored Dosage Systems

EDOXABAN

Adjust dose for RENAL FUNCTION, BODY WEIGHT and consider INTERACTIONS

DOSING : Treatment of DVT/PE and prevention of recurrent DVT/PE

Standard dose: Initial treatment with at least 5 days of **parenteral anticoagulant**. Then **60mg edoxaban once daily** for at least 3 months with longer durations based on permanent risk factors or idiopathic DVT/PE

CrCl 15-50 ml/min **or** low body weight (≤ 60 kg) **or** concomitant ciclosporin, dronedarone, erythromycin or ketoconazole (P-gp-inhibitors) (based on clinical data)	30mg once daily
NOT RECOMMENDED in CrCl < 15 ml/min or in patients undergoing dialysis	

Interactions: this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
CAUTION: co-administration of aspirin in elderly patients. The concomitant chronic use of high dose aspirin (>300mg) is not recommended, doses higher than 100mg should only be performed under medical supervision
CAUTION (increased bleeding risk): P-gp **inhibitors** – see dosing guidance opposite for dose reduction recommendations
CAUTION (risk of reduced efficacy): P-gp **inducers** (e.g. phenytoin, carbamazepine, phenobarbital, St. John's Wort)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents, SSRIs/SNRIs
Caution in mild to moderate hepatic impairment, not recommended in severe hepatic impairment and contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*

NOTE: Edoxaban is predominately absorbed in the upper gastrointestinal tract. Therefore medicines or disease conditions that increase gastric emptying and gut motility may reduce edoxaban dissolution and absorption.

RIVAROXABAN

Adjust dose for RENAL FUNCTION and consider INTERACTIONS

DOSING : Treatment of DVT/PE and prevention of recurrent DVT/PE

Standard Dose: Initial dose of 15mg **twice daily** (BD) for first **21** days **then reduce** to 20mg **once daily** thereafter for at least 3 months (longer durations determined according to risk factors). If extended prevention of recurrent DVT/PE is indicated (after ≥ 6 months therapy for DVT/PE), the recommended dose is 10mg once daily. Refer to SmPC for further details.

CrCl 30-49 ml/min	15mg BD for first 21 days then reduce to 15mg or 20mg **once daily** thereafter depending on bleeding risk versus risk of recurrent DVT/PE. Limited evidence for 15mg dose – based on pharmacokinetic modelling. EXTREME CAUTION if CrCl < 30 ml/min
CrCl 15-29 ml/min (**EXTREME CAUTION**)	
NOT RECOMMENDED in CrCl < 15 ml/min	

Interactions: this list is not exhaustive; See SmPC for full details

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): Strong **inhibitor**s of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors)
AVOID CONCURRENT USE: dronedarone - limited clinical data
AVOID CONCURRENT USE (risk of reduced efficacy): Strong **inducers** of CYP3A4 (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION: moderate to strong **inhibitors** of CYP3A4 and/or P-gp (e.g. clarithromycin, erythromycin, fluconazole) in patients with renal impairment
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*

- **Important information: 15mg and 20mg tablets should be taken WITH FOOD**

PROPHYLAXIS OF THROMBOEMBOLISM IN ADULT PATIENTS AFTER ELECTIVE TOTAL KNEE REPLACEMENT (TKR) OR TOTAL HIP REPLACEMENT (THR) SURGERY

Individual Summary of Product Characteristics (SmPCs) are available on www.hpra.ie

GENERAL INFORMATION — **Creatinine Clearance (CrCl) should be measured using Cockroft-Gault equation (SI units): CrCl = (140 – Age (yrs)) x Weight (kg) x constant [1.23 for males & 1.04 for females] / Serum Creatinine (μmol/L)**

APIXABAN

Remain aware of possible risks with older AGE, lower BODY WEIGHT, RENAL FUNCTION, and consider INTERACTIONS

DOSING	Prevention of venous thromboembolic events (VTE) in adult patients who have undergone elective TKR or THR surgery
Standard dose	2.5mg twice daily (BD) for 10-14 days (TKR) or for 32-38 days (THR). Initial dose should be taken 12-24 hours after surgery.
CrCl 15-29 ml/min	Use with caution if CrCl < 30 ml/min
NOT RECOMMENDED in CrCl < 15 ml/min or in patients undergoing dialysis	

Interactions : this list is not exhaustive; See Summary of Product Characteristics (SmPC) for full details (www.hpra.ie)

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): strong **inhibitors** of CYP3A4 and P-gp such as azole-antimycotics (e.g. ketoconazole, itraconazole, posaconazole, voriconazole) and HIV protease inhibitors (e.g. ritonavir) - check SmPC for more details
CAUTION (risk of reduced efficacy): strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*
Not recommended in severe hepatic impairment.

DABIGATRAN

Adjust dose for AGE, RENAL FUNCTION, GORD, and INTERACTIONS

DOSING	Prevention of VTE in adult patients who have undergone elective TKR or THR surgery
Less than 75 years (see also options below)	110mg after surgery* then 220mg **once daily** (starting the first day after surgery) (TKR: 10 days, THR: 28-35 days)
≥ 75 years (treat with caution) **or** CrCl 30-50 ml/min **or** concomitant P-gp inhibitors i.e. verapamil, amiodarone, quinidine (take these agents at same time as dabigatran)	75mg after surgery* then 150mg **once daily** (starting the first day after surgery) (TKR: 10 days, THR: 28-35 days) * 1-4 hours post-surgery once haemostasis is achieved. If haemostasis is not secured, initiation of treatment should be delayed. If treatment is not started on the day of surgery then treatment should be started with the higher dose once daily.
CrCl 30-50 ml/min **AND** on concomitant verapamil	75mg after surgery* then 75mg **once daily** (starting the first day after surgery) should be considered
GORD/Gastritis/Oesophagitis	No adjustment – dose according to the above recommendations
CONTRAINDICATED in CrCl < 30 ml/min	

Interactions : this list is not exhaustive; See SmPC for full details (www.hpra.ie)

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
CONTRAINDICATED with **P-gp inhibitors**: ciclosporin, dronedarone, glecaprevir/pibrentasvir, itraconazole, ketoconazole
AVOID CONCURRENT USE: P-gp **inhibitor** - tacrolimus
AVOID CONCURRENT USE (reduced efficacy): P-gp **inducers** (e.g. carbamazepine, phenytoin, rifampicin, St. John's Wort)
CAUTION (increased bleeding risk) with **P-gp inhibitors**: amiodarone, clarithromycin, posaconazole, quinidine, ticagrelor, verapamil (see dosing section, important to take verapamil and dabigatran at the same time)
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Not recommended in hepatic impairment and contraindicated in hepatic impairment *or liver disease that is expected to have any impact on survival.*

Important information: DO NOT OPEN OR CRUSH CAPSULE
Blister: Store in the ORIGINAL PACKAGE in order to protect from moisture - not suitable for Monitored Dosage Systems

RIVAROXABAN

Adjust dose for RENAL FUNCTION and consider INTERACTIONS

DOSING	Prevention of VTE in adult patients who have undergone elective TKR or THR surgery
Standard Dose	10mg once daily for 14 days (TKR) or for 35 days (THR). Initial dose should be taken 6-10 hours after surgery, provided haemostasis has been established.
CrCl 30-49 ml/min	No dose adjustment required – 10mg once daily for 14 days (TKR) or 35 days (THR) (initial dose as above)
CrCl 15-29 ml/min	EXTREME CAUTION if CrCl < 30 ml/min
NOT RECOMMENDED in CrCl < 15 ml/min	

Interactions : this list is not exhaustive; See SmPC for full details (www.hpra.ie)

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): Strong **inhibitors** of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors)
AVOID CONCURRENT USE: dronedarone - limited clinical data
AVOID CONCURRENT USE (risk of reduced efficacy): Strong **inducers** of CYP3A4 (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION: moderate to strong **inhibitors** of CYP3A4 and/or P-gp (e.g. clarithromycin, erythromycin, fluconazole) in patients with renal impairment
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*

Important information: 10mg tablets can be taken with or without food.

PREVENTION OF ATHEROTHROMBOTIC EVENTS IN ADULT PATIENTS WITH CORONARY ARTERY DISEASE (CAD) OR SYMPTOMATIC PERIPHERAL ARTERY DISEASE (PAD) AT HIGH RISK OF ISCHAEMIC EVENTS (co-administered with aspirin).

Individual Summary of Product Characteristics (SmPCs) are available on www.hpra.ie

GENERAL INFORMATION	**Creatinine Clearance (CrCl) should be measured using Cockroft-Gault equation (SI units): CrCl = (140 – Age (yrs)) x Weight (kg) x constant [1.23 for males & 1.04 for females] / Serum Creatinine ($\mu mol/L$)**
RIVAROXABAN	**Ensure correct DOSE for indication, ensure cardiovascular risk factors have been optimised prior to initiation and consider CONTRAINDICATIONS, CAUTIONS and INTERACTIONS**

DOSING	**Prevention of atherothrombotic events in adult patients with CAD or symptomatic PAD at high risk of ischaemic events (with aspirin).**
Standard Dose	2.5mg twice daily (BD) (with aspirin)
CrCl 30-49 ml/min	2.5mg BD (with aspirin)
CrCl 15-29 ml/min	2.5mg BD (with aspirin) – **EXTREME CAUTION**
NOT RECOMMENDED in CrCl < 15 ml/min	

Care should be taken when prescribing, transcribing, dispensing and administering all DOACs due to the risk of medication errors e.g. potential for confusion between rivaroxaban 2.5mg twice daily (CAD/PAD) and apixaban 2.5mg twice daily (NVAF and other licensed indications, pages 2-4).

Interactions : this list is not exhaustive; See SmPC for full details (www.hpra.ie)

CONTRAINDICATED with other anticoagulants (unless switching, then refer to SmPC)
AVOID CONCURRENT USE (increased bleeding risk): Strong **inhibitors** of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors)
AVOID CONCURRENT USE: dronedarone – limited clinical data
AVOID CONCURRENT USE (risk of reduced efficacy): Strong **inducers** of CYP3A4 (e.g. carbamazepine, phenytoin, phenobarbital, rifampicin, St. John's Wort)
CAUTION: moderate to strong **inhibitors** of CYP3A4 and/or P-gp (e.g. clarithromycin, erythromycin, fluconazole) in patients with renal impairment
CAUTION (increased bleeding risk): NSAIDs, antiplatelet agents including aspirin, SSRIs/SNRIs
Contraindicated in hepatic disease *associated with coagulopathy and clinically relevant bleeding risk.*

Important information: 2.5mg tablets can be taken with or without food.

There is a **reimbursement application system** in place for the use of rivaroxaban 2.5mg film-coated tablets (with aspirin) for this indication.
Refer to Managed Access Protocol for Rivaroxaban 2.5mg (Xarelto®) available on www.hse.ie/yourmedicines.

- To be eligible for reimbursement of rivaroxaban (Xarelto®) 2.5mg, patients must satisfy criteria at the time of application, including that the following cardiovascular risk factors have been optimised; lipids, blood pressure and diabetes mellitus.
- GPs and hospital prescribers, once user-registered with the HSE-Primary Care Reimbursement Service (PCRS), will be authorised to apply for reimbursement. A reimbursement application can be made through the Special Drug Request (SDR) section on the GP Application Suite or under "Services for Hospitals" on the PCRS website (www.pcrs.ie).
- The reimbursement application should be made by the prescriber responsible for the initiation of treatment due to the mandatory information required for reimbursement to be approved.
- Applications submitted will be reviewed by the HSE-Medicines Management Programme (MMP) before a reimbursement recommendation is made. This recommendation will be communicated to the prescriber through the online reimbursement application system.
- Once a patient is approved for reimbursement there will be no expiry on the duration of this approval.