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 and www.medicines.ie)

The Medicines Management Programme consider **WARFARIN** or **APIXABAN** to be the agents of choice for most patients with **Non-Valvular Atrial Fibrillation (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** and may be considered 1st line treatment, particularly if there are tolerability issues and/or labile international normalised ratios (INRs) with warfarin

The following points should be considered when prescribing a DOAC:

1. **Initiation and follow-up**: Ensure correct dose (and frequency) of individual DOAC is chosen at initiation and reviewed at all subsequent appointments based on: Age, renal function, licensed indication, weight, concomitant medicines etc.[2-5] Renal function should be assessed regularly and dose adjusted or therapy reviewed as appropriate (at least every six months 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 for requirement to continue treatment after 3 and/or 6 months.
3. **For treatment of NVAF:** refer to ICGP reference guide "Practical use of Direct Oral Anti-Coagulants (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. Poor compliance with DOAC therapies carries a risk of thrombotic events due to the **short half-life of these agents**.[2-5]

Abbreviations: ATC: Anatomical therapeutic classification; DOAC: Direct oral anticoagulant; DVT: Deep vein thrombosis; GMS: General Medical Services; ICGP: Irish College of General Practitioners; INR: International normalised ratio; HPRA: Health Products Regulatory Authority; NVAF: non-valvular atrial fibrillation; PE: Pulmonary embolism; SmPC: Summary of Product Characteristics; TTR: time in therapeutic range

NOTE: AGE

Less than 20% of patients in key licensing trials for NVAF were ≥ 80 years of age. Data (Jan-June 2019) shows that at least 40% of patients in receipt of DOACs under the GMS scheme are aged ≥ 80 years.[7]

SAFETY ALERT

A review published by the State Claims Agency detailed medication incidents reported by Irish acute hospitals (2017-2018). Anti-thrombotic agents were responsible for the greatest number of incidents in medication group ATC level 3. There were four antithrombotic agents in the top ten drugs involved in medication incidents including apixaban and rivaroxaban. Among the top ten antithrombotic agents involved in medication incidents, apixaban and rivaroxaban appeared in second and fourth places, respectively.[8]

REPORTING OF SUSPECTED ADVERSE REACTIONS

Reporting suspected adverse reactions after authorisation of the 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 reactions to the Health Products Regulatory Authority (HPRA) (www.hpra.ie).

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) 150 mg hard capsules. Summary of Product Characteristics. Last revised May 2020. Accessed on www.medicines.ie on 30/09/2020
3. Xarelto® (Rivaroxaban) 20 mg film-coated tablets. Summary of Product Characteristics. Last revised October 2019. Accessed on www.medicines.ie on 30/09/2020
4. Eliquis® (Apixaban) 5 mg film-coated tablets. Summary of Product Characteristics. Last revised August 2020. Accessed on www.medicines.ie on 30/09/2020
5. Lixiana® (Edoxaban) 60 mg film-coated tablets. Summary of Product Characteristics. Last revised June 2020. Accessed on www.medicines.ie on 30/09/2020
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]
7. PCERS database. January-June 2019. Number of patients aged 80 and over on DOACs. GMS data. On file
8. State Claims Agency. Medication Incidents Report. A review of medication incidents reported by Irish acute hospitals (2017-2018). January 2020. [Available on www.stateclaims.ie]

Version 2.0 MMP October 2020 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.medicines.ie or 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 ($\mu mol/L$)**

APIXABAN

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

DOSING	Stroke prevention in NVAF
Standard dose	5 mg twice daily (BD)
Serum creatinine > 133 micromol/L (measured) ***AND*** ≥ 80 yrs ***OR*** weight ≤ 60 kg (Or any two of three above i.e. serum creatinine, age ≥ 80, weight ≤ 60 kg)	2.5 mg BD
CrCl 15-29 ml/min [use Cockroft-Gault equation (SI units)] (regardless of age or weight)	2.5 mg BD – **EXTREME CAUTION**, consider alternative (review HAS-BLED and other risk factors)
CONTRAINDICATED in CrCl < 15 ml/min or if patient is undergoing dialysis	

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

CONTRAINDICATED with other anticoagulants (unless switching, then refer to individual 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, phenobarbitone, rifampicin, St Johns Wort)
CAUTION (increased bleeding risk): NSAIDs including aspirin
Antiplatelet agents including **aspirin** will increase risk of bleeding
Contraindicated *in patients with* ***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 consider INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard dose	150 mg twice daily (BD)
75-80 years	150 mg BD or 110 mg BD should be selected based on an individual assessment of the thromboembolic risk and the risk of bleeding
GORD/Gastritis/Oesophagitis	
Over 80 years	110 mg BD
Renal Impairment (CrCl 30 ml/min – 50 ml/min)	150 mg BD (110 mg BD if high bleeding risk)
CONTRAINIDICATED in CrCl < 30 ml/min	
Concomitant Verapamil (take verapamil at the same time as dabigatran)	110 mg BD

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

CONTRAINDICATED with other anticoagulants (unless switching, then refer to individual SmPC)
CONTRAINDICATED: Ciclosporin, dronedarone, itraconazole, ketoconazole.
AVOID CONCURRENT USE (reduced efficacy): P-gp **inducers** (e.g. carbamazepine, phenytoin, rifampicin, St Johns Wort
CAUTION: P-gp inhibitors (e.g. amiodarone, clarithromycin, quinidine, tacrolimus, ticagrelor)
Verapamil (P-gp inhibitor **– increased bleeding risk**) – **REDUCE DOSE** of dabigatran (take both drugs at the same time)
CAUTION (increased bleeding risk): NSAIDs, including aspirin
SSRI/SNRIs – increased risk of bleeding
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 (MDS)

EDOXABAN

Adjust dose for RENAL FUNCTION, BODY WEIGHT and consider INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard dose	60 mg once daily
Renal impairment (CrCl 15 ml/min - 50 ml/min) **or** low body weight (≤ 60 kg)	30 mg once daily
Concomitant ciclosporin, dronedarone, erythromycin or ketoconazole (P-gp inhibitors)	30 mg once daily (based on clinical data)
According to clinical data no dose adjustment is needed if concomitant use with amiodarone, quinidine or verapamil (P-gp inhibitors)	
CONTRAINDICATED in CrCl < 15 ml/min or if the patient is 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 (>300 mg daily) is not recommended, doses higher than 100 mg daily should only be performed under medical supervision
CAUTION: P-gp inhibitors – (increased bleeding risk) see dosing guidance opposite for dose reduction recommendations
CAUTION: (increased bleeding risk) chronic use of NSAIDS with edoxaban is not recommended
CAUTION: P-gp inducers (reduced efficacy) e.g. Phenytoin, carbamazepine, phenobarbital, St. Johns Wort
Caution in mild to moderate hepatic impairment, not recommended in severe hepatic impairment and contraindicated in patients with 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. Can be taken with or without food.
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

RIVAROXABAN

Adjust dose for RENAL FUNCTION and consider INTERACTIONS

DOSING	Stroke prevention in NVAF
Standard Dose	20 mg once daily
CrCl: 30-49 ml/min	15 mg once daily (caution with concomitant medications which increase rivaroxaban plasma concentration)
CrCl: 15-30 ml/min (**CAUTION**)	15 mg once daily – **EXTREME CAUTION**, consider alternative
CONTRAINDICATED 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 individual SmPC for guidance)
AVOID CONCURRENT USE (increased bleeding risk): Strong **inhibitor**s of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors)
AVOID: Dronedarone – (limited clinical data) **CAUTION**: Strong **inhibitors** of CYP3A4 (e.g. clarithromycin) **AND** renal impairment
CAUTION (risk of reduced efficacy): Strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns Wort). Avoid unless closely observed.
CAUTION (increased bleeding risk): NSAIDs, Platelet aggregation inhibitors including aspirin, SSRIs, SNRIs
Contraindicated *in* ***hepatic disease*** *associated with coagulopathy and clinically relevant bleeding risk*

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

Reference: SmPC for Eliquis® (apixaban), Pradaxa® (dabigatran), Lixiana® (edoxaban) and Xarelto® (rivaroxaban)
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TREATMENT OF DEEP VEIN THROMBOSIS (DVT) AND PULMONARY EMBOLISM (PE)

Individual Summary of Product Characteristics (SmPCs) are available on www.medicines.ie or 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 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 10 mg BD before reducing to 5 mg 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	10 mg **twice daily** for **7** days **then reduce** to **5 mg twice daily** for at least 3 months
CrCl 15-29ml/min	No dose adjustment recommended, use with CAUTION
CONTRAINDICATED in CrCl <15 ml/min or if the patient is undergoing dialysis	
Prevention of recurrent DVT and PE	2.5 mg twice daily; this dose should be started following completion of 6 months treatment with apixaban 5 mg twice daily or another anticoagulant. The duration of overall therapy should be individualised after careful assessment of the treatment benefit against the risk of 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
CAUTION (risk of reduced efficacy): Strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns Wort)
CAUTION (increased bleeding risk): NSAIDS including aspirin
Antiplatelet agents including **aspirin** will increase risk of bleeding
Not recommended in severe hepatic impairment and contraindicated *in patients with* ***hepatic disease*** *associated with coagulopathy and clinically relevant bleeding risk.*

DABIGATRAN

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

DOSING : Treatment of DVT/PE	
Standard Dose: Initial treatment with 5 days of **parenteral anticoagulant. Then 150 mg dabigatran twice daily** (BD) for at least 3 months (longer durations determined according to risk factors)	
Less than 75 years (see also options below)	150 mg BD
75-80 years or GORD/gastritis/oesophagitis	150 mg BD or 110 mg BD* should be selected based on an individual assessment of the thromboembolic risk and the risk of bleeding
80 years and over OR concomitant Verapamil (take at the same time)	110 mg BD* *** NOTE**: For DVT/PE the recommendation for the use of 110 mg BD is based on pharmacokinetic and pharmacodynamic analyses and **has not been studied in this clinical setting**.
CrCl 30 ml/min – 50 ml/min	150 mg BD (110 mg BD if high bleeding risk)*
CONTRAINIDICATED 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 individual SmPC)
CONTRAINDICATED: Ciclosporin, dronedarone, itraconazole, ketoconazole.
AVOID CONCURRENT USE (reduced efficacy): P-gp **inducers** (e.g. carbamazepine, phenytoin, rifampicin, St Johns Wort
CAUTION: P-gp **Inhibitors** (e.g. amiodarone, clarithromycin, quinidine, tacrolimus, ticagrelor)
Verapamil (P-gp inhibitor – **increased bleeding risk**) – **REDUCE DOSE** of dabigatran (take both drugs at the same time)
CAUTION (increased bleeding risk): NSAIDs, including aspirin
SSRI/SNRIs – increased risk of bleeding
Contraindicated *in* ***hepatic impairment*** *or liver disease expected to have any impact on survival. Not recommended in hepatic impairment.*
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 (MDS)

EDOXABAN

Adjust dose for RENAL FUNCTION, BODY WEIGHT and consider INTERACTIONS

DOSING : Treatment of DVT/PE	
Standard dose: Initial treatment with at least 5 days of **parenteral anticoagulant**. **Then 60 mg edoxaban once daily** for at least 3 months with longer durations based on permanent risk factors or idiopathic DVT/PE	
Renal impairment (CrCl 15 ml/min - 50 ml/min) or low body weight (≤ 60 kg) or concomitant use with ciclosporin, dronedarone, erythromycin, ketoconazole (P-gp inhibitors) (based on clinical data)	30 mg once daily
CONTRAINDICATED in CrCl < 15 ml/min or if on 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 (>300 mg daily) is not recommended, doses higher than 100 mg daily should only be performed under medical supervision
CAUTION (increased bleeding risk): chronic use of NSAIDS with edoxaban is not recommended
CAUTION: P-gp inducers **(reduced efficacy)** e.g. Phenytoin, carbamazepine, phenobarbital, St. JohnsWort
Contraindicated in patients with hepatic disease associated with coagulopathy and clinically relevant bleeding risk. Not recommended in severe hepatic impairment, caution in mild to moderate hepatic impairment
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. Can be taken with or without food.

RIVAROXABAN

Adjust dose for RENAL FUNCTION and consider INTERACTIONS

DOSING : Treatment of DVT/PE	
Standard Dose: Initial dose of 15 mg **twice daily** (BD) for first **21** days **then reduce** to 20 mg **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 at least 6 months therapy for DVT/PE), the recommended dose is 10mg once daily. Refer to SmPC for further details and dosing if risk of recurrence is high.	
CrCl: 30-49 ml/min	15 mg BD for first 21 days then reduce to 15 mg or 20 mg **once daily** thereafter depending on bleeding risk versus risk of recurrent DVT/PE. Limited evidence for 15 mg once daily dose – based on pharmacokinetic modelling EXTREME CAUTION if CrCl < 30 ml/min, consider alternative
CrCl: 15-30 ml/min (**EXTREME CAUTION**)	
CONTRAINDICATED 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 individual SmPC for guidance)
AVOID CONCURRENT USE (increased bleeding risk): Strong **inhibitor**s of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors).
AVOID: Dronedarone – (limited clinical data)
CAUTION: Strong **inhibitors** of CYP3A4 (e.g. clarithromycin) ***AND*** renal impairment
CAUTION (risk of reduced efficacy): Strong **inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns Wort). Avoid unless closely observed.
CAUTION (increased bleeding risk): NSAIDs, platelet aggregation inhibitors including aspirin, SSRIs, SNRIs
Contraindicated *in* ***hepatic disease*** *associated with coagulopathy and clinically relevant bleeding risk*

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

Ref: SmPC for Eliquis® (apixaban), Pradaxa® (dabigatran), Lixiana® (edoxaban) and Xarelto® (rivaroxaban) **Version 2.0 MMP October 2020**

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

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 ($\mu mol/L$)**

APIXABAN

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

DOSING	**Prevention of VTE in adult patients who have undergone elective TKR or THR surgery**	**Interactions** : this list is not exhaustive; See Summary of Product Characteristics (SmPC) for full details (www.medicines.ie or www.hpra.ie)
Standard dose	2.5 mg twice daily for 10-14 days (TKR) or for 32-38 days (THR). Initial dose should be taken 12-24 hours after surgery	• **CONTRAINDICATED** with other anticoagulants (unless switching, then refer to individual SmPC for guidance) • **AVOID CONCURRENT USE** (increased bleeding risk): Strong **inhibitors** of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, posaconazole, voriconazole) –Anti-retrovirals – check SmPC for details • **USE WITH CAUTION (risk of reduced efficacy):** Strong **Inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns Wort) • **CAUTION (increased bleeding risk):** NSAIDS including aspirin • **CAUTION**: Antiplatelet agents including aspirin will increase risk of bleeding ***Contraindicated** in patients with **hepatic disease** associated with coagulopathy and clinically relevant bleeding risk. Not recommended in severe hepatic impairment.*
CONTRAINDICATED in CrCl < 15 ml/min or if patient is undergoing dialysis		

DABIGATRAN

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

DOSING	**Prophylaxis of DVT post TKR and THR surgery**	**Interactions** : this list is not exhaustive; See SmPC for full details (www.medicines.ie or www.hpra.ie)
Less than 75 years (see also options below)	110 mg after surgery* then 220 mg **once daily** (TKR: 10 days, THR: 28-35 days)	• **CONTRAINDICATED** with other anticoagulants (unless switching, refer to SmPCs for guidance) • **CONTRAINDICATED**: Ciclosporin, dronedarone, itraconazole, ketoconazole. • **AVOID CONCURRENT USE** (reduced efficacy): P-gp **inducers** (e.g. carbamazepine, phenytoin, rifampicin, St Johns Wort) • **CAUTION**: P-gp **inhibitors** (e.g. amiodarone, clarithromycin, quinidine, tacrolimus, ticagrelor) • Verapamil (P-gp **inhibitor**) – REDUCE DOSE of dabigatran (take verapamil and dabigatran at the same time) • **CAUTION** (increased bleeding risk): NSAIDs, including aspirin • SSRI/SNRIs – increased risk of bleeding ***Contraindicated** in **hepatic impairment** or liver disease which is expected to have any impact on survival. Not recommended in hepatic impairment.*
> 75 years (treat with caution)	75 mg after surgery* then 150 mg **once daily** (TKR: 10 days, THR: 28-35 days)	
Renal Impairment (CrCl 30 ml/min – 50 ml/min)	75 mg after surgery* then 150 mg **once daily** (TKR: 10 days, THR: 28-35 days) – treat with caution	
CONTRAINIDICATED in CrCl < 30 ml/min		
GORD/Gastritis/Oesophagitis	No adjustment – dose according to the above recommendations	**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 (MDS)**
Concomitant P-gp inhibitors i.e. verapamil, amiodarone, quinidine (take these agents at same time as dabigatran)	75 mg after surgery* then 150 mg **once daily** (see also renal impairment)	
Moderate renal impairment (CrCl 30 -50 ml/min) AND on concomitant verapamil	75 mg after surgery* then 75 mg **once daily** should be considered	* After surgery: 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.

RIVAROXABAN

Adjust dose for RENAL FUNCTION and consider INTERACTIONS

DOSING	**Prophylaxis of DVT post TKR or THR surgery**	**Interactions** : this list is not exhaustive; See SmPC for full details (www.medicines.ie or www.hpra.ie)
Standard Dose	10 mg once daily for 14 days (TKR) or for 35 days (THR)**	• **CONTRAINDICATED** with other anticoagulants (unless switching, then refer to individual SmPC for guidance) • **AVOID CONCURRENT USE** (increased bleeding risk): Strong **inhibitor**s of CYP3A4 and P-gp (e.g. ketoconazole, itraconazole, voriconazole, posaconazole, HIV protease inhibitors) • **AVOID**: Dronedarone – (limited clinical data) • **CAUTION**: Strong **inhibitors** of CYP3A4 (e.g. clarithromycin) ***AND*** renal impairment – **CAUTION** • **CAUTION (risk of reduced efficacy): Strong inducers** of CYP3A4 and P-gp (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns Wort). Avoid unless closely observed. • **CAUTION (increased bleeding risk):** NSAIDs, platelet aggregation inhibitors including aspirin, SSRIs, SNRIs ***Contraindicated** in **hepatic disease** associated with coagulopathy and clinically relevant bleeding risk*
CrCl: 30 – 49 ml/min	No dose adjustment required – 10 mg once daily for 14 days (TKR) or 35 days (THR)**	
CrCl: 15 - 29 ml/min	**Extreme Caution required**	

**Initial dose taken 6-10 hours after surgery provided haemostasis has been established
CONTRAINDICATED in CrCl < 15 ml/min

Reference: SmPC for Eliquis® (apixaban), Pradaxa® (dabigatran) and Xarelto® (rivaroxaban) **Version 2.0 MMP October 2020**