PHARMACY BULLETIN

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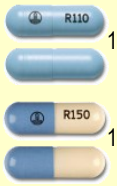
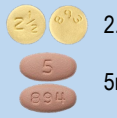
Non-vitamin K Oral Anti-Coagulants in HCTM

Non-vitamin K Oral Anticoagulants (NOAC), or Direct Oral Anticoagulants (DOAC) are new generation of oral anticoagulants that do not require frequent blood monitoring and have fewer drug interactions compared to warfarin.

The term "novel" was initially referred to Dabigatran when it was introduced is the market in 2010. When the other anticoagulants in the same group was introduced, the term "novel" was no longer relevant and the acronym were revised.

Summary on the dose of each NOAC is in Page 2. Recommendations in special population group are listed below:

Drugs / Condi-	Dabigatran (Pradaxa®)	Rivaroxaban (Xarelto®)	Apixaban (Eliquis®)	Edoxaban (Lixiana®)
Renal impairment	CrCl <30mL/min: Contraindicated	CrCl <15mL/min: Avoid Use	CrCl <15mL/min: Avoid use	CrCl <15mL/min: Avoid use
Crush/cut	Swallow the capsule whole	Tablets may be crushed and mixed with applesauce immediately prior to use. Stable up to 4 hours	Tablets may be crushed and suspended in water, or 5% glucose in water, or apple juice or mixed with apple puree immediately before administration. Stable up to	Tablets may be crushed and mixed with applesauce immediately prior to use. Stable up to 4 hours
Nasogastric (NG) tube	Not recommended. Capsule should no be opened as it will increase the absorption thus increase the risk of bleeding	Tablets may be crushed and suspended in 50 mL of water and administered via an NG tube or gastric feeding tube. Stable up to 4 hours	Tablets may be crushed and suspended in 60 mL of water or dextrose 5%. Stable up to 4 hours	Tablets may be crushed and suspended in a small amount of water and immediately delivered through a gastric tube after which it should be flushed with water.
Conversion from Warfarin to NOAC	Discontinue Warfarin and start Dabigatran when INR <2.0	Discontinue Warfarin and start Rivaroxaban when INR <3.0	Discontinue Warfarin and start Apixaban when INR <2.0	Discontinue Warfarin and start Edoxaban when INR <2.5
Conversion from NOAC to warfarin	CrCl ≥ 50 mL/min: start warfarin 3 days before discontinuing Dabigatran CrCl ≥ 30 to < 50 mL/min: start warfarin 2 days before discontinuing Dabigatran	Discontinue Rivaroxaban and begin both a parenteral anticoagulant and warfarin at the time the next dose of Rivaroxaban would have been taken. INR testing may be done reliably 24 hours after the last dose of Rivaroxaban	Stop Apixaban and begin both a parenteral anticoagulant and warfarin at the time the next dose of Apixaban would have been taken. Discontinue parenteral agent when INR is in range	For patients on 60mg dose: co-administer Edoxaban 30mg with warfarin For patient on 30mg dose: co-administer Edoxaban 15mg with warfarin Stop Edoxaban when INR ≥ 2.0. Patients should not take a loading dose of warfarin in order to promptly achieve a stable INR

Drugs \ Indications	Prophylaxis of DVT/PE after KNEE or HIP replacement surgery	Non-Valvular Atrial Fibrillation (NVAF)	Treatment of DVT & prevention of recurrent DVT	Treatment of PE & prevention of recurrent DVT & PE after acute PE
DABIGATRAN (Pradaxa®)  110mg 150mg	**Day 1**: 110mg within 1-4 hours of completed surgery **Day 2 onwards**: 220mg OD **Duration:** Knee - 10 days Hip - 28-35 days Special patient population: • Elderly >75yo • CrCl 30-50 ml/min • Taking Amiodarone **Day 1**: 75mg within 1-4 hours of completed surgery **Day 2 onwards**: 150mg OD	150mg BD lifelong Reduce dose to 110mg BD if: • Elderly >80 yo • Taking verapamil	150mg BD (After at least 5 days of parenteral anticoagulant), Duration of treatment should be individualized. Reduce dose to 110mg BD if: • Elderly ≥80 yo (due to risk of bleeding) • Taking verapamil	
		For these group of patients, daily dose should be selected based on an individual assessment of the thromboembolic risk and the risk of bleeding: • Between 75-80 years • Moderate renal impairment • Patients with gastritis, esophagitis or gastroesophageal reflux • Other patients at increased risk of bleeding		
HCTM Policy	Pay full price at NF Pharmacy RM 4.50/tab	NFS: Cardiologist & Neurologist only. **With subsidy card: RM 150/month	Pay full price at NF Pharmacy RM 4.50/tab	
RIVAROXABAN (Xarelto®)  10mg 15mg 20mg	10mg OD **Duration:** Knee– 12 days Hip - 35 days Initial dose should be taken 6-10 hours after surgery provided hemostasis has been achieved.	20mg OD with evening meal Reduce dose to 15mg OD if : • ClCr 15-50ml/min	**Treatment dose:** 15mg BD with food for first 21 days 20mg OD with food on Day 22 onwards **Prevention dose:** 10mg OD, after at least standard anticoagulant treatment.	
HCTM Policy	A*: Orthopedic Surgeons only. Only for 100 patients Others to pay full price: RM8.70/tab	NFS: Cardiologist & Neurologist only. **With subsidy card: RM150/month	Pay full price at NF Pharmacy RM 8.70/tab	A*: Respiratory Specialists only (Sharing quota with tab. Apixaban—30 pts/year for 6 months only)
APIXABAN (Eliquis®)  2.5mg 5mg	2.5mg BD Initial dose should be taken 12-24 hours post surgery **Duration:** Knee- 10-14 days Hip- 32-38 days	5mg BD long-term Reduce dose to 2.5mg BD if (at least 2 of the following): • Age ≥80 yo • Wt ≤ 60 kg • SrCr ≥ 1.5mg/dL(133µmol/L)	Treatment dose: 10mg BD for first 7 days followed by 5mg BD for at least 3 months Prevention dose: 2.5mg BD following the completion of 6 months of treatment with 5 mg BD or with another anticoagulant	
HCTM Policy	Pay full price at NF Pharmacy RM 4.50/tab	NFS: Cardiologist & Neurologist only. **With subsidy card: RM150/month	Pay full price at NF Pharmacy RM 4.50/tab	A*: Respiratory Specialists only (Sharing quota with tab. Rivaroxaban—30 pts/year for 6 months only)
EDOXABAN (Lixiana®)  30mg 60mg	Safety and efficacy data are not establish	60mg OD long-term	60mg OD Following initial dose of parenteral anticoagulant for at least 5 days	
		Reduce dose to 30mg OD if (one or more of the following): • Renal impairment (CrCl 15-50 ml/min) • Patient weight ≤ 60kg • Concomitant use of P-glycoprotein (P-gp) inhibitors (Ciclosporin, Dronedarone, Erythromycin or Ketoconazole)		
HCTM Policy	-	NFS: Cardiologist & Neurologist only. **With subsidy card: RM150/month	Pay full price at NF Pharmacy RM 8.70/tab	

**Subsidy cards allocated for only 300 patients for the combination all the four drugs. Cards are with Cardiologists & Neurologists.

References : Product monographs of Pradaxa, Xarelto, Eliquis and Lixiana. Pictures of tablets and capsules: Webmd

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