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The “Princesses” of Oral Anticoagulants—A Comparison by: PRP Fei Yee & Ms Izyan

Warfarin has long been the “King” of oral anticoagulants since it was first discovered in 1940-s. Since its discovery, there are no other oral anticoagulant available in the market, until recently. The introduction of the “princesses” of anticoagulants - novel oral anticoagulants (NOACs), as an alternative to warfarin, provides more options for treatment/prevention of several health conditions, namely venous thrombo-embolic events (VTE) as well as non-valvular atrial fibrillation (NVAF) without extensive dietary restrictions and the need of routine INR testing for dosing purposes. The table below illustrates a comparison between the NOACs and warfarin from various perspectives in clinical application.

Anticoagulants		Apixaban by Pfizer 	Dabigatran by Boehringer-Ingelheim 	Rivaroxaban by Bayer 	Warfarin
Brand name		<i>Eliquis</i> (apixaban) tablets	<i>Pradaxa</i> dabigatran etexilate	 <i>Xarelto</i> [®] rivaroxaban tablets	Various
Mechanism of action		Factor Xa inhibitor	Thrombin Factor IIa inhibitor	Factor Xa inhibitor	Vitamin K antagonist
Time to peak levels (hours) ^{1,2}		3	3	3	4
Half life ^{1,2}		9—14 hours	12—17 hours	5—13 hours	1 week
VTE prevention after elective hip/knee replacement surgery ^{2,3,4}	Licenced by BPFK/FDA	☑ 2.5 mg tablets	☑ 75 mg & 110 mg capsules	☑ 10 mg tablets	☑ 2, 3, 5 mg tablets
	Approval status in PPUKM	Not listed in PPUKM	Not indicated	☑ 10 mg tablets Prescribers: Consultants only.	☑ 2, 3, 5 mg tablets
Prevention of stroke and systemic embolism with NVAF with ≥1 risk factors ^{2,3,4} eg: <ul style="list-style-type: none">• Prior stroke or transient ischaemic attack (TIA)• Age ≥ 75 years• Hypertension• Diabetes mellitus• Symptomatic heart failure (NYHA Class ≥ II)	Licenced by BPFK/FDA	☑ 2.5 & 5 mg tablets	☑ 110 & 150 mg capsules	☑ 15 & 20 mg tablets	☑ 2, 3, 5 mg tablets
	Approval status in PPUKM	Not listed in PPUKM	☑ 110 & 150 mg capsules	☑ 15 & 20 mg tablets	<div><p>Card System</p><p>Prescribers: Consultant Cardiologists & Consultant Neurologists only.</p><p>*Patients with card can purchase at Kedai Farmasi with flat rate: RM100.00 monthly (150 patients only for both dabigatran and rivaroxaban).</p><p>*Patients without card may purchase at <u>full price</u>.</p></div>
Treatment of pulmonary embolism (PE) and prevention of recurrent DVT & PE following an acute PE in adults ^{2,3,4}	Licenced by BPFK/FDA	Not indicated	Not indicated	☑ 15 & 20 mg tablets	
	Approval status in PPUKM	Not listed in PPUKM	Not indicated	☑ 15 & 20 mg tablets Prescribers: A* Respiratory Specialists only.	☑ 2, 3, 5 mg tablets
Administration via enteral feeding tubes		Can be crushed and administered through NG tube ⁵	Not recommended to open the capsules ⁴	15 & 20 mg tablets: may be crushed and suspended in 50 mL water, followed by enteral feeding via the tube immediately ⁶	Can be crushed and suspended in water ⁷

	Apixaban by Pfizer 	Dabigatran by Boehringer-Ingelheim 	Rivaroxaban by Bayer 	Warfarin
Typical effective dose ^{2,3,4}	<p>VTE prevention after elective hip/knee replacement surgery: 2.5 mg twice daily, 12 to 24 hours after surgery.</p> <ul style="list-style-type: none"> - 10-14 days for knee replacement - 32-38 days for hip replacement <p>Prevention of stroke and systemic embolism with NVAF: 5mg twice daily</p>	<p>VTE prevention after elective hip/knee replacement surgery: Day of surgery (1-4 hours post surgery): 110 mg followed by 220 mg once daily</p> <ul style="list-style-type: none"> - Day 2-10 for knee replacement surgery - Day 2-35 for hip replacement surgery <p>(75 mg 1-4 hours post surgery followed by 150 mg once daily for >75 years old)</p> <p>Prevention of stroke and systemic embolism with NVAF: 150 mg twice daily</p> <p>(110 mg twice daily for ≥ 80 years old)</p>	<p>VTE prevention after elective hip/knee replacement surgery: 10 mg once daily initiated 6-10 hours after surgery, provided haemostasis has been established.</p> <ul style="list-style-type: none"> - for 2 weeks following knee replacement - for 5 weeks following hip replacement <p>Prevention of stroke and systemic embolism with NVAF: 20mg once daily</p> <p>Treatment of PE and prevention of recurrent DVT & PE following acute PE in adults: 15 mg twice daily for 21 days followed by 20 mg daily as long as the risks persists.</p>	INR-guided
Dose adjustment in renal impairment ^{2,3,4}	<p>Prevention of stroke and systemic embolism in NVAF patients:</p> <p>SeCr ≥ 133 µmol/l associated with age ≥ 80 years or body weight ≤ 60 kg; CrCl 15- 29 mL/min: 2.5 mg twice daily.</p> <p>Not recommended for patients with creatinine clearance <15 mL/min</p>	<p>Moderate renal impairment (CrCl 30-50 mL/min):</p> <p>Primary VTE prevention after elective hip/knee replacement surgery: Day of surgery (1-4 hours post surgery): 75 mg followed by 150 mg once daily</p> <p>Reduction of the Risk of Stroke and Systemic Embolism in NVAF Patients: 150 mg twice daily</p> <p>Contraindicated if creatinine clearance <30 mL/min</p>	<p>Moderate or severe renal impairment (CrCl 15-49 mL/min):</p> <p>Prevention of Stroke and Systemic Embolism in NVAF patients: 15 mg once daily</p> <p>Treatment of DVT and Prevention of Recurrent DVT and PE: Initially, 15 mg twice daily for the first 3 weeks. Thereafter, 15 mg once daily</p> <p>Use is not recommended in patients with creatinine clearance <15 mL/min</p>	No dosage adjustment necessary. However, patients with renal failure have an increased risk of bleeding complications; monitor closely ²
Dose adjustment in liver impairment ^{2,3,4}	<p>Mild -moderate impairment (Child Pugh A or B): Use with caution, no dosage adjustment required</p> <p>Severe impairment: Not recommended</p>	Contraindicated in hepatic impairment or liver disease expected to have any impact on survival	<p>Contraindicated in hepatic disease associated with coagulopathy and clinically relevant bleeding risk including cirrhotic patients with Child-Pugh B and C</p> <p>Other hepatic diseases: No dose adjustment necessary</p>	No dosage adjustment provided in manufacturer's labeling. However, the response to oral anticoagulants may be markedly enhanced in obstructive jaundice, hepatitis, and cirrhosis. INR should be closely monitored ²

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ANNOUNCEMENT: DEPOSIT FOR PUREGON (NEW!!!)

Dear doctors,

Please kindly inform your patients that starting **1st June 2014**, patients requiring supply of **cool bag for Puregon Inj** are required to pay a deposit of **RM50** per bag to **Kedai Farmasi**. This deposit is required to ensure that the bags are returned to Kedai Farmasi once patients no longer use it as it is on **loan basis**. Patients' understanding and cooperation are greatly appreciated. Thank you.

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DRUG INFORMATION CENTRE
Pharmacy Department , UKMMC

Izyan Diyana Binti Ibrahim
izyandi@ppukm.ukm.edu.my
Ext 5415

Michelle Tan Hwee Pheng
hptan@ppukm.ukm.edu.my
Ext 5401
<http://pharmacy.hukm.ukm.my>
(for previous bulletin issues)