The following newer oral anticoagulants are available in Australia. Patients may be initiated on these agents in hospital or in the community for a number of indications (refer page 2)

- Rivaroxaban (Xarelto®)
- Dabigatran (Pradaxa®)
- Apixaban (Eliquis®)

**Background**

The TGA advise they have received 297 adverse drug reports related to the use of rivaroxaban (20), warfarin (23) and dabigatran (258) between May 2011 and September 2011. Many of these were bleeding events.

The TGA notes that some bleeding events with dabigatran have occurred in patients during the transition from warfarin to dabigatran, and in patients on the lower recommended dose.

The TGA has released safety information about Dabigatran (see http://www.tga.gov.au/safety/alerts-medicine-dabigatran-111005.htm )

**The newer anticoagulants have no specific reversal agent**, unlike warfarin (reversed with vitamin K and plasma/factor concentrates)

**Risk Factors**

Risk factors to be considered when using all oral anticoagulants include:
- renal impairment;
- older age and/or low body weight; (elderly patients are at significant risk of bleeding)
- other medications may reduce clearance and increase plasma levels of some agents including p-glycoprotein inhibitors (amiodarone, verapamil), CYP3A4 inhibitors (eg macrolides, azoles, protease inhibitors).

**Steps to minimise risk**

- Patients receiving these newer oral anticoagulants have an increased risk of bleeding and should not routinely be given other anticoagulants (including heparin or low molecular weight heparins).
- Patients stable on warfarin may not benefit from switching to a newer oral anticoagulant.
- Any suspicion of moderate to severe bleeding requires a consultation with senior medical staff or haematologist or, if unavailable, through the NSW Poisons Information Centre at www.chw.edu.au/poisons/ or by calling 131126.
- Assess renal function before commencing therapy. Calculate creatinine clearance because small body mass will disguise poor renal function if eGFR is used.
- Ensure prescribers recognise the newer agents as anticoagulants and understand the risks.
- Check for drug interactions. Great caution should be used if prescribing antiplatelet agents and NSAIDS with these agents.
- Refer to the relevant product information for specific advice on perioperative management of patients.

**Suggested Actions by Local Health Districts/ Networks**

1. Ensure that this Safety Notice and attachments are distributed to all relevant stakeholders including GP’s.
2. Report suspected adverse drug reactions to the TGA at adr.reports@tga.gov.au
### Newer Oral anticoagulants

<table>
<thead>
<tr>
<th>Anticoagulant action</th>
<th>Dabigatran (Pradaxa®)</th>
<th>Rivaroxaban (Xarelto®)</th>
<th>Apixaban (Eliquis®)</th>
<th>Warfarin (Coumadin®, Marevan®)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Competitive reversible direct thrombin inhibitor</td>
<td>Factor Xa inhibitor</td>
<td>Factor Xa inhibitor</td>
<td>Inhibits synthesis of vitamin K-dependent clotting factors, proteins C and S.</td>
</tr>
</tbody>
</table>

| TGA approved indication | Prevention of VTE post major orthopaedic surgery of lower limb | Prevention of VTE post major orthopaedic surgery of lower limb | Prevention of VTE after elective total hip or knee replacement surgery. | Treatment and prevention of VTE Prevention of embolism in prosthetic heart valves Prevention of stroke with previous MI and increased embolic risk Non-valvular AF with risk of stroke or systemic embolism. |

| Use in renal impairment | Increased plasma levels and haemorrhagic risk in moderate renal impairment (30-50mL/min CrCl) | Increased plasma levels and haemorrhagic risk in moderate and severe renal impairment | Increased plasma levels and haemorrhagic risk in moderate renal impairment (15-29mL/min CrCl) | No adjustment required |
| Contraindicated in severe renal impairment (CrCl < 30mL/min) | Contraindicated in severe renal impairment (CrCl < 15mL/min) | Contraindicated in severe renal impairment (CrCl < 15mL/min) | |

| Drug interactions | Proton pump inhibitors reduce absorption Possible interactions with P-glycoprotein inhibitors and inducers | Strong inhibitors of both CYP3A4 and P-glycoprotein's may lead to reduced hepatic and renal clearance significantly increased systemic exposure of rivaroxaban. | CYP 3A4 inhibitors and p-glycoprotein inhibitors and inducers (eg rifampicin, phenytoin, carbamazepine or St. John's Wort), NSAIDs and anticoagulants | Numerous – See product information or AMH |

| Reversal agent | nil | nil | nil | Immediate reversal with plasma or factor concentrate Reversal within hours of Vitamin K |

### Further Information

3. Australian Prescriber Volume 33, Number 2 April 2010
6. MIMS Online: Rivaroxaban, Full Product Information. 30/7/10. Accessed 29th Sept 2011