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Guidelines for Anticoagulation using Warfarin

Ward:
Bed no.:

Before Initiating Warfarin Therapy

- Consider if the benefits of anticoagulation outweigh the risks for each patient, eg bleeding.
- Ensure **INR**, platelets and liver function tests are normal. If not, seek senior/specialist advice.

Dosing Principles

- Warfarin should be **prescribed** in the **designated** area of the medication chart.
- The initiating team must complete **target INR**, **indication**, **initial dose** and consider **duration** of therapy.
- Check the patient has received **education** and **warfarin leaflets** before discharge. Ask your pharmacist to assist.

Starting Warfarin Therapy

- **Acute DVT** or **PE**: Start warfarin on the same day as heparin. **Overlap warfarin** with full dose heparin for a minimum of five (5) days **and** until the INR has been therapeutic for at least two (2) consecutive days.[1]
- **Chronic AF** and **valve replacements**: Start **warfarin alone** (may overlap with prophylactic heparin).
- **Post operative patients**: Restart with their **'normal'** pre-operative maintenance dose – **DO NOT RE-LOAD**.
- Assess each patient for **risk factors** (see below±) for increased sensitivity to warfarin and therefore bleeding:
  - If **no risk factors** exist, **start at 5mg daily**, monitor **INR daily** and adjust dose **using nomogram below**;
  - If **risk factors exist** consider a smaller loading dose (2 - 4mg) and seek senior/specialist advice.
- **High loading doses**, such as 10mg, should **not** be used due to an **increase in the risk of bleeding**.

Recommended starting nomogram for patients with no risk factors for increased sensitivity to warfarin[2]

Day of Initiation	INR	Dose
1	< 1.4	5 mg
2	< 1.8	5 mg
	1.8 – 2.0	1 mg
	> 2.0	Nil
3	< 2.0	5 mg
	2.0 – 2.5	4 mg
	2.6 – 2.9	3 mg
	3.0 – 3.2	2 mg
	3.3 – 3.5	1 mg
	> 3.5	Nil
4	< 1.4	10 mg
	1.4 – 1.5	7 mg
	1.6 – 1.7	6 mg
	1.8 – 1.9	5 mg
	2.0 – 2.3	4 mg
	2.4 – 3.0	3 mg
	3.1 – 3.2	2 mg
	3.3 – 3.5	1 mg
	> 3.5	Nil

After Day 4, dose is based on clinical judgement

±Risk factors for increased sensitivity to warfarin [3,4,5]

- Age > 75 years;
- History of bleeding;
- Baseline INR > 1.4;
- Concomitant drugs affecting warfarin metabolism (see "Warfarin Drug Interactions" on reverse page);
- Co-morbid diseases i.e. hypertension, cerebrovascular disease, ischaemic stroke, heart disease, renal insufficiency, hepatic impairment or low platelets;
- Presence of malignancy;
- History of falls;
- Major surgery < 10-14 days.

Recommended target INR ranges[4,6]

Indication	INR
AF, DVT, PE and bio-prosthetic heart valve in patients with sinus rhythm for 6 weeks post-op	2.0 - 3.0
Mechanical prosthetic heart valves	2.5 - 3.5

Minimum recommended duration[1,4,5]

Indication	Transient risks	Non-transient risks
DVT/PE	3 months	6 – 12 months
AF	Life long, balanced against risks	
Irreversible, clinically hyper-coagulable states	Life long, balanced against risks	

Managing warfarin therapy during invasive procedures according to risk of thromboembolism[7]

NB simple dental or dermatological procedures may not require interruption to warfarin therapy[7]

	Before surgery	After surgery
LOW thromboembolic risk *eg AF*	• Withhold warfarin 4-5 days before surgery. • **Night before surgery**: If INR > 2.0, give 1 - 2mg vitamin K IV. • **Day of surgery**: If INR < 1.5, surgery can proceed. If INR > 1.5, defer surgery or, if urgent give Prothrombinex™-HT (25-50units/kg) plus FFP (150-300mL) or FFP (10-15mL/kg) if Prothrombinex™-HT not available.	• Start warfarin on the day of surgery at the **previous** '**normal**' maintenance dose as long as there is no evidence of bleeding. • Employ thrombo-prophylaxis as per hospital policy.

HIGH thromboembolic risk
eg recurrent DVT/PE, mechanical valve
	• Withhold warfarin 4-5 days before surgery.
	• **2-3 days before surgery**: Commence treatment dose of unfractionated heparin IV or treatment dose of LMWH* subcutaneously:
	  • If using unfractionated heparin IV, cease infusion 4-6hrs before surgery.
	  • If using LMWH*, last dose should be given **at least** 24hrs before surgery.
		• Recommence warfarin as soon as possible at the **previous 'normal'** maintenance dose as long as there is no evidence of bleeding – DO NOT RE-LOAD;
		• Start heparin or LMWH* 12-24 hrs post-operatively;
		• If using LWMH*, give a thrombo-prophylactic dose;
		• If using unfractionated heparin IV, aim to prolong APTT as recommended by your site;
		• Cease heparin or LMWH* 48 hours after the target INR is reached.

INR = international normalised ratio, FFP = fresh frozen plasma, LMWH = low molecular weight heparin e.g. enoxaparin, APTT = activated partial thromboplastin time
*Exercise caution in patients with impaired renal function (calc Clcr < 30ml/min) where LMWH can accumulate and contribute to bleeding.

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Recommendations for reversal of warfarin [7] Seek early advice if any bleeding occurs

INR > therapeutic range but < 5.0 and **NO** bleeding		Withhold next dose of warfarin and resume lower dose of warfarin when INR approaches therapeutic range.
INR 5.0 – 9.0 and **NO** bleeding		Cease warfarin. If bleeding risk **high**, give vitamin K, 1 - 2mg orally or 0.5 - 1mg IV. Check INR within 24hrs. Resume lower dose of warfarin once INR approaches therapeutic range.
INR > 9.0 and **NO** bleeding	**Low risk of bleed**	Cease warfarin. Give vitamin K up to 5 mg orally or 0.5 - 1mg IV. Check INR in 6-12hrs. Resume lower dose of warfarin once INR < 5.0.
	High risk of bleed	Cease warfarin. Give vitamin K 1mg IV. Consider Prothrombinex™-HT (25-50units/kg) and FFP (150-300mL). Check INR in 6-12hrs. Resume lower dose of warfarin once INR < 5.0.
Any clinically significant bleeding where warfarin-induced coagulopathy considered a contributing factor		**SEEK SENIOR ADVICE**: Cease warfarin. Give vitamin K 5-10 mg IV, Prothrombinex™-HT (25-50units/kg) and FFP (150-300mL). Assess INR frequently until INR < 5.0 and bleeding stops. If Prothrombinex™-HT is unavailable, increase FFP dose to 10-15mL/kg and assess INR frequently until INR < 5.0 and bleeding stops.

Warfarin Drug Interactions [8,9]

- **Drug interactions** are a common and significant cause of morbidity and mortality.
- Consider **all concomitant therapy** including **herbal/complementary** and **over-the-counter** medications (OTCs).
- Whenever **starting** or **stopping** a drug, particularly **antibiotics**, the **INR** must be **re-checked** 48 to 72 hours after change in therapy.
- Do not pre-empt a change. Make dose adjustments only after checking INR at 48 to 72 hours.

✓ Refers to a review that states the interaction is not likely to be clinically significant, or less than two case reports with no clinically significant outcomes (i.e. bleeding, bruising, haematoma, death).

✓✓ Refers to a review containing no information regarding clinical significance or a single case study with a clinically significant outcome.

✓✓✓ Refers to a review which states that the interaction is clinically significant.

This list is not comprehensive or exhaustive. Contact your pharmacist for further information.

Interacting Medication (Drug or Class)	↑ Effect	↓ Effect
Aminoglutethimide		✓✓
Amiodarone	✓✓✓	
Amoxycillin	✓✓	
Anabolic Steroids/Androgens *eg nandrolone, oxandralone*	✓✓✓	
Anticoagulants/Antiplatelets *eg low molecular weight heparin, clopidogrel, aspirin*	✓✓✓	
Antithyroid agents *eg carbimazole, propylthiouracil*		✓✓
Aprepitant		✓✓✓
Azathioprine/Mercaptopurine		✓✓
Capecitabine	✓✓	
Carbamazepine		✓
Cephalosporins *eg cephazolin*	✓	
Cholestyramine		✓✓
Ciprofloxacin	✓✓✓	
Cyclosporin		✓
Danazol	✓✓	
Dicloxacillin		✓✓
Disulfiram	✓✓	
Fibrates *eg fenofibrate, gemfibrozil*	✓✓	
5-Fluorouracil	✓✓	
Gatifloxacin	✓✓	
Griseofulvin		✓
Imidazole antifungals *eg ketaconazole, miconazole*	✓✓	
Isoniazid	✓	
Leflunomide	✓✓	
Macrolides *eg azithromycin, clarithromycin, erythromycin, roxithromycin*	✓✓✓	
Metronidazole	✓✓✓	
Moxifloxacin	✓✓	
Norfloxacin	✓✓✓	
NSAIDs/COX-2 inhibitors *eg naproxen, celecoxib*	✓✓✓	
Paracetamol *(if taking >3.5 - 7.0g/week)*	✓✓✓	
Phenobarbitone		✓✓✓
Phenytoin	✓✓✓ (initially)	✓ (long-term)
Proton Pump Inhibitors *eg omeprazole, esomeprazole, pantoprazole*	✓✓	

Interacting Medication (Drug or Class)	↑ Effect	↓ Effect
Quetiapine	✓✓	
Quinidine	✓✓	
Quinine	✓✓	
Ranitidine	✓	
Rifabutin		✓✓✓
Rifampicin		✓✓✓
Salicylates (topical) *eg methyl salicylate*	✓✓	
Statins *eg fluvastatin, simvastatin*	✓	
SSRIs *eg fluoxetine, sertraline, paroxetine*	✓✓	
Sucralfate		✓
Sulfamethoxazole *(in co-trimoxazole)*	✓✓✓	
Tamoxifen	✓✓✓	
TCAs *eg amitryptiline*	✓✓	
Tetracyclines *eg doxycycline*	✓	
Thrombolytic Agents *eg tenecteplase*	✓✓✓	
Thyroxine	✓	
Tramadol	✓✓	
Triazole antifungals *eg fluconazole, itraconazole, voriconazole*	✓✓	
Vancomycin	✓	

This list is not comprehensive or exhaustive.
Contact your pharmacist for further information.

Interacting Complementary Medication	↑ Effect	↓ Effect
Cranberry	✓✓	
Dong Quai *Angelica sinensis*	✓✓	
Garlic *Allium sativum*	✓✓	
Ginkgo	✓✓	
Ginseng *Panax ginseng*		✓
Glucosamine +/- Chondroitin	✓	
Papaya extract (containing Papain)*Carica papaya*	✓	
St John's Wort *Hypericum perforatum*		✓✓✓
Tan-shen *(also known as Danshen)*	✓✓	
Vitamin E	✓✓	

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