# Warfarin Initiation / Restarting with INR < 1.2



- Check contraindications. See box 1.
- Check FBC, LFTs, INR, APTT
- Choose warfarin brand (Marevan most common) or continue existing brand
- In most cases current aspirin can be stopped, except in metallic heart valves (discuss with cardiology if relevant)

# AF/Atrial Flutter

#### **Target INR**

- AF: 2-3
- AF + DVT/PE: 2.5-3.5
- AF + left atrial thrombus: 2.5 3.5

# 

1	-	3mg
2	•	3mg
3	•	3mg
4	-	3mg
5	<2.0	4mg
	2.0-3.0	3mg
	3.0-3.5	2mg
	>3.5	1mg
>6		Adjust dose in <i>small</i>

increments

Once stabilised, check INR weekly for 3 weeks, then 6-8 weekly

Check interactions – see box 2.

Duration of warfarin treatment: indefinite

## DVT / PE

If active solid malignancy- see box 6.

#### Target INR

- DVT/PE: 2-3
- Left atrial thrombus: 2.5-3.5
- Start warfarin, and start enoxaparin 1.5mg/kg once daily (if patient >100kg consult with medical team)
- Continue enoxaparin for a minimum of 4 days and stop once INR >=2
   Hospital doctors <u>click here</u> for enoxaparin protocol

Check interactions - see box 2.

Day   INR   Warfarin dose (mg)	<b>▼</b>			
1	Fast loading			
Low Risk (*See box 3.) = 10mg.  >1.4 Seek Advice  2 <1.8 5  1.8-2.0 1  >2.0 0  3 <2.0 5  2.0-2.5 4  2.6-2.9 3  3.0-3.2 2  3.3-3.5 1  >3.5 0  4 <1.4 10  1.4-1.5 7  1.6-1.7 6  1.8-1.9 5  2.0-2.3 4  2.4-3.0 3  3.1-3.2 2  3.3-3.5 1	Day	INR	Warfarin dose (mg)	
= 10mg.  >1.4 Seek Advice  2 <1.8 5  1.8-2.0 1  >2.0 0  3 <2.0 5  2.0-2.5 4  2.6-2.9 3  3.0-3.2 2  3.3-3.5 1  >3.5 0  4 <1.4 10  1.4-1.5 7  1.6-1.7 6  1.8-1.9 5  2.0-2.3 4  2.4-3.0 3  3.1-3.2 2  3.3-3.5 1	1	<1.4		
>1.4 Seek Advice  2 <1.8 5 1.8-2.0 1 >2.0 0 3 <2.0 5 2.0-2.5 4 2.6-2.9 3 3.0-3.2 2 3.3-3.5 1 >3.5 0 4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1			Low Risk (*See box 3.)	
2			= 10mg.	
1.8-2.0 1 >2.0 0 3 <2.0 5 2.0-2.5 4 2.6-2.9 3 3.0-3.2 2 3.3-3.5 1 >3.5 0 4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		>1.4	Seek Advice	
>2.0 0 0  3 <2.0 5 2.0-2.5 4 2.6-2.9 3 3.0-3.2 2 3.3-3.5 1 >3.5 0  4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1	2	<1.8	5	
3 <2.0 5 2.0-2.5 4 2.6-2.9 3 3.0-3.2 2 3.3-3.5 1 >3.5 0 4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1	[	1.8-2.0	1	
2.0-2.5 4 2.6-2.9 3 3.0-3.2 2 3.3-3.5 1 >3.5 0  4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		>2.0	0	
2.6-2.9 3 3.0-3.2 2 3.3-3.5 1 >3.5 0  4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1	3	<2.0	5	
3.0-3.2 2 3.3-3.5 1 >3.5 0  4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		2.0-2.5	4	
3.3-3.5 1 >3.5 0  4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		2.6-2.9	3	
>3.5 0 4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		3.0-3.2	2	
4 <1.4 10 1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		3.3-3.5	1	
1.4-1.5 7 1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		>3.5	0	
1.6-1.7 6 1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1	4	<1.4	10	
1.8-1.9 5 2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		1.4-1.5	7	
2.0-2.3 4 2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		1.6-1.7	6	
2.4-3.0 3 3.1-3.2 2 3.3-3.5 1		1.8-1.9	5	
3.1-3.2 2 3.3-3.5 1		2.0-2.3	4	
3.3-3.5 1		2.4-3.0	3	
		3.1-3.2	2	
>3.5 0		3.3-3.5	1	
		>3.5	0	

Day 5 onwards – if INR therapeutic use Day 4 dose as maintenance dose; otherwise seek specialist advice.

# Duration of warfarin treatment:

- DVT: see box 4.
- PE: see box 5.

# Artificial (Metallic) Heart Valve

#### **Target INR**

- Aortic bileaflet mechanical valve:
   2-3
- Other prosthetic/mechanical: 2.5-3.5

Check interactions – see box 2.

Duration of warfarin treatment: indefinite

## **Instructions for discharging hospital doctors**

- Refer to hospital pharmacist for patient education, or if unavailable: educate and give red warfarin booklet
- Inform GP of latest INR result and recent warfarin doses
- Inform GP of intended duration of warfarin treatment and of target INR

#### **Box 1.**

#### **Absolute contraindications:**

- Large oesophageal varices or decompensated liver disease
- Within 72 hours of major surgery
- A platelet count of less than 50
- Hypersensitivity to the drug, such as skin ischemic necrosis or priapism
- Pregnancy and within 48 hours of delivery
- Coagulation defects at baseline such that the INR is over 1.5 or uncorrected major bleeding disorder e.g. haemophilia
- Renal failure

#### **Relative contraindications:**

- Previous history of intracranial haemorrhage
- Recent history of a major extracranial bleed without known cause
- History of peptic ulceration within the past three months (wait until treatment of peptic ulcer is completed then continue treatment along with warfarin)
- Recent history of repeated falling episodes with a patient at higher risk for bleeds
- Unsupervised patients with conditions associated with potential high level of noncompliance (e.g. dementia, alcoholism, psychosis)
- Severe hypertension which is poorly controlled, or not under treatment
- Concomitant use of other drugs that interact with warfarin, increasing the risk of bleeding
- Major regional or lumbar block anaesthesia
- Spinal puncture and other diagnostic or therapeutic procedures with potential for uncontrollable bleeding

#### Box 3.

## Low Risk =

- Age < 60 years</li>
- Body weight > 50kg
- No liver disease
- No cardiac failure
- Serum albumin > 35g/L
- No known bleeding risk
- Not taking medication that enhance the effect of anticoagulants
- Previously anticoagulated and maintenance dose > 2mg daily

#### **Box 2.**

- For interactions, refer to the Interactions Checker at http://nzf.org.nz/
- Don't forget to check for complementary/natural medicines and over the counter (OTC) products

# **Box 4.**

#### **DVT**

- Proximal
  - 1. Provoked: 3 months anticoagulation
  - 2. Unprovoked or recurrent DVT or persistent risk factors (e.g. thrombophilia, family history, immobility): lifelong anticoagulation\*
- Distal
  - 1. Symptomatic
    - Provoked: 3 months anticoagulation
    - Unprovoked or recurrent DVT or persistent risk factors (as above): lifelong anticoagulation \*
  - 2. Asymptomatic or patient does not want anticoagulation: observe and repeat ultrasound weekly for two weeks. If DVT shows extension: 3 months anticoagulation, if not then no anticoagulation.
- \* NB *Lifelong* anticoagulation may not be appropriate for some patients. If risk factors for bleeding are present consider shorter treatment duration (use validated risk score, eg **HAS-BLED** score)- see <a href="http://www.mdcalc.com/">http://www.mdcalc.com/</a>

# **Box 5.**

#### **Pulmonary embolism**

- Provoked: 6 months anticoagulation
- Unprovoked or large or recurrent PE or persistent risk factors: lifelong anticoagulation, and refer haematology for further testing

#### **Box 6.**

# **DVT/PE in Active Solid Malignancy**

- Not for warfarin
- Use indefinite enoxaparin (or until malignancy resolved)- download special authority form for enoxaparin here- http://www.pharmac.govt.nz/2016/ 10/01/SA1174.pdf

#### **References**

- Baglin TP, Keeling DM, Watson HG, the British Committee for Standards in Haematology. Guidelines on oral anticoagulation (warfarin): third edition, 2005 update. British Society for Haematology 2005; 132(3):277-85.
- Mahtani KR, Heneghan CJ, Nunan D, et al. Optimal loading dose of warfarin for the initiation of oral anticoagulation. *Cochrane Database of Systematic Reviews* 2012, Issue 12.
- Holbrook A, Schulman S, Witt DM, et al Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed.: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141;e44S-e88S
- Kovacs MJ, Rodger M, Anderson DR, et al. Comparison of 10-mg and 5-mg Warfarin Initiation Nomograms Together with Low-Molecular-Weight Heparin for Outpatient Treatment of Acute Venous Thromboembolism: A Randomized, Double-Blind, Controlled Trial. Ann Intern Med. 2003;138(9):714-719
- Guyatt GH, Akl EA, Crowther M, et al, "Executive Summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed.: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines," Chest, 2012, 141(2 Suppl):7-47. [PubMed 22315257]
- Nutescu EA and Dager W, "Heparin, Low Molecular Weight Heparin, and Fondaparinux," *Managing Anticoagulation Patients in the Hospital*, Gulseth M ed., American Society of Health-System Pharmacists®, Bethesda, MD: 2007, 181
- Uptodate- <u>www.uptodate.com</u>