Management of Subtherapeutic INRs in Patients on Warfarin

NHS
Bath and North East Somerset, Swindon and Wiltshire
Integrated Care Board

This protocol provides guidance for managing adult patients on oral anticoagulation with a vitamin K antagonist (e.g. warfarin), with an International Normalised Ratio (INR) result below their target range.

Clinical decisions in these scenarios require individual patient considerations, including determining a reason for the result (e.g. missed dose), risk factors for thrombosis / bleeding, and patient preference. The decision to bridge may also be affected by anticipated poor compliance either with administration of low molecular weight heparin (LMWH) injections or with subsequent INR testing. Complex patients should be discussed with local anticoagulation service.

Low Thrombosis Risk

The following groups of patients have low thrombotic risk and do not require bridging with LMWH. However, consider a review with local anticoagulation service if the INR remains low (i.e. <1.7) for >10 days despite dose adjustment. Increase regular dose of warfarin. If INR < 1.4 consider a loading dose of warfarin for 1-2 days. Management should focus on warfarin dose adjustment, adherence assessment, interacting medicines, dietary factors and increased INR monitoring frequency.

- Atrial fibrillation (AF) without significant additional thrombotic risk factors (CHADs-Vasc score ≤6, no recent thrombotic event within past 3 months or significant valve disease)
- Venous thromboembolism (VTE) >4 weeks (unless significant thrombosis such as extensive pulmonary embolism (PE)/right heart strain, iliofemoral deep vein thrombosis (DVT)) or recurrent VTE (not whilst on anticoagulant) with target INR 2.5
- Low risk aortic valve replacement with no additional risk factors (see *Table 1* below))

High Thrombosis Risk

- VTE within 4 weeks (or within 12 weeks if significant thrombosis such as extensive PE/right heart strain, iliofemoral vein DVT)
- AF with CVA/TIA/embolism within 3 months, rheumatic mitral disease, or mitral stenosis or CHADs-Vasc score 7-8
- Non-AF cardiac embolism within 4 weeks
- Mitral or aortic valve replacement of high or medium thrombotic risk (see *Table 1* below for classifying risk of valves)
- Recurrent VTE whilst on anticoagulant (often elevated INR target such as 3-4 if recurrent event on warfarin)
- Severe thrombophilia such as antiphospholipid syndrome / Anti-thrombin deficiency / protein S/C deficiency

For patients at higher risk of thrombosis, including those specified by a consultant, consider prescribing bridging therapy with treatment dose LMWH (enoxaparin (Inhixa) recommended) – see *Table 2* and *3* - until INR within therapeutic range if **INR ≤1.7 (for target 2.5) or ≤1.9 (for target ≥ 3.0)**

Table 1: Risk stratification for mechanical prostheses:

Risk	Type of valve
Low	Carbomedics, Medtronic Hall, ATS, Medtronic Open-Pivot, ST Jude Medical, Sorin Bicarbon
Medium	Other bileaflet valves with insufficient data
High	Lillehei-Kaster, Omniscience, Starr-Edwards (ball-cage), Bjork-Shiley / tilting-disc valves

Patient related risk factors (if present raise the risk):

-Mitral/tricuspid value replacement; previous thromboembolism, AF; mitral stenosis (any degree); LVEF < 35%

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Table 2: Doses of enoxaparin (Inhixa) with CrCl >30ml/min

Standard dosing of enoxaparin (Inhixa) with CrCL ≥30ml/min: 1.5mg/kg OD SC	
Weight range	**Dose**
< 40kg	1.5mg/kg OD - Please discuss with haematology or the anticoagulation team if needed
>40-48kg	60mg OD
>48-60kg	80mg OD
>60-73kg	100mg OD
>73-88kg	120mg OD
>88-110kg	150mg OD
>110-125kg	180mg OD (i.e. 100mg + 80mg)
>125-150kg	1.5mg/kg as a split dose (dose divided BD and rounded to nearest syringe size. This may lead to asymmetric dosing)
>150kg	Please discuss with haematology or the anticoagulation team

** Please note that although the standard bridging dose for enoxaparin in patients with subtherapeutic INR is 1.5mg/kg OD some high-risk patients particularly those newly started on warfarin and discharged from secondary care may be given enoxaparin at a dose of 1mg/kg BD initially during the highest risk period until established on warfarin.*

Table 3: Doses of enoxaparin (Inhixa) if CrCl < 30ml/min

Dosing of enoxaparin (Inhixa) with CrCL <30ml/min: 1mg/kg OD		
Weight range	**Renal dose**	**Additional administration information**
< 45kg	1mg/kg OD – Please discuss with haematology or the anticoagulation team if needed	
>45-55kg	50mg OD	0.5ml from 60mg syringe
>55-65kg	60mg OD	-
>65-75kg	70mg OD	0.7ml from 80mg syringe
>75-85kg	80mg OD	-
>85-95kg	90mg OD	0.9ml from 100mg syringe
>95-105kg	100mg OD	-
>105-115kg	110mg OD	60mg + 0.5ml (i.e. 50mg) from a 60mg syringe
>115-125kg	120mg OD	-
>125-135kg	130mg OD	80mg + 0.5ml (i.e. 50mg) from a 60mg syringe
>135-145kg	140mg OD	80mg + 60mg
>145-155kg	150mg OD	-
>155kg	Discuss with haematology or the anticoagulation team	

There is a video for patients provided by the manufacturer to support injection technique available online here: [Patient Video_Techdow Pharma England Ltd]

References:

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