INTRODUCTION
Warfarin is a vitamin K epoxide reductase inhibitor that exerts its anticoagulant effect by preventing the activation of the vitamin K-dependent clotting factors II, VII, IX and X. The incidence of warfarin-related bleeding is approximately 5% per year and generally the risks tend to be greater when the INR increases to > 5 and especially when the result is > 8.

Factor II has a half-life of at least 48 hours hence the reason why it can take 72 hours for the INR to fall effectively after stopping warfarin. Vitamin K is a direct antagonist which can be used to lower the INR more rapidly:
- Intravenous - 6-12 hours
- Oral - 12 to 24 hours

MANAGEMENT OF OVER-ANTICOAGULATED PATIENTS IN PRIMARY CARE
Adult patients with high INR who are asymptomatic or with modest bruising only can be safely managed in primary care, particularly if cause of high INR is known i.e. anorexia, diarrhoea or drug-induced such as antibiotics.

Exclusion criteria
The following clinical criteria would exclude patients from management in primary care anticoagulation services:
- Significant bleeding - referred to the secondary care on call medical team at Dorset County Hospital Switchboard on 01305 251150
- Mechanical heart valve - refer to on-call medical team or Cardiologist via Dorset County Hospital Switchboard on 01305 251150
- Patients aged <18 years

The above exclusions are not exhaustive and clinical judgement should be applied in referring patients to secondary care specialist services appropriately.

GUIDELINES FOR MANAGEMENT OF HIGH INR

<table>
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<tr>
<th>INR &gt; 8.0</th>
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<tr>
<td>• Omit warfarin.</td>
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<td>• Repeat INR test to confirm result and if *Point of Care (POC) send a venous blood sample for a laboratory INR test.</td>
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<td>• Give oral Vitamin K (Konakion MM Paediatric™(phytomenadione 2mg in 0.2 mL)). **See instructions on page 2 for administration.</td>
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<td>• Advise patient to seek urgent medical attention if they develop significant spontaneous bruising or bleeding.</td>
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*NOTE - To avoid delay in treatment Vitamin K can be prescribed based on POC INR test (CoaguChek®) without waiting for a lab-based INR result. Vitamin K given in advance of a laboratory INR result should be noted on the blood test request.

Follow-up
- Repeat INR test after 1-3 days as clinically appropriate. This should ideally be a laboratory INR test if practical.
- Review the patient to assess why the INR was high e.g. interacting drugs, vomiting/diarrhoea.
- If repeat INR >8 give further oral 2 mg Vitamin K or seek specialist advice if clinically indicated e.g. signs of bleeding or bruising.
- Restart warfarin when INR <5.
- Reduce warfarin maintenance dose by 10-20%.
INR 4.5 – 7.9

- Omit warfarin
- Repeat INR test to confirm result.
- Advise patient to seek urgent medical attention if they develop significant spontaneous bruising or bleeding.

**Follow-up**
- Repeat INR test after 1-3 days as clinically appropriate. This should ideally be a laboratory INR test if practical.
- Review the patient to assess why the INR was high e.g. interacting drugs, vomiting/diarrhoea.
- Restart warfarin when INR <5
- Reduce warfarin maintenance dose by 10-20%

**Responsibility**

In general practice it is the GP’s responsibility to administer, or direct the administration of, the vitamin K to patients in this situation. Patient Group Directions (PGDs) should not be used. Vitamin K should not be prescribed on an FP10 prescription for this indication.

In the DHUFT anticoagulant service different arrangements, including PGDs, may apply.

**Vitamin K Administration**

Konakion MM Paediatric™ (phytomenadione 2mg in 0.2 mL) 0.2 mL ampoules should be used to manage high INRs. Although this product is licensed for several routes of administration this protocol refers to oral use, which is off-label in adolescents and adults. To administer Vitamin K (Konakion MM Paediatric™ 2mg in 0.2ml) orally:

- Check expiry date of ampoule and ensure the product is in date before use
- Break ampoule
- Using the oral dispenser withdraw the solution to the appropriate mark (2mg = 0.2ml);
- Hold dispenser in patient’s mouth (at the back of the tongue) and press plunger
- Offer patient a glass of water as the solution has a very bitter taste

All primary care anticoagulation services are required to maintain a stock of Vitamin K – (Konakion MM Paediatric™) and ensure that this stock is checked for expiry date and re-ordered on a regular basis, from an authorised supplier e.g. a community pharmacy using a signed order or from the GP’s regular wholesaler.

**Reference**


Primary Care Vitamin K Pathway

INR >8

Omit Warfarin
Repeat INR if POC and send venous blood sample for lab INR test

Give 2 mg Vitamin K by mouth (Konakion MM Paediatric™ 2mg in 0.2ml)

Arragne for post Vitamin K INR in 1-3 days (preferably lab-based test) as clinically appropriate and consider repeat oral Vitamin K 2mg if INR remains >8 or seek specialist advice if clinically indicated e.g. signs of bleeding/bruising

Review patient to assess cause of high INR e.g. drug interaction, vomiting/diarrhoea
Recommence Warfarin when INR <5 reducing the preceding dose by 10-20%

To avoid delay in treatment while waiting for a laboratory result, Vitamin K can be given based on a confirmed ‘Point of Care’ INR test obtained using CoaguCheck® machine.
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<tr>
<th>Approval date</th>
<th>April 2017, by Anticoagulant Working Group</th>
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<tbody>
<tr>
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<td>July 2017 by DMAG</td>
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<tr>
<td>Review date</td>
<td>April 2019 by Anticoagulant Working Group, or sooner in the light of new information or evidence</td>
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<tr>
<td>Contact for this policy</td>
<td>Dr Jason Mainwaring - Consultant Haematologist, Dorset Hospitals</td>
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<td>Ruth Doe - Program Lead, Cardiovascular, Dorset CCG</td>
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<td>Vanessa Sherwood - Senior Pharmacist Dorset CCG</td>
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<td>Adam Hocking - Lead Pharmacist Community Services</td>
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