GUIDELINES FOR MANAGEMENT OF BLEEDING AND EXCESSIVE ANTICOAGULATION WITH ORAL ANTICOAGULANTS

This guideline covers the management of patients being treated with
- Vitamin K antagonists (VKA):
  - Warfarin
  - Acenocoumarol
  - Phenindione
- Novel oral anticoagulants (NOACs):
  - Apixaban (see also Appendix I)
  - Rivaroxaban (see also Appendix II)
  - Dabigatran (see also Appendix III)

Management of paediatric patients should be in discussion with their named Consultant

INTERPRETATION OF THE COAGULATION SCREEN

Warfarin/Phenindione/Acenocoumarol
- Prolongs the PT significantly more than the APTT.
- PT/INR is used to monitor anticoagulation

Apixaban/Rivaroxaban/Dabigatran
- Prolongs PT more than the APTT
- Neither the PT nor the APTT can be used to monitor anticoagulation
- A normal PT makes therapeutic anticoagulation unlikely but cannot be fully excluded

GENERAL NON-PHARMACOLOGICAL MEASURES IN A BLEEDING PATIENT
- Stop the antithrombotic drug
- Document the timing and amount of the last drug dose and presence of pre-existing renal or hepatic impairment
- Assess the source of bleeding
- Request full blood count, prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen
  - concentration, creatinine concentration
- Correct haemodynamic compromise with intravenous fluids and red cell
- Transfusion
- Apply mechanical pressure if possible
- Use endoscopic, radiological or surgical measures if possible.

MAJOR/LIFE THREATENING (irrespective of INR):
- STOP THE DRUG
**Warfarin (or phenindione/acenocoumarol)**
- Give vitamin K 5mg IV.
- **Emergency anticoagulation reversal should be with prothrombin complex concentrate (PCC) – BERIPLEX** – refer to Beriplex Policy
- It is NOT mandatory to discuss use of Beriplex with the Haematology Consultant on call.

The dose is dependent on the INR and on the weight of the patient. The dose can be calculated from the table below.
The maximum dose is 5000 units.

<table>
<thead>
<tr>
<th>INR</th>
<th>Units/kg</th>
</tr>
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<tbody>
<tr>
<td>2.0 - 3.9</td>
<td>25 units/kg</td>
</tr>
<tr>
<td>4.0 - 6.0</td>
<td>35 units/kg</td>
</tr>
<tr>
<td>&gt; 6.0</td>
<td>50 units/kg</td>
</tr>
</tbody>
</table>

- Fresh Frozen Plasma (FFP) can be given (only if Beriplex unavailable)
- **Repeat INR should be done 30 minutes after giving Fresh frozen plasma or Beriplex.**

**Apixaban/Rivaroxaban/Dabigatran**
- There is NO SPECIFIC REVERSAL agent
- Consider IV tranexamic acid 1g bolus over 10 minutes and repeat if bleeding persists.
- Beriplex 50units/kg (maximum 5000 units)
  
  *(NB Recommendation for Beriplex is based on animal/ healthy volunteer/laboratory studies only)*

In the event of a major bleed, anticoagulation should not be restarted until the patient is haemodynamically stable and there is stabilisation of haemoglobin (Hb).

- **HEAD INJURY**
  - All patients on anticoagulants presenting to Accident and Emergency departments with head injury should have their INR measured as soon as possible.
  - A lower threshold for performing a head CT scan should be used for patients on anticoagulants
  - Patients on warfarin presenting with a strong suspicion of intracerebral bleed should have their anticoagulation reversed before the results of any investigations
  - In intracranial haemorrhage, anticoagulation should be restarted only after discussions with Neurosurgeons.
NON MAJOR BLEEDING

Local measures to control bleeding

Warfarin (or phenindione/acenocoumarol)

- If INR in therapeutic range – Warfarin should be temporarily discontinued. Clinician to investigate source of bleeding.
- If INR above therapeutic range – Vitamin K 1 to 3mg IV

Apixaban/Rivaroxaban/Dabigatran

- Delay next dose or discontinue as appropriate

Patients on warfarin, phenindione or acenocoumarol who are overanticoagulated based on a elevated INR

No bleeding – Treat according to INR:

<table>
<thead>
<tr>
<th>INR</th>
<th>MANAGEMENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.0 to 5.9 (if target 2.5) OR 4.0 to 5.9 (if target 3.5)</td>
<td>Decrease or discontinue warfarin temporarily.</td>
</tr>
<tr>
<td>6.0 to 8.0 (no bleeding)</td>
<td>Discontinue warfarin temporarily.</td>
</tr>
<tr>
<td>8.0 to 12.0 (no additional risk factors for bleeding*)</td>
<td>Stop warfarin</td>
</tr>
<tr>
<td></td>
<td>Give Konakion MM paediatric(vitamin K)** 1 to 2mg orally</td>
</tr>
<tr>
<td>8.0-12.0 (additional risk factors for bleeding*) &gt; 12.0</td>
<td>Give Konakion MM paediatric(vitamin K)** 2 to 5mg orally</td>
</tr>
</tbody>
</table>

* Additional risk factors include Elderly (>65yrs), previous GI or intracranial bleed, renal or liver failure, anaemia, cancer, recent stroke, recent surgery are at increased risk of bleeding

** Konakion MM can be given intravenously or orally but NOT intramuscularly.

REFERENCE

Guideline on the management of bleeding in patients on antithrombotic agents – British Committee for Standards in Haematology (BCSH) – 2012

Dr S Kaul, Consultant Haematologist / Lee Wilson, Consultant Pharmacist
Approved by Trust Drug and Therapeutics Committee: May 2015
Review Date: May 2017
Appendix 1: Guidelines For The Management Of Apixaban-Related Bleeding

- Apixaban is an oral direct factor Xa inhibitor
- Apixaban has a half-life of approximately 12 hours
- Apixaban is metabolised 25% renally and 75% hepatic
- There is NO SPECIFIC REVERSAL agent for apixaban

Apixaban-related bleeding

STOP Apixaban

- Assess clinical bleeding and resuscitate patient as appropriate
- Use local haemostatic measures to control bleeding
- Mechanical compression
- Consider surgical/radiological/endoscopic intervention or wound packing
Check: FBC, G&S, U&E and clotting screen for PT, APTT, TT and fibrinogen

Interpretation of Coagulation Screen

- PT or APTT cannot be used to determine the effect of apixaban

Minor Bleeding

Local measures
Delay next dose of apixaban or discontinue as appropriate

Moderate/Severe and Life-Threatening Bleeding

Discuss with Haematology

Fluid replacement to maintain good urine output
Blood support to keep:
- Hb > 8.0x10^9 g/dL
- Platelets > 80x10^9/L
- Fibrinogen > 1.0 g/L
PT/APTT may not be correct in the presence of apixaban with blood products
Consider IV tranexamic acid (1g bolus over 10 minutes and repeat bolus if bleeding persists

Repeat FBC and clotting screen after blood product replacement

For life-threatening bleeding consider:
- Beriplex 50 units/kg (maximum 5000 units)
(NB this recommendation is based on animal/healthy volunteer/laboratory studies only)
Appendix 2: Guidelines For Management Of Rivaroxaban-Related Bleeding

- Rivaroxaban is an oral direct factor Xa inhibitor
- Rivaroxaban has a plasma half-life of 7 to 9 hours
- Rivaroxaban is metabolised 25% renally and 75% hepatic
- There is NO SPECIFIC REVERSAL agent for rivaroxaban

**Rivaroxaban-related bleeding**

STOP Rivaroxaban

- Assess clinical bleeding and resuscitate patient as appropriate
- Use local haemostatic measures to control bleeding
- Mechanical compression
- Consider surgical/radiological/endoscopic intervention or wound packing

Check: FBC, G&S, U&E and clotting screen for PT, APTT, TT and fibrinogen

**Interpretation of Coagulation Screen**

- Rivaroxaban prolongs the PT more than the APTT
- Neither the PT or APTT can be used to monitor rivaroxaban anticoagulation
- Normal PT makes therapeutic anticoagulation unlikely but cannot be fully excluded

**Minor Bleeding**

Local measures

Delay next dose of rivaroxaban or discontinue as appropriate

**Moderate/Severe and Life-Threatening Bleeding**

Discuss with Haematology

 Fluid replacement to maintain good urine output
 Blood support to keep:
  - Hb > 8.0x10^9 g/dL
  - Platelets > 80x10^9/L
  - Fibrinogen > 1.0 g/L

PT/APTT may not be correct in the presence of rivaroxaban with blood products
Consider IV tranexamic acid (1g bolus over 10 minutes and repeat bolus if bleeding persists

Repeat FBC and clotting screen after blood product replacement

For life-threatening bleeding consider:
- Beriplex 50 units/kg (maximum 5000 units)
(NB this recommendation is based on animal/healthy volunteer/laboratory studies only)
Appendix 3: Guidelines For Management Of Dabigatran-Related Bleeding

- Dabigatran is a direct oral thrombin inhibitor with a plasma half-life of 12 to 18 hours
- Dabigatran is primarily renally excreted and the half-life is prolonged in renal impairment. Diuresis must be maintained to promote adequate drug clearance.
- There is no SPECIFIC REVERSAL agent for dabigatran

Dabigatran-related bleeding

STOP Dabigatran

- Assess clinical bleeding and resuscitate patient as appropriate
- Use local haemostatic measures to control bleeding
- Mechanical compression
- Consider surgical/radiological/endoscopic intervention or wound packing

Check: FBC, G&S, U&E and clotting screen for PT, APTT, TT and fibrinogen

Interpretation of Coagulation Screen

- Dabigatran prolongs the APTT more than the PT and markedly prolongs TT
- The PT, APTT and TT cannot be used to monitor dabigatran anticoagulation
- A normal APTT makes therapeutic anticoagulation unlikely
- A normal TT excludes the presence of dabigatran

Minor Bleeding

Local measures

Delay next dose of dabigatran or discontinue as appropriate

Repeat FBC and clotting screen after blood product replacement

Moderate/Severe and Life-Threatening Bleeding

Discuss with Haematology

Fluid replacement to maintain good urine output
Blood support to keep:
- Hb > 8.0x10^9 g/dL
- Platelets > 80x10^9/L
- Fibrinogen > 1.0 g/L

PT/APTT may not be correct in the presence of dabigatran with blood products
Consider IV tranexamic acid (1g bolus over 10 minutes and repeat bolus if bleeding persists

Repeat FBC and clotting screen after blood product replacement

For life-threatening bleeding consider:
- Beriplex 50 units/kg (maximum 5000 units)

(NB this recommendation is based on animal/healthy volunteer/laboratory studies only)