Adults with Haemophilia and Related Bleeding Disorders
Acute Treatment Guidelines

Adult Comprehensive Care Centres (CCC) Ireland

- The National Centre for Hereditary Coagulation Disorders (NCHCD),
  St. James’s Hospital, Dublin 8. Ph: 01 4162141
  [http://www.stjames.ie/Departments/DepartmentsAZ/N/NationalCentreforHereditaryCoagulationDisorders](http://www.stjames.ie/Departments/DepartmentsAZ/N/NationalCentreforHereditaryCoagulationDisorders)

- Cork Coagulation Centre, Cork University Hospital. Ph: 021 4922278
  [www.cuh.hse.ie](http://www.cuh.hse.ie)
<table>
<thead>
<tr>
<th>Document Owner</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position Title</td>
</tr>
<tr>
<td>Chair, NHC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reviewer(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position Title</td>
</tr>
<tr>
<td>Consultant Haematologist</td>
</tr>
<tr>
<td>Nurse Manager, NCHCD</td>
</tr>
<tr>
<td>Consultant Haematologist</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Approver(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Position Title</td>
</tr>
<tr>
<td>Chair, NHC</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dates</th>
</tr>
</thead>
<tbody>
<tr>
<td>29.01.15</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Version</th>
</tr>
</thead>
<tbody>
<tr>
<td>Version 1</td>
</tr>
</tbody>
</table>
Table of Contents

1.0 Introduction

2.0 Factor VIII Deficiency Management
   2.1 General Information
   2.2 Disease Severity
   2.3 Bleeding Episode Management
      Step 1- Patient Assessment
      Step 2- Communication to Comprehensive Care Centres (CCC)
      Step 3 - Treatment Selection & Administration
      Step 4 - Documentation / Records
      Step 5 - PRICE for Joint Bleeds
   2.4 Surgery Management
   2.5 Pregnancy Management

3.0 Factor IX Deficiency Management
   3.1 General Information
   3.2 Disease Severity
   3.3 Bleeding Episode Management
      Step 1- Patient Assessment
      Step 2- Communication to Comprehensive Care Centres (CCC)
      Step 3 - Treatment Selection & Administration
      Step 4 - Documentation / Records
      Step 5 - PRICE for Joint Bleeds
   3.4 Surgery Management
   3.5 Pregnancy Management

4.0 Von Willebrand Disease Management
   4.1 General Information
   4.2 Disease Severity
   4.3 Bleeding Episode Management
      Step 1- Patient Assessment
      Step 2- Communication to Comprehensive Care Centres (CCC)
      Step 3 - Treatment Selection & Administration
      Step 4 - Documentation / Records
      Step 5 - PRICE for Joint Bleeds
   4.4 Surgery Management
   4.5 Pregnancy Management

5.0 Platelet Function Disorders (PFDs) Management
   5.1 General Information
   5.2 Disease Severity
   5.3 Bleeding Episode Management
      Step 1- Patient Assessment
      Step 2- Communication to Comprehensive Care Centres (CCC)
Step 3 - Treatment Selection & Administration
Step 4 - Documentation / Records
Step 5 - PRICE for Joint Bleeds
5.4 Surgery Management
5.5 Pregnancy Management

6.0 Rare Bleeding Disorders (RBDs) Management
6.1 General Information
6.2 Disease Severity
6.3 Bleeding Episode Management
   Step 1- Patient Assessment
   Step 2- Communication to Comprehensive Care Centres (CCC)
   Step 3 - Treatment Selection & Administration
   Step 4 - Documentation / Records
   Step 5 - PRICE for Joint Bleeds
6.4 Surgery Management
6.5 Pregnancy Management

7.0 Appendices

   Appendix 1: Haemophilia Acute Pain Management

   Appendix 2: FVIII Deficiency - Clotting Factor Concentrate Dose Calculation Guide

   Appendix 3: FIX Deficiency - Clotting Factor Concentrate Dose Calculation Guide
1.0 Introduction

The National Haemophilia Council (NHC) was set up in response to the findings of the Lindsay Tribunal in 2001 and established as a statutory body in 2004 (S.I. No. 451 of 2004.) The principal function of the NHC is to provide advice, information, support and education on all aspects of haemophilia to the Health Minister, Health Service Agencies and Persons with or affected by haemophilia. Under this remit the Council works continuously to provide Clinicians with current and comprehensive evidence-based guidelines for the safe and effective management of persons with haemophilia and related bleeding disorders.

Haemophilia refers to inherited bleeding disorders caused by the absence or low level of specific proteins called clotting factors (specifically factor VIII or factor IX in the blood). Related bleeding disorders are caused by deficiencies in other clotting factors such as VWF or by abnormalities in blood platelets. The most common bleeding disorders are:

- Factor VIII Deficiency (Haemophilia A)
- Factor IX Deficiency (Haemophilia B)
- Von Willebrand Disease (VWD)
- Platelet Function Disorders (PFDs)
- Rare Bleeding Disorders (RBDS0 i.e. Inherited deficiencies of Factors I, II, V, VII, X, XI, XIII)

Due to the complexity of haemophilia and its treatment, care of persons with these bleeding disorders should be co-ordinated by a specialist centre known as a Comprehensive Care Centre (CCC).

The specialist multidisciplinary services and care that these centres provide have been shown to contribute significantly to improved outcomes and better quality of life for persons with bleeding disorders. The NHC recommends that all persons diagnosed with a bleeding disorder should be registered with and monitored by one of the designated CCCs in Ireland, which are:

- The National Centre for Hereditary Coagulation Disorders (NCHCD), St. James’s Hospital, Dublin 8
- Cork Coagulation Centre, Cork University Hospital.
- Paediatric CCC - Our Lady’s Children’s Hospital Crumlin (OLCHC), Dublin 12 – All persons <16 years

However, the NHC recognises that on occasion persons with haemophilia may present to a non-specialist service requiring treatment and/or intervention e.g. with a bleed. In these circumstances non-specialist clinicians are required to assess the patients and initiate management in collaboration with the patient’s CCC. Accordingly, the NHC has commissioned these guidelines to assist healthcare professionals in the immediate management of adult persons with haemophilia. The information is presented in condition-specific chapters in which the following information is included:

- General Information
- Disease Severity
- Bleed / Suspected Bleed Management
- Surgery / Interventional Procedure Management (Elective and/or Emergency)
Pregnancy Management
- General Pregnancy
- Labour
- Infant

Key Statements

- Acute treatment of all persons with an inherited bleeding disorder should be co-ordinated by the CCC with which the patient is registered.

- In the event a person with a diagnosis of haemophilia or related bleeding disorder presents to a hospital requiring assessment and/or treatment and/or intervention the treating Clinician should:
  - Contact the CCC (the patient should have a registration card detailing their diagnosis and CCC)
  - Confirm the bleeding disorder diagnosis, factor level and treatment of choice with the CCC
  - Agree a management and follow up plan with the CCC.

- Prescribers must ensure that they prescribe the correct clotting factor concentrate e.g. Advate for FVIII deficiency and Benefix for FIX deficiency.

  The Prescriber must note that not all patients with mild FVIII or FIX deficiency require clotting factor concentrate as the use of alternative treatments may be indicated e.g. DDAVP (some types of FVIII deficiency only) or Tranexamic Acid. The patient’s treatment of choice must be confirmed with the relevant CCC.

- These guidelines should be used in the management of persons with bleeding disorders as an adjunct to advice received from the CCC.

- Persons under the age of 16 years (Children) should be treated in accordance with paediatric guidelines.

Scope

These Guidelines apply to:
- Adults with Inherited Bleeding Disorders including the following:
  - Factor VIII Deficiency (Haemophilia A)
  - Factor IX Deficiency (Haemophilia B)
  - Von Willebrand Disease
  - Rare bleeding disorders (inherited deficiencies of factors I (Fibrinogen), II, V, VII, X, XI, XIII)
  - Inherited disorders of Platelet function

- Immediate treatment / intervention in non-specialist centres.
Definitions / Glossary

Throughout this document the following abbreviations / acronyms are used:

- **VWD** = Von Willebrand Disease
- **VWF** = Von Willebrand Factor
- **CCC** = Comprehensive Care Centre
- **CFC** = Coagulation Factor Concentrates
1.0: Factor VIII Deficiency (Haemophilia A)

1.1 General Information

Factor VIII deficiency (Haemophilia A) is a bleeding disorder caused by a deficiency of clotting factor VIII. This condition affects 1 in 5,000 male live births and is five times more common than Factor IX deficiency (Haemophilia B). Female carriers of Haemophilia may have low FVIII levels and one third have levels similar to mild Haemophilia i.e. 5-40% (0.05-0.40 IU/ml). These affected females may also need treatment for bleeding, menorrhagia, prior to surgery or labour and delivery.

1.2 Disease Severity

Disease severity relates to the baseline level of factor VIII.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Factor VIII Activity Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe disease</td>
<td>&lt;1% (&lt;0.01 IU/ml)</td>
</tr>
<tr>
<td>Moderate disease</td>
<td>1–5% (0.01-0.05 IU/ml)</td>
</tr>
<tr>
<td>Mild disease</td>
<td>&gt;5% (&gt;0.05 IU/ml)</td>
</tr>
</tbody>
</table>

Table 1.0: Factor VIII Disease Severity Categories

1.3 Bleeding Episode Management

In the event a person with FVIII Deficiency presents with a bleed / potential bleed the Clinician should take the following steps:

Step 1: Patient Assessment

- Perform initial evaluation and assessment.
- Identify the site of the suspected bleed.
- Assess for compression of vital structures e.g. airway, nerves or blood vessels, and manage accordingly.
- Undertake pain assessment and treat accordingly- Refer to Pain Management Guidelines (Appendix 1).
- Where possible, obtain details from patient or relative regarding bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice.
- Check patient registration card.
- Weigh the patient or estimate weight where necessary.
- Undertake initial blood testing to include: FBC, Biochemistry, Group and Cross-match, Coagulation and Factor Levels.
- Arrange appropriate imaging but **DO NOT DELAY** haemostatic treatment if a bleed is suspected. Treat first, image after.
- If in doubt manage as a bleed, but consider alternative diagnosis and investigate accordingly.
Step 2: Communication to CCC

- Contact the patient’s CCC **IMMEDIATELY** following the initial assessment
- Confirm the patient’s bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Agree a management plan and follow up with the CCC

Step 3: Treatment Administration

- Prescribers must ensure that they prescribe the correct clotting factor concentrate e.g. Advate for FVIII deficiency
- The Prescriber must note that not all patients with mild FVIII deficiency require clotting factor concentrate and the use of alternative treatments may be indicated e.g. DDAVP or Tranexamic Acid
- The patient’s treatment of choice must be confirmed with the relevant CCC.

- The Clinician should establish the treatment of choice i.e. Advate, DDAVP®/Desmopressin Injection and/or Tranexamic Acid.

- The selected treatment should be prepared and administered as follows:

  **Clotting Factor Concentrate – Advate**

  - Advate is the factor used in the treatment and prophylaxis of bleeding in patients with congenital factor VIII deficiency.
  - Advate comes as a powder and solvent that must be reconstituted for solution
  - Can be administered as a bolus infusion or as a continuous infusion
  - The required dose must be determined by calculating the patients weight and the required post treatment factor level which is determined by the severity and location of the bleed (See Appendix 2: FVIII Deficiency - Clotting Factor Concentrate Dose Calculation Guide).
  - Advate must be reconstituted for use using an aseptic technique (Refer to Factor Reconstitution Procedure - Appendix 3)

  **Administration**

  - Factor concentrate should be administered as a slow intravenous push over 5 minutes
  - A post treatment factor level should be drawn 20 minutes post administration (two coagulation samples, send to local laboratory for forwarding to the CCC for analysis)
  - Liaise with CCC regarding the post treatment level result in case further treatment is required.
Reactions

In the event of a reaction or suspected reaction the Clinician should undertake the following:

- Discontinue the Factor Concentrate
- Assess the patient
- Contact the relevant CCC for advice on alternative treatments.

In the event of **mild to moderate reaction** the Clinician should undertake the following:

- Administer Chlorpheniramine 10-20 mg IM or slow IV (at least over one minute)
- If required, add Hydrocortisone 100 - 200mg slow IV (over three minutes)

In the event of **severe allergic or anaphylactic reaction** local hospital resuscitation / response protocols should be followed. The use of the following medications is recommended:

- Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500 micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
- Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given.
- Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir
- Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).

**DDAVP®/Desmopressin Injection**

- DDAVP® Injection (Desmopressin Acetate) is a synthetic analogue of the natural hormone arginine vasopressin. It is indicated for use in managing bleeds in some persons with Factor VIII deficiency and Von Willebrand disease/Low VWF by increasing plasma levels of FVIII and VWF.

- DDAVP use should be avoided in the following circumstances:
  - Persons over 55 years of age
  - Persons with a history of heart failure or other conditions being treated with diuretic agents
  - Persons with known atherosclerosis or ischaemic heart disease

- DDAVP should be used with caution in the following circumstances:
  - Persons with risk factors for ischaemic heart disease
  - Pregnant persons
  - Children less than two years of age (Refer to Paediatric Guidelines)

**Dose Calculation**

- DDAVP is administered intravenously at a dose of 0.3 micrograms/kg
- The maximum total dose recommended for any patient is 27 micrograms
- Example: A 60kg patient requiring DDAVP, the dose should be calculated as 60 kg x 0.3 micrograms = 18 micrograms.
**Dose Administration**

- DDAVP comes in 1ml ampoule which contains Desmopressin acetate 4 micrograms per ml in a sterile, aqueous solution for injection
- DDVAP should be added to 100mls of normal saline using an aseptic technique
- The 100ml solution should be administered intravenously over 30-60 minutes
- The patient’s serum sodium (Na) level should be >135 mmol/L prior to administration
- Blood pressure must be monitored before, during and after the infusion
- The patients must be maintained on a fluid restriction of 1.5 L/24 hours following the infusion
- Post treatment blood levels should be taken and reviewed 30 minutes following the infusion
- **Example:** A 60kg patient requiring DDAVP - The intravenous preparation has a concentration of 4 micrograms /ml. Therefore, the intravenous dose for a 60kg patient (18 micrograms) will be prepared by diluting 4.5mls of DDAVP in 100mls of normal saline and this will be administered IV over 30-60 minutes.

**Reactions to DDAVP**

- Reactions to DDAVP can be common

  - **Mild reactions** commonly include the following:
    - Vasodilatation
    - Hypotension
    - Facial flushing
  
  Mild reactions should be treated by slowing the intravenous infusion so that it is administered over 60 minutes.

  - **Moderate reactions** should be treated as follows:
    - Discontinue DDAVP
    - Assess the patient
    - Administer Chlorpheniramine 10-20 mg IM or slow IV (over one minute)
    - If required, add Hydrocortisone 100 - 200 mg IM or slow IV (over three minutes)
    - If required, add Oxygen (10-12 litre/min) +/- inhaled Salbutamol (2.5mg)
    - The DDAVP infusion can be restarted at a slower rate with close monitoring of the patient
    - In the event a reaction recurs, the infusion should be stopped and the clinician should contact the relevant CCC for advice on alternative treatments.
- **Severe allergic reactions** should be treated in accordance with local resuscitation / response protocols. The use of the following medications is recommended:

  - Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
  - Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given as above.
  - Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir.
  - Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).
  - The clinician should contact the relevant CCC for advice on alternative treatments.

- **Tranexamic Acid (Cyclokapron)**

  - Tranexamic Acid is an antifibrinolytic agent indicated in patients with haemophilia for short-term use (two to eight days) to reduce or prevent haemorrhage
  - Tranexamic Acid is available in tablet and Intravenous Injection form

  - **Oral / Tablet form** (500 mg Tranexamic Acid)
    - Recommended dose 15-25 mg/kg TDS or QDS (usually 1g TDS or QDS)

  - **Intravenous** Injection (500mg in 5ml ampoule)
    - Recommended dose 10 mg/kg TDS
    - Bolus injection – The required dose can be administered undiluted slowly i.e. at a rate of 100mg/min
    - Intravenous Infusion – The required dose can be diluted in 100mls normal saline and given as an infusion over 30 minutes.

- **Contraindications/Cautions**

  Should not be used in the following circumstances
  - Patients with a history of thromboembolic disease
  - Patient with Disseminated Intravascular Coagulation (DIC)
  - Persons with bleeding from the upper urinary tract (risk of ureteric clot colic and obstruction)

  Caution should be used when administering Tranexamic acid to patients receiving FEIBA or recombinant factor VIIIa (risk of thrombosis).

- **Adverse effects**
  - Nausea, vomiting, and diarrhoea
  - Rapid intravenous injection may cause dizziness and hypotension (do not administer faster than 100 mg/min).
**Step 4: Documentation**

- In addition to routine prescribing and recording, the dose and batch number of all Factor Concentrates administered must be recorded in the patient’s medical notes and as per local hospital/laboratory policy.

**Step 5: Initiate ‘PRICE’ for all Joint Bleeds**

- **Protection:** Reduce weight bearing or stress on the affected joint or muscle by providing crutches or other supports such as a 'collar and cuff' for the arm. Avoid putting weight on the affected side completely for the first 48 hours; and possibly longer if it is a severe bleed.

- **Rest:** The affected arm or leg should be gently placed on a pillow or in a sling or bandage. The individual should not move the bleeding joint.

- **Ice:** Wrap an ice pack in a damp towel and place over bleed. After 5 minutes, remove ice for 10 minutes. Repeat this step for as long as the joint feels hot. This may help decrease pain and bleeding.

- **Compression:** Gentle pressure from a tensor bandage (e.g. Tubigrip, size appropriate for the patient’s limb) can help to limit bleeding and support the joint. Use compression carefully with muscle bleeds if a nerve injury is suspected.

- **Elevation:** Raise the affected area above the heart. This may slow blood loss by lowering pressure in the area of the bleed.

- Ensure that the patient is referred to a physiotherapist for assessment and treatment.

**1.4 Surgery Management**

- Patients with bleeding disorders should ideally have surgery in a hospital where there is a Haemophilia Comprehensive Care Centre and haemostatic management should be supervised by the CCC Team

- In rare circumstances surgery may need to be performed in a hospital without a CCC, such as in emergencies or where the person needs to avail of specialist surgical services.

- In these circumstances, haemostatic management must be determined by the patient’s CCC and it is recommended that the local Haematology service provides on-site consultation.
In the event a person with FVIII Deficiency is undergoing surgery in a non-specialist CCC the Clinical staff should ensure the following steps are undertaken:

Pre-Operative

- Confirm the patient’s known bleeding diagnosis, baseline levels, inhibitor status and treatment of choice with the patient and the relevant CCC.
- Confirm the patient’s virology (i.e. Hepatitis A, B, C and HIV) and TSE at-risk status with the CCC.
- Obtain a written management plan from the CCC
- Liaise with local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate
- Ensure a ‘No NSAIDS, No Aspirin, No Heparin and No IM injections’ note is communicated and recorded clearly in the drug idiosyncrasies section of the patient’s prescription form, the front cover of their medical chart and in all other relevant healthcare records e.g. Nursing Care Plans etc.
- Ensure that the local Anaesthetic Department / Team are informed that epidural and spinal anaesthesia are contra-indicated in patients with bleeding disorders. This must be clearly documented in the patient’s healthcare record.

Post-Operative

- Liaise with the relevant CCC to determine the requirement for ongoing haemostatic treatment and factor levels.
- Ensure that the patient is provided with adequate haemostatic cover for all invasive procedures e.g. placement of central lines or removal of sutures, clips, drains etc. As these procedures are likely to occur some days after the surgery the patient’s CCC should be contacted to advise regarding additional treatment requirements.

1.5 Pregnancy Management

- Women who are carriers of FVIII deficiency should have an individual management plan for labour and delivery determined collaboratively by the woman, her CCC and the woman’s Obstetrician. This plan should be made available to the patient, the woman’s Obstetrical Department / Provider, the local Haematologist and the woman’s GP.
- It is recommended to determine foetal sex by ultrasound from 18 weeks onwards. The CCC should be informed of the sex of the foetus
- Significant proportions of carriers for FVIII deficiency have low levels of FVIII and may need haemostatic treatment peripartum. This will be determined by the woman’s CCC.
• The woman’s Obstetrical Department / Provider should liaise with their local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate, if indicated.

Maternal Labour, Delivery and Postpartum Period Management

Patients with FVIII levels of <0.5 IU/ml (<50%) will require treatment at the time of delivery to maintain levels >0.50 IU/ml (>50%). The CCC should be contacted to advise on the appropriate treatment, dose and required blood testing

- **Epidural Anaesthesia**
  - The use of Epidural Anaesthesia is contra-indicated in patients with FVIII levels <0.50 IU/ml (<50%) in the third trimester.
  - Patients with confirmed normal FVIII levels in the third trimester may receive epidural anaesthesia if required.

- **Analgesia**
  - The use of Intramuscular injections e.g. Pethidine are contra-indicated in women with low FVIII levels.
  - Alternative analgesia such as inhaled nitrous oxide and oxygen or intravenous Remifentanil is acceptable for patients with low FVIII levels.
  - For women with low FVIII levels, appropriate options for analgesia MUST be discussed with the local Maternity unit Anaesthetic service in advance.

- **Post Partum Management**
  - Normal factor levels should be maintained for 3 days following vaginal delivery and for 5 days after caesarean section.
  - In the event the patient has received haemostatic treatment to cover the delivery, it will be necessary to send factor levels daily for 3 days following vaginal delivery and for 5 days following caesarean section.
  - Postpartum, factor VIII levels can fall quickly in women who have low baseline levels but who have had a pregnancy-induced rise in levels and therefore have not needed treatment for labour.
  - If a patient with FVIII deficiency has excessive bleeding post-partum, factor levels should be sent and advice obtained from the CCC in addition to usual obstetrical management.
  - Delayed post-partum haemorrhage is a feature of inherited bleeding disorders and affected women should be provided with emergency contact numbers for their CCC and Obstetric Unit / Provider following discharge.
• **Management of the infant During Labour and Delivery**

- Ultrasound should be performed to determine sex and position.
- There should be a low threshold for caesarean section.
- Foetal scalp sampling and electrodes should be avoided.
- The use of ventouse and/or mid-cavity forceps is contraindicated due to the increased risk of intracranial haemorrhage.
- Lift out forceps can be performed if deemed necessary by a Consultant Obstetrician.
- If delivery is instrumental, then an urgent cranial ultrasound and factor VIII measurement of cord blood should be obtained.
- Factor VIII should be administered to the child in the presence of severe deficiency being detected if the delivery is instrumental and after liaison with the Paediatric CCC in Our Lady’s Children’s Hospital, Crumlin or Cork University hospital.
- Factor VIII levels should be measured from a cord blood sample from all potentially affected infants. The cord blood sample should be sent in a 2.5 mls citrate tube via the local laboratory to the laboratory at Our Lady’s Hospital, Crumlin or Cork University hospital. The sex of the baby and specific factor deficiency should be clearly documented on the laboratory request form.
- In the event the child was delivered using a ventouse or forceps delivery the factor level analysis should be undertaken as an emergency. The receiving laboratory must be informed that the factor level is required urgently.
- The use of intramuscular injections should be avoided.
- Vitamin K should be administered by the oral and not the intramuscular route.
- The Bacillus Calmette-Guérin (BCG) vaccine can be administered without haemostatic support.
- A Heel-Prick test can be undertaken for Guthrie card analysis without haemostatic support.
- In the event the factor level is found to be reduced, the child should be referred to the Paediatric Haematologist on–call at Our Lady’s Children’s Hospital, Crumlin or Cork University Hospital.
2.0: Factor IX Deficiency (Haemophilia B)

2.1 General Information

Factor IX deficiency (Haemophilia B) is a bleeding disorder caused by a deficiency of clotting factor IX. This condition affects around 1 in 25,000 to 30,000 males (about 5 times rarer than haemophilia A). Female carriers of Haemophilia may have low FIX levels and one third have levels similar to mild Haemophilia i.e. 5-40% (0.05-0.40 IU/ml). These affected females may also need treatment for bleeding, menorrhagia or prior to surgery or labour and delivery.

2.2 Disease Severity

Disease severity relates to the baseline level of factor IX.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Factor IX Activity Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe disease</td>
<td>&lt;1% (&lt;0.01 IU/ml)</td>
</tr>
<tr>
<td>Moderate disease</td>
<td>1–5% (0.01-0.05 IU/ml)</td>
</tr>
<tr>
<td>Mild disease</td>
<td>&gt;5% (&gt;0.05 IU/ml)</td>
</tr>
</tbody>
</table>

Table 2.0: Factor IX Disease Severity Categories

2.3 Bleeding Episode Management

In the event a person with FIX Deficiency presents with a bleed / potential bleed the Clinician should take the following steps:

Step 1: Patient Assessment

- Perform initial evaluation and assessment.
- Identify the site of the suspected bleed.
- Assess for compression of vital structures e.g. airway, nerves or blood vessels, and manage accordingly.
- Undertake pain assessment and treat accordingly- Refer to Pain Management Guidelines (See Appendix 1)
- Where possible, obtain details from patient or relative regarding bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice.
- Check patient registration card.
- Weigh the patient or estimate weight where necessary.
- Undertake initial blood testing to include: FBC, Biochemistry, Group and Cross-match, Coagulation and Factor Levels.
- Arrange appropriate imaging but DO NOT DELAY haemostatic treatment if a bleed is suspected. Treat first, image after.
- If in doubt manage as a bleed, but consider alternative diagnosis and investigate accordingly.
Step 2: Communication to CCC

- Contact the patient’s CCC IMMEDIATELY following the initial assessment
- Confirm the patient’s bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Agree a management plan and follow up with the CCC

Step 3: Treatment Administration

- Prescribers must ensure that they prescribe the correct clotting factor concentrate e.g. i.e. BeneFIX for FIX deficiency
- In doing so the Prescriber must note that not all patients with mild FIX deficiency require clotting factor concentrate and the use of alternative treatments may be indicated e.g. Tranexamic Acid
- The patient’s treatment of choice must be confirmed with the relevant CCC.

- The Clinician should establish the treatment of choice i.e. BeneFIX, and/or Tranexamic Acid.
- The selected treatment should be prepared and administered as follows:

Clotting Factor Concentrate – BeneFIX

- BeneFIX is the clotting factor concentrate used as the first line treatment and prophylaxis of bleeding in patients with FIX deficiency.
- BeneFIX comes as a powder with an accompanying solvent of sodium chloride solution
- Can be administered as a bolus infusion or as a continuous infusion
- The required dose must be determined by calculating the patient’s weight and the required post treatment factor level that is determined by the severity and location of the bleed and the patient’s clinical condition (See Appendix 3: FIX Deficiency - Clotting Factor Concentrate Dose Calculation Guide).
- BeneFIX must be reconstituted for use using an aseptic technique.

Administration

- BeneFIX should be administered as a slow intravenous push over 5 minutes
- A sample for post treatment factor level should be drawn 20 minutes post administration (two coagulation samples, send to local laboratory for forwarding to the CCC for analysis)
- Liaise with CCC regarding the post treatment level result in case further treatment is required
Reactions

In the event of a reaction or suspected reaction the Clinician should undertake the following:
- Discontinue the Factor Concentrate
- Assess the patient
- Contact the relevant CCC for advice on alternative treatments.

In the event of **mild to moderate reaction** the Clinician should undertake the following:
- Administer Chlorpheniramine 10-20 mg IM or slow IV (at least over one minute)
- If required, add Hydrocortisone 100 - 200mg slow IV (over three minutes)

In the event of **severe allergic or anaphylactic reaction** local hospital resuscitation / response protocols should be followed. The use of the following medications is recommended:
- Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500 micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
- Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given.
- Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir
- Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).

Tranexamic Acid (Cyclokapron)

- Tranexamic Acid is an antifibrinolytic agent indicated in patients with haemophilia for short-term use (two to eight days) to reduce or prevent haemorrhage
- Tranexamic acid should not be used in combination with either FEIBA or Factor XI Concentrate (risk of thrombosis).
- Tranexamic Acid is available in tablet and Intravenous Injection form
- Oral / Tablet form (500 mg Tranexamic Acid)
  - Recommended dose 15-25 mg/kg TDS or QDS (usually 1g TDS or QDS)
- Intravenous Injection (500mg in 5ml ampoule)
  - Recommended dose 10 mg/kg TDS
  - Bolus injection – The required dose can be administered undiluted slowly i.e. at a rate of 100mg/min
  - Intravenous Infusion – The required dose can be diluted in 100mls normal saline and given as an infusion over 30 minutes.

- **Contraindications/Cautions**
  Should not be used in the following circumstances
  - Patients with a history of thromboembolic disease
  - Patient with Disseminated Intravascular Coagulation (DIC)
  - Persons with bleeding from the upper urinary tract (risk of ureteric clot colic and obstruction)

- **Caution should be used when administering Tranexamic acid to patients receiving FEIBA or recombinant factor VIIa (risk of thrombosis)**
- **Adverse effects**
  - Nausea, vomiting, and diarrhoea
  - Rapid intravenous injection may cause dizziness and hypotension (do not administer faster than 100 mg/min).

### Step 4: Documentation

- In addition to routine prescribing and recording, the dose and batch number of all Factor Concentrates administered must be recorded in the patient’s medical notes and as per local hospital/laboratory policy.

### Step 5: Initiate ‘PRICE’ for all Joint Bleeds

- **Protection**: Reduce weight bearing or stress on the affected joint or muscle by providing crutches or other supports such as a ‘collar and cuff’ for the arm. Avoid putting weight on the affected side completely for the first 48 hours; and possibly longer if it is a severe bleed.

- **Rest**: The affected arm or leg should be gently placed on a pillow or in a sling or bandage. The individual should not move the bleeding joint.

- **Ice**: Wrap an ice pack in a damp towel and place over bleed. After 5 minutes, remove ice for 10 minutes. Repeat this step for as long as the joint feels hot. This may help decrease pain and bleeding.

- **Compression**: Gentle pressure from a tensor bandage (e.g. Tubigrip, size appropriate for the patient’s limb) can help to limit bleeding and support the joint. Use compression carefully with muscle bleeds if a nerve injury is suspected.

- **Elevation**: Raise the affected area above the heart. This may slow blood loss by lowering pressure in the area of the bleed.

- **Ensure that the patient is referred to a physiotherapist for assessment and treatment.**

### 2.4 Surgery Management

- Patients with bleeding disorders should ideally have surgery in a hospital where there is a Haemophilia Comprehensive Care Centre and haemostatic management should be supervised by the CCC Team

- In rare circumstances surgery may need to be performed in a hospital without a CCC, such as in emergencies or where the person needs to avail of specialist surgical services.

- In these circumstances, haemostatic management must be determined by the patient’s CCC and it is recommended that the local Haematology service provides on-site consultation.
In the event a person with FIX Deficiency is undergoing surgery in a non-specialist CCC the Clinical staff should ensure the following steps are undertaken:

**Pre-Operative**

- Confirm the patient’s known bleeding diagnosis, baseline levels, inhibitor status and treatment of choice with the patient and the relevant CCC.
- Confirm the patient’s virology (i.e. Hepatitis A, B, C and HIV) and TSE at-risk status with the CCC.
- Obtain a written management plan from the CCC
- Liaise with local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate
- Ensure a ‘No NSAIDS, No Aspirin, No Heparin and No IM injections’ note is communicated and recorded clearly in the drug idiosyncrasies section of the patient’s prescription form, the front cover of their medical chart and in all other relevant healthcare records e.g. Nursing Care Plans etc.
- Ensure that the local Anaesthetic Department / Team are informed that epidural and spinal anaesthesia are contra-indicated in patients with bleeding disorders. This must be clearly documented in the patient’s healthcare record.

**Post-Operative**

- Liaise with the relevant CCC to determine the requirement for ongoing haemostatic treatment and factor levels.
- Ensure that the patient is provided with adequate haemostatic cover for all invasive procedures e.g. placement of central lines or removal of sutures, clips, drains etc. As these procedures are likely to occur some days after the surgery the patient’s CCC should be contacted to advise regarding additional treatment requirements.

### 2.5 Pregnancy Management

- Women who are carriers of FIX deficiency should have an individual management plan for labour and delivery determined collaboratively by the woman, her CCC and the woman’s Obstetrician. This plan should be made available to the patient, the woman’s Obstetrical Department / Provider, the local Haematologist and the woman’s GP.

- It is recommended to determine foetal sex by ultrasound from 18 weeks onwards. The CCC should be informed of the sex of the foetus.

- Significant proportions of carriers for FIX deficiency have low levels of FIX and may need haemostatic treatment peripartum. This will be determined by the woman’s CCC.

- The woman’s Obstetrical Department / Provider should liaise with their local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate, if indicated.
Maternal Labour, Delivery and Postpartum Period Management

- Patients with FIX levels of <0.5 IU/ml (<50%) will require treatment at the time of delivery to maintain levels >0.50 IU/ml (>50%). The CCC should be contacted to advise on the appropriate treatment, dose and required blood testing.

Epidural Anaesthesia

- The use of Epidural Anaesthesia is contra-indicated in patients with FIX levels <0.50 IU/ml (<50%) in the third trimester.
- Patients with confirmed normal FIX levels in the third trimester may receive epidural anaesthesia if required.

Analgesia

- The use of Intramuscular injections e.g. Pethidine are contra-indicated in women with low FIX levels.
- Alternative analgesia such as inhaled nitrous oxide and oxygen or intravenous Remifentanil is acceptable for patients with low FVIII or FIX levels.
- For women with low FIX levels, appropriate options for analgesia MUST be discussed with the local Maternity unit Anaesthetic service in advance.

Post partum Management

- Normal factor levels should be maintained for 3 days following vaginal delivery and for 5 days after caesarean section.
- In the event the patient has received haemostatic treatment to cover the delivery, it will be necessary to send factor levels daily for 3 days following vaginal delivery and for 5 days following caesarean section.
- Postpartum, factor IX levels can fall quickly in women who have low baseline levels but who have had a pregnancy-induced rise in levels and therefore have not needed treatment for labour.
- If a patient with FIX deficiency has excessive bleeding post-partum, factor levels should be sent and advice obtained from the CCC in addition to usual obstetrical management.
- Delayed post-partum haemorrhage is a feature of inherited bleeding disorders and affected women should be provided with emergency contact numbers for their CCC and Obstetric Unit / Provider following discharge.

Management of the infant During Labour and Delivery

- Ultrasound should be performed to determine sex and position.
- There should be a low threshold for caesarean section.
- Foetal scalp sampling and electrodes should be avoided.
o The use of ventouse and/or mid-cavity forceps is contraindicated due to the increased risk of intracranial haemorrhage.

o Lift out forceps can be performed if deemed necessary by a Consultant Obstetrician.

o If delivery is instrumental, then an urgent cranial ultrasound and factor VIII measurement of cord blood should be obtained.

o Factor IX should be administered to the child in the presence of severe deficiency being detected if the delivery is instrumental and after liaison with the Paediatric CCC in Our Lady’s Children’s Hospital, Crumlin.

o Factor IX levels should be measured from a cord blood sample from all potentially affected infants. The cord blood sample should be sent in a 2.5 mls citrate tube via the local laboratory to the laboratory at Our Lady’s Hospital, Crumlin. The sex of the baby and specific factor deficiency should be clearly documented on the laboratory request form.

o In the event the child was delivered using a ventouse or forceps delivery the factor level analysis should be undertaken as an emergency. The receiving laboratory must be informed that the factor level is required urgently.

o The use of intramuscular injections should be avoided.

o Vitamin K should be administered by the oral and not the intramuscular route.

o The Bacillus Calmette-Guérin (BCG) vaccine can be administered without haemostatic support.

o A Heel-Prick test can be undertaken for Guthrie card analysis without haemostatic support.

o In the event the factor level is found to be reduced, the child should be referred to the Paediatric Haematologist on-call at Our Lady’s Children’s Hospital, Crumlin or Cork University Hospital.
3.0: Von Willebrand Disease (VWD)

3.1 General Information

Von Willebrand Disease (VWD) is a bleeding disorder resulting from deficiency or abnormal function of Von Willebrand Factor (VWF). VWF is a multimeric glycoprotein gene which has two main functions:

- To assist in platelet plug formation by binding circulating platelets to the site of vessel damage
- To bind to coagulation factor VIII preventing its clearance from the plasma

Disease Classification

VWD is subdivided into three types determined by the nature of the mutations in the VWF gene. The 3 types are as follows:

- **Type 1 VWD**: Persons who have true Type 1 have levels of VWF antigen and/or activity of <0.3 IU/ml (level is measured by the Ricof or collagen binding (CBA) assays). FVIII may also be low.

- **Type 2 VWD** is further subdivided into types 2A, 2B, 2M, 2N.
  - Type 2 VWD is characterised by abnormal function of the VWF protein and the Ricof or CBA assays are lower than the VWF antigen in types 2A, 2B and 2M.
  - In Type 2N VWD, the functional abnormality involves the binding of VWF to FVIII and the FVIII is low but the VWF levels may not be low.

- **Type 3 VWD**: Persons with Type 3 have very low levels of VWF and FVIII and have the most severe bleeding phenotype which is akin to severe haemophilia.

In addition the following subcategories are recognised

- **Low VWF**: This relates to persons who have low VWF levels between 0.3 and 0.5 IU/ml. The low levels are not caused by mutations in the gene for VWF but are reduced in a number of ways including for example by faster clearance of the VWF protein from the blood as happens in people who are blood group O.
  - Some people with low VWF levels have bleeding symptoms and may need to have preventative treatment if they are having surgery or other invasive procedures.

- **Platelet-type VWD** is a rare condition caused by a mutation in the glycoprotein on the surface of platelets which interacts with VWF.
3.2 Disease Severity

The disease severity relates to the VWF level and activity. The severity and associated presentation are described in Table 3.0 below.

<table>
<thead>
<tr>
<th>VWF antigen and /or activity</th>
<th>Clinical bleeding phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low VWF</td>
<td></td>
</tr>
<tr>
<td>0.3-0.5 IU/ml</td>
<td>Some patients may bleed with invasive procedures, or have menorrhagia or mucocutaneous bleeding</td>
</tr>
<tr>
<td>Type 1</td>
<td></td>
</tr>
<tr>
<td>&lt;0.3 IU/ml</td>
<td>Bleeding after invasive dental or surgical procedures, menorrhagia, mucocutaneous bleeding</td>
</tr>
<tr>
<td>Type 2</td>
<td></td>
</tr>
<tr>
<td>&lt;0.3 IU/ml (Ricof or CBA)</td>
<td>Variable bleeding tendency.</td>
</tr>
<tr>
<td>Ratio of activity to antigen</td>
<td></td>
</tr>
<tr>
<td>&lt;0.5-0.7</td>
<td></td>
</tr>
<tr>
<td>Type 3</td>
<td></td>
</tr>
<tr>
<td>Levels are very low or undetectable</td>
<td>Mucocutaneous bleeding, menorrhagia, post operative bleeding. May have haemarthrosis, muscle haematomas</td>
</tr>
</tbody>
</table>

3.3 Bleeding Episode Management

In the event a person with VWF or Low VWF presents with a bleed / potential bleed the Clinician should take the following steps:

Step 1: Patient Assessment

- Perform initial evaluation and assessment.
- Identify the site of the suspected bleed
- Assess for compression of vital structures e.g. airway, nerves or blood vessels, and manage accordingly.
- Undertake pain assessment and treat accordingly- Refer to (See Appendix 1: Pain Management Guidelines)
- Where possible, obtain details from patient or relative regarding bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Check patient registration card
- Weigh the patient or estimate weight where necessary
- Undertake initial blood testing to include: FBC, Biochemistry, Group and Cross-match, Coagulation and Factor Levels
- Arrange appropriate imaging but **DO NOT DELAY** haemostatic treatment if a bleed is suspected. Treat first, image after.
- If in doubt manage as a bleed, but consider alternative diagnosis and investigate accordingly.
Step 2: Communication to CCC

- Contact the patient’s CCC IMMEDIATELY following the initial assessment
- Confirm the patient’s bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Agree a management plan and follow up with the CCC

Step 3: Treatment Administration

- Prescribers must ensure that they prescribe the correct clotting factor concentrate e.g. Wilate for VWD
- In doing so the Prescriber must note that not all patients with low VWF require clotting factor concentrate and the use of alternative treatments may be indicated e.g. DDAVP or Tranexamic Acid
- The patient’s treatment of choice must be confirmed with the relevant CCC.

- Minor bleeding involving mucosal surfaces of the nose, mouth or female genital tract can be treated with Tranexamic acid alone.

- Excessive menstrual bleeding can be treated with the addition of hormonal therapy i.e. the combined oral contraceptive pill or consideration can be given to progesterone releasing intra-uterine system (Mirena).

- For more extensive or major bleeding, DDAVP or VWF concentrate should be used. The choice of agent will depend on the age of the patient, the presence of or risk factors for arteriovascular disease and the documented response of the patient to DDAVP. The CCC will advise on the appropriate treatment to use.

- The Clinician should establish the treatment of choice i.e. Wilate, DDAVP®/Desmopressin Injection and/or Tranexamic Acid.

- The selected treatment should be prepared and administered as follows:

Clotting Factor Concentrate – Wilate

- Wilate is the clotting factor concentrate recommended for use in the prevention and treatment of haemorrhage or surgical bleeding in von Willebrand disease (VWD)

- The required dose must be determined by calculating the patient’s weight and the required post treatment factor level which is determined by the severity and location of the bleed and the patient’s clinical condition.
Wilate comes as a powder and should be reconstituted using the accompanying solvent (i.e. water for injections with 0.1 % Polysorbate 80) which comes in Mix2Vial™

Wilate should be reconstituted using aseptic technique in accordance with the Wilate Reconstituted Procedure.

**Administration**

- Factor concentrate should be administered as a slow intravenous push over 5 minutes
- A post treatment factor level should be drawn 20 minutes post administration (two coagulation samples, send to local laboratory for forwarding to the CCC for analysis)
- Liaise with CCC regarding the post treatment level result in case further treatment is required.

**Reactions**

In the event of a reaction or suspected reaction the Clinician should undertake the following:
- Discontinue the Factor Concentrate
- Assess the patient
- Contact the relevant CCC for advice on alternative treatments.

In the event of **mild to moderate reaction** the Clinician should undertake the following:
- Administer Chlorpheniramine 10-20 mg IM or slow IV (at least over one minute)
- If required, add Hydrocortisone 100 - 200mg slow IV (over three minutes)

In the event of **severe allergic or anaphylactic reaction** local hospital resuscitation / response protocols should be followed. The use of the following medications is recommended:
- Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500 micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
- Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given.
- Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir
- Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).

**DDAVP®/Desmopressin Injection**

- DDAVP® Injection (Desmopressin Acetate) is a synthetic analogue of the natural hormone arginine vasopressin. It is indicated for use in managing bleeds in persons with hemophilia (Factor VIII) and some Von Willebrands by increasing plasma levels.
- DDAVP Injection 4 mcg/mL is provided as a sterile, aqueous solution for injection
- DDAVP use should be avoided in the following circumstances:
  - Persons over 55 years of age
  - Persons with a history of heart failure or other conditions being treated with diuretic agents
  - Persons with known arteriosclerosis or ischaemic heart disease
- DDAVP should be used with caution in the following circumstances:
  - Persons with risk factors for ischaemic heart disease
  - Pregnant persons
  - Children less than two years of age (Refer to Paediatric Guidelines)

- **Dose Calculation**
  - DDAVP is administered intravenously at 0.3 µg/kg
  - The maximum total dose recommended for any patient is 27µg
  - Example: A 60kg patient requiring DDAVP, the dose should be calculated as 60 kg x 0.3 µg = 18µg.

- **Dose Administration**
  - DDAVP comes in 1ml ampoule which contains Desmopressin acetate 4 micrograms per ml
  - DDAVP should be added to 100mls of normal saline using an aseptic technique
  - The 100ml solution should be administered intravenously over 30-60 minutes
  - The patient’s serum Na level should be >135 mmol/L prior to administration
  - Blood pressure must be monitored before, during and after the infusion
  - The patients must be maintained on a fluid restriction of 1.5 L/24 hours following the infusion
  - Post treatment blood levels should be taken and reviewed 30 minutes following the infusion
  - **Example:** A 60kg patient requiring DDAVP - The intravenous preparation has a concentration of 4 µg/ml. Therefore, the intravenous dose for this 60kg patient will be prepared from 4.5mls of DDAVP (at a concentration of 4 µg/ml) diluted in 100mls of normal saline and administered over 30-60 minutes.

- **Reactions to DDAVP**
  - Reactions to DDAVP can be common
  - **Mild reactions** commonly include the following:
    - Vasodilatation
    - Hypotension
    - Facial flushing
    - Mild reactions should be treated by slowing the intravenous infusion so that it is administered over 60 minutes.
  - **Moderate reactions** should be treated as follows:
    - Discontinue DDAVP
    - Assess the patient
    - Administer Chlorpheniramine 10-20 mg IM or slow IV (over one minute)
    - If required, add Hydrocortisone 100 - 200 mg IM or slow IV (over three minutes)
- If required, add Oxygen (10-12 litre/min) +/- inhaled Salbutamol (2.5mg)
- The DDAVP infusion can be restarted at a slower rate with close monitoring of the patient
- In the event a reaction recurs, the infusion should be stopped and the clinician should contact the relevant CCC for advice on alternative treatments.

- **Severe allergic reactions** should be treated in accordance with local resuscitation / response protocols. The use of the following medications is recommended:
  - Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
  - Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given as above.
  - Oxygen should be administered as soon as possible (15 litres/min) using a mask with a oxygen reservoir.
  - Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).
  - The clinician should contact the relevant CCC for advice on alternative treatments.

**Tranexamic Acid (Cyclokapron)**

- Tranexamic Acid is an antifibrinolytic agent indicated in patients with haemophilia for short-term use (two to eight days) to reduce or prevent haemorrhage
- Tranexamic acid should not be used in combination with either FEIBA or factor XI concentrate (risk of thrombosis).
- Tranexamic Acid is available in tablet and Intravenous Injection form
- Oral / Tablet form (500 mg Tranexamic Acid)
  - Recommended dose 15-25 mg/kg TDS or QDS (usually 1g TDS or QDS)
- Intravenous Injection (500mg in 5ml ampoule)
  - Recommended dose 10 mg/kg TDS
  - Bolus injection – The required dose can be administered undiluted slowly i.e. at a rate of 100mg/min
  - Intravenous Infusion – The required dose can be diluted in 100mls normal saline and given as an infusion over 30 minutes.

**Contraindications**

- Should not be used in the following circumstances
  - Patients with a history of thromboembolic disease
- Patient with Disseminated Intravascular Coagulation (DIC)
- Persons with bleeding from the upper urinary tract (risk of ureteric clot colic and obstruction)

- **Adverse effects**
  - Nausea, vomiting, and diarrhoea
  - Rapid intravenous injection may cause dizziness and hypotension (do not administer faster than 100 mg/min).

### Step 4: Documentation

- In addition to routine prescribing and recording, the dose and batch number of all Factor Concentrates administered must be recorded in the patient’s medical notes and as per local hospital/laboratory policy.

### Step 5: Initiate ‘PRICE’ for all Joint Bleeds

- **Protection**: Reduce weight bearing or stress on the affected joint or muscle by providing crutches or other supports such as a ‘collar and cuff’ for the arm. Avoid putting weight on the affected side completely for the first 48 hours; and possibly longer if it is a severe bleed.

- **Rest**: The affected arm or leg should be gently placed on a pillow or in a sling or bandage. The individual should not move the bleeding joint.

- **Ice**: Wrap an ice pack in a damp towel and place over bleed. After 5 minutes, remove ice for 10 minutes. Repeat this step for as long as the joint feels hot. This may help decrease pain and bleeding.

- **Compression**: Gentle pressure from a tensor bandage (e.g. Tubigrip, size appropriate for the patient’s limb) can help to limit bleeding and support the joint. Use compression carefully with muscle bleeds if a nerve injury is suspected.

- **Elevation**: Raise the affected area above the heart. This may slow blood loss by lowering pressure in the area of the bleed.

- **Ensure that the patient is referred to a physiotherapist for assessment and treatment.**
### 3.4 Surgery Management

- Patients with bleeding disorders should ideally have surgery in a hospital where there is a Haemophilia Comprehensive Care Centre and haemostatic management should be supervised by the CCC Team.

- In rare circumstances surgery may need to be performed in a hospital without a CCC, such as in emergencies or where the person needs to avail of specialist surgical services.

- In these circumstances, haemostatic management must be determined by the patient’s CCC and it is recommended that the local Haematology service provides on-site consultation.

**Pre-Operative**

- Confirm the patient’s known bleeding diagnosis, baseline levels, inhibitor status and treatment of choice with the patient and the relevant CCC.

- Confirm the patient’s virology (i.e. Hepatitis A, B, C and HIV) and TSE at-risk status with the CCC.

- Obtain a written management plan from the CCC.

- Liaise with local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate.

- Ensure a ‘No NSAIDS, No Aspirin, No Heparin and No IM injections’ note is communicated and recorded clearly in the drug idiosyncrasies section of the patient’s prescription form, the front cover of their medical chart and in all other relevant healthcare records e.g. Nursing Care Plans etc.

- Ensure that the local Anaesthetic Department / Team are informed that epidural and spinal anaesthesia are contra-indicated in patients with bleeding disorders. This must be clearly documented in the patient’s healthcare record.

**Post-Operative**

- Liaise with the relevant CCC to determine the requirement for ongoing haemostatic treatment and factor levels.

- Ensure that the patient is provided with adequate haemostatic cover for all invasive procedures e.g. placement of central lines or removal of sutures, clips, drains etc. As these procedures are likely to occur some days after the surgery the patient’s CCC should be contacted to advise regarding additional treatment requirements.
3.5 Pregnancy Management

- Women who have VWD or low VWF should have an individual management plan for labour and delivery determined collaboratively by the woman, her CCC and the woman’s Obstetrician. This plan should be made available to the patient, the woman’s Obstetrical Department / Provider, the local Haematologist and the woman’s GP.

- Many women with low VWF or type 1 VWD will have a physiological increase in FVIII and VWF levels during pregnancy. This should be determined by taking a von Willebrand screen in the late second trimester and early third trimester.

- Women whose FVIII and VWF levels have normalised in pregnancy do not need haemostatic cover for labour and delivery and may have epidural analgesia or caesarean delivery if indicated without specific haemostatic treatment.

- Women with type 3 VWD and some women with type 1 or 2 VWD will not normalise their FVIII or VWF levels in pregnancy. These women will need haemostatic treatment peripartum. This may either consist of DDAVP or VWF concentrate and will be determined by the CCC.

- The woman’s Obstetrical Department / Provider should liaise with their local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate, if indicated.

Maternal Labour, Delivery and Postpartum Period Management

- Patients with FVIII and/or VWF levels of <0.5 IU/ml (<50%) will require treatment at the time of delivery to maintain levels >0.50 IU/ml (>50%). The CCC should be contacted to advise on the appropriate treatment, dose and required blood testing

Epidural Anaesthesia

- The use of Epidural Anaesthesia is contra-indicated in patients with FVIII and/or VWF levels <0.50 IU/ml (<50%) in the third trimester
- Patients with confirmed normal FVIII and/or VWF levels in the third trimester may receive epidural anaesthesia if required.

Analgesia

- The use of Intramuscular injections e.g. Pethidine are contra-indicated in women with low FVIII and/or VWF levels.
- Alternative analgesia such as inhaled nitrous oxide and oxygen or intravenous Remifentanil is acceptable for patients with low FVIII and/or VWF levels
- For women with low FVIII and/or VWF levels, appropriate options for analgesia MUST be discussed with the local Maternity unit Anaesthetic service in advance.
Post partum management

- Normal factor levels should be maintained for 3 days following vaginal delivery and for 5 days after caesarean section.

- In the event the patient has received haemostatic treatment to cover the delivery, it will be necessary to send factor levels daily for 3 days following vaginal delivery and for 5 days following caesarean section.

- Postpartum, factor VIII and/or VWF levels can fall quickly in women who have low baseline levels but who have had a pregnancy-induced rise in levels and therefore have not needed treatment for labour.

- If a patient with VWD or low VWF has excessive bleeding post-partum, factor levels should be sent and advice obtained from the CCC in addition to usual obstetrical management.

- Delayed post-partum haemorrhage is a feature of inherited bleeding disorders and affected women should be provided with emergency contact numbers for their CCC and Obstetric Unit / Provider following discharge.

Management of the infant During Labour and Delivery

- Ultrasound should be performed to determine position.

- There should be a low threshold for caesarean section.

- Foetal scalp sampling and electrodes should be avoided.

- The use of ventouse and/or mid-cavity forceps is contraindicated due to the increased risk of intracranial haemorrhage.

- Lift out forceps can be performed if deemed necessary by a Consultant Obstetrician.

- If delivery is instrumental, then an urgent cranial ultrasound and VWF measurement of cord blood should be obtained.

- VWF levels should be measured from a cord blood sample from all potentially affected infants. The cord blood sample should be sent in a 2.5 mls citrate tube via the local laboratory to the laboratory at Our Lady's Hospital, Crumlin. The specific factor deficiency should be clearly documented on the laboratory request form.

- In the event the child was delivered using a ventouse or forceps delivery the factor level analysis should be undertaken as an emergency. The receiving laboratory must be informed that the factor level is required urgently.

- The use of intramuscular injections should be avoided.

- Vitamin K should be administered by the oral and not the intramuscular route.
- The Bacillus Calmette-Guérin (BCG) vaccine can be administered without haemostatic support.

- A Heel-Prick test can be undertaken for Guthrie card analysis without haemostatic support.

- In the event the factor level is found to be reduced, the child should be referred to the Paediatric Haematologist on-call at Our Lady’s Children’s Hospital, Crumlin or Cork University Hospital.
4.0: Platelet Function Disorders

4.1 General Information

Platelet function disorders (PFDs) are a heterogeneous group of conditions affecting the function of platelets in primary haemostasis. Inherited PFDs may be caused by specific genetic mutations e.g. Glanzmann’s Thrombasthenia or Bernard Soulier Syndrome. More often, the genetic cause of the PFD is not known and the conditions are described as Non-Specific PFDs. Persons with PFDs are likely to present with symptoms of mucocutaneous bleeding including recurrent epistaxis, easy bruising, excessive bleeding after dental extraction or surgery, menorrhagia and post-partum haemorrhage in women and.

There are a variety of treatment options for platelet function disorders. The patient’s CCC MUST be contacted to determine the optimal treatment for each patient and clinical scenario.

4.2 Disease Severity

The severity of the bleeding disorder is variable and the patient’s previous bleeding history will be informative if they have had previous haemostatic challenges. Certain PFDs are very likely to be associated with a bleeding phenotype e.g. Glanzmann’s thrombasthenia or Bernard Soulier syndrome. The patient’s CCC will be able to advise on the bleeding severity for individual patients.

4.3 Bleeding Episode Management

In the event a person with a platelet function disorder presents with a bleed / potential bleed the clinician should take the following steps:

Step 1: Patient Assessment

- Perform initial evaluation and assessment.
- Identify the site of the suspected bleed
- Assess for compression of vital structures e.g. airway, nerves or blood vessels, and manage accordingly.
- Undertake pain assessment and treat accordingly- Refer to Pain Management Guidelines (refer to Appendix)
- Where possible, obtain details from patient or relative regarding bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Check patient registration card
- Weigh the patient or estimate weight where necessary
- Undertake initial blood testing to include: FBC, Biochemistry, Group and Cross-match, Coagulation and Factor Levels
- Arrange appropriate imaging but DO NOT DELAY haemostatic treatment if a bleed is suspected. Treat first, image after.
- If in doubt manage as a bleed, but consider alternative diagnosis and investigate accordingly.
Step 2: Communication to CCC

- Contact the patient’s CCC IMMEDIATELY following the initial assessment
- Confirm the patient’s bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Agree a management plan and follow up with the CCC

Step 3: Treatment Administration

- Prescribers must ensure that they prescribe the correct treatment. Treatment options include the use of the following:
  - Random Donor Platelets
  - Human Leukocyte Antigen (HLA) Matched Platelets
  - Recombinant Factor VIIa
  - DDAVP
  - Tranexamic Acid

- In doing so the Prescriber must note that not all patients with PFDs require platelet transfusion and the use of alternative treatments may be indicated e.g. DDAVP or Tranexamic Acid

- The patient’s treatment of choice must be confirmed with the relevant CCC.

- The Clinician should establish the treatment of choice in consultation with the CCC and prepare and administer as follows:

  Platelet Transfusion

  - Where platelet transfusion is indicated the Clinician should order, prescribe and administer platelets in accordance with local protocols.

  - Where the CCC direct that the use of HLA matched platelets is indicated they must be ordered from the Irish Blood Transfusion Service

  Recombinant Factor VIIa / Novo Seven

  - Recombinant Factor VIIa / Novo Seven is a factor concentrate indicated for use to control bleeding in some cases of PFD.

  - The required dose must be determined by calculating the patient’s weight and the required post treatment factor level which is determined by the severity and location of the bleed and the patient’s clinical condition. Establish the of Recombinant Factor VIIa / Novo Seven dose required in consultation with the Consultant Haematologist on-call in St. James’s Hospital.

  - Recombinant Factor VIIa / Novo Seven comes as a powder with a solvent for reconstitution

  - Recombinant Factor VIIa / Novo Seven should be reconstituted using aseptic technique in accordance with the Reconstituted Procedure (refer to Appendix)
### Administration

- Factor concentrate should be administered as a slow intravenous push over 5 minutes.
- There is no requirement for monitoring of NovoSeven therapy. Severity of bleeding condition and clinical response to NovoSeven administration must guide dosing requirements.
- Liaise with CCC regarding on-going management requirements.

### Reactions

In the event of a reaction or suspected reaction the Clinician should undertake the following:
- Discontinue the Factor Concentrate
- Assess the patient
- Contact the relevant CCC for advice on alternative treatments.

In the event of **mild to moderate reaction** the Clinician should undertake the following:
- Administer Chlorpheniramine 10-20 mg IM or slow IV (at least over one minute)
- If required, add Hydrocortisone 100 - 200mg slow IV (over three minutes)

In the event of **severe allergic or anaphylactic reaction** local hospital resuscitation / response protocols should be followed. The use of the following medications is recommended:
- Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500 micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
- Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given.
- Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir
- Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).

### DDAVP®/Desmopressin Injection

- DDAVP® Injection (Desmopressin Acetate) is a synthetic analogue of the natural hormone arginine vasopressin. It is indicated for use in managing bleeds in persons with hemophilia (Factor VIII) and some Von Willebrands by increasing plasma levels.
- DDAVP Injection 4 mcg/mL is provided as a sterile, aqueous solution for injection
- DDAVP use should be avoided in the following circumstances:
  - Persons over 55 years of age
  - Persons with a history of heart failure or other conditions being treated with diuretic agents
  - Persons with known arteriosclerosis or ischaemic heart disease
- DDAVP should be used with caution in the following circumstances:
  - Persons with risk factors for ischaemic heart disease
  - Pregnant persons
  - Children less than two years of age (Refer to Paediatric Guidelines)
▪ **Dose Calculation**
  - DDAVP is administered intravenously at 0.3 µg/kg
  - The maximum total dose recommended for any patient is 27 µg
  - Example: A 60kg patient requiring DDAVP, the dose should be calculated as 60 kg x 0.3 µg = 18 µg.

▪ **Dose Administration**
  - DDAVP comes in 1ml ampoule which contains Desmopressin acetate 4 micrograms per ml
  - DDAVP should be added to 100mls of normal saline using an aseptic technique
  - The 100ml solution should be administered intravenously over 30-60 minutes
  - The patient’s serum Na level should be >135 mmol/L prior to administration
  - Blood pressure must be monitored before, during and after the infusion
  - The patients must be maintained on a fluid restriction of 1.5 L/24 hours following the infusion
  - Post treatment blood levels should be taken and reviewed 30 minutes following the infusion
  - **Example**: A 60kg patient requiring DDAVP - The intravenous preparation has a concentration of 4 µg/ml. Therefore, the intravenous dose for this 60kg patient will be prepared from 4.5mls of DDAVP (at a concentration of 4 µg/ml) diluted in 100mls of normal saline and administered over 30-60 minutes.

▪ **Reactions to DDAVP**
  - Reactions to DDAVP can be common
  - **Mild reactions** commonly include the following:
    ▪ Vasodilatation
    ▪ Hypotension
    ▪ Facial flushing
    ▪ Mild reactions should be treated by slowing the intravenous infusion so that it is administered over 60 minutes.
  - **Moderate reactions** should be treated as follows:
    ▪ Discontinue DDAVP
    ▪ Assess the patient
    ▪ Administer Chlorpheniramine 10-20 mg IM or slow IV (over one minute)
    ▪ If required, add Hydrocortisone 100 - 200 mg IM or slow IV (over three minutes)
    ▪ If **required**, add Oxygen (10-12 litre/min) +/- inhaled Salbutamol (2.5mg)
    ▪ The DDAVP infusion can be restarted at a slower rate with close monitoring of the patient
In the event a reaction recurs, the infusion should be stopped and the clinician should contact the relevant CCC for advice on alternative treatments.

- **Severe allergic reactions** should be treated in accordance with local resuscitation / response protocols. The use of the following medications is recommended:
  - Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
  - Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given as above.
  - Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir.
  - Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).
  - The clinician should contact the relevant CCC for advice on alternative treatments.

- **Tranexamic Acid (Cyklokapron)**
  - Tranexamic Acid is an antifibrinolytic agent indicated in patients with haemophilia for short-term use (two to eight days) to reduce or prevent haemorrhage
  - Tranexamic acid should not be used in combination with either FEIBA or factor XI concentrate (risk of thrombosis).
  - Tranexamic Acid is available in tablet and Intravenous Injection form
  - Oral / Tablet form (500 mg Tranexamic Acid)
    - Recommended dose 15-25 mg/kg TDS or QDS (usually 1g TDS or QDS)
  - Intravenous Injection (500mg in 5ml ampoule)
    - Recommended dose 10 mg/kg TDS
    - Bolus injection – The required dose can be administered undiluted slowly i.e. at a rate of 100mg/min
    - Intravenous Infusion – The required dose can be diluted in 100mls normal saline and given as an infusion over 30 minutes.

- **Contraindications**
  - Should not be used in the following circumstances
    - Patients with a history of thromboembolic disease
    - Patient with Disseminated Intravascular Coagulation (DIC)
    - Persons with bleeding from the upper urinary tract (risk of ureteric clot colic and obstruction)
- **Adverse effects**
  - Nausea, vomiting, and diarrhoea
  - Rapid intravenous injection may cause dizziness and hypotension (do not administer faster than 100 mg/min).

### Step 4: Documentation

- In addition to routine prescribing and recording, the dose and batch number of all Factor Concentrates administered must be recorded in the patient’s medical notes and as per local hospital/laboratory policy.

### Step 5: Initiate ‘PRICE’ for all Joint Bleeds

- **Protection:** Reduce weight bearing or stress on the affected joint or muscle by providing crutches or other supports such as a ‘collar and cuff’ for the arm. Avoid putting weight on the affected side completely for the first 48 hours; and possibly longer if it is a severe bleed.

- **Rest:** The affected arm or leg should be gently placed on a pillow or in a sling or bandage. The individual should not move the bleeding joint.

- **Ice:** Wrap an ice pack in a damp towel and place over bleed. After 5 minutes, remove ice for 10 minutes. Repeat this step for as long as the joint feels hot. This may help decrease pain and bleeding.

- **Compression:** Gentle pressure from a tensor bandage (e.g. Tubigrip, size appropriate for the patient’s limb) can help to limit bleeding and support the joint. Use compression carefully with muscle bleeds if a nerve injury is suspected.

- **Elevation:** Raise the affected area above the heart. This may slow blood loss by lowering pressure in the area of the bleed.

- **Ensure that the patient is referred to a physiotherapist for assessment and treatment.**

### 4.4 Surgery Management

- Patients with bleeding disorders should ideally have surgery in a hospital where there is a Haemophilia Comprehensive Care Centre and haemostatic management should be supervised by the CCC Team

- In rare circumstances surgery may need to be performed in a hospital without a CCC, such as in emergencies or where the person needs to avail of specialist surgical services.

- In these circumstances, haemostatic management must be determined by the patient’s CCC and it is recommended that the local Haematology service provides on-site consultation.
In the event a person with PFD is undergoing surgery in a non-specialist CCC the Clinical staff should ensure the following steps are undertaken:

**Pre-Operative**

- Confirm the patient’s known bleeding diagnosis, baseline levels, inhibitor status and treatment of choice with the patient and the relevant CCC.
- Confirm the patient’s virology (i.e. Hepatitis A, B, C and HIV) and TSE at-risk status with the CCC.
- Obtain a written management plan from the CCC.
- Liaise with local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate.
- Ensure a ‘No NSAIDS, No Aspirin, No Heparin and No IM injections’ note is communicated and recorded clearly in the drug idiosyncrasies section of the patient’s prescription form, the front cover of their medical chart and in all other relevant healthcare records e.g. Nursing Care Plans etc.
- Ensure that the local Anaesthetic Department / Team are informed that epidural and spinal anaesthesia are contra-indicated in patients with bleeding disorders. This must be clearly documented in the patient’s healthcare record.

**Post-Operative**

- Liaise with the relevant CCC to determine the requirement for ongoing haemostatic treatment and factor levels.
- Ensure that the patient is provided with adequate haemostatic cover for all invasive procedures e.g. placement of central lines or removal of sutures, clips, drains etc. As these procedures are likely to occur some days after the surgery the patient’s CCC should be contacted to advise regarding additional treatment requirements.

### 4.5 Pregnancy Management

- Women who have PFDs should have an individual management plan for labour and delivery determined collaboratively by the woman, her CCC and the woman’s Obstetrician. This plan should be made available to the patient, the woman’s Obstetrical Department / Provider, the local Haematologist and the woman’s GP.
- Some women with PFDs may need haemostatic treatment peri-partum. This will be determined by the woman’s CCC.
- The woman’s Obstetrical Department / Provider should liaise with their local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate, if indicated.
Maternal Labour, Delivery and Postpartum Period Management

- Haemostatic treatment if recommended by the CCC should be administered in accordance with the delivery plan

Epidural Anaesthesia
- The use of Epidural Anaesthesia is contra-indicated in patients with PFDs

Analgesia
- The use of Intramuscular injections e.g. Pethidine are contra-indicated in women with PFDs.
- Alternative analgesia such as inhaled nitrous oxide and oxygen or intravenous Remifentanil is acceptable for patients with PFDs.
- For women with PFDs appropriate options for analgesia MUST be discussed with the local Maternity unit Anaesthetic service in advance

Post partum management
- In the event a person with PFD has excessive bleeding post-partum, advice should be obtained from the CCC in addition to obstetrical management.
- Delayed post-partum haemorrhage is a feature of inherited bleeding disorders and affected women should be provided with emergency contact numbers for their CCC and Obstetric Unit/Provider following discharge.

Management of the infant During Labour and Delivery
The inheritance of platelet function disorders is variable according to the type of disorder. Some are inherited in autosomal recessive manner, some are autosomal dominant and others have undetermined inheritance patterns. The CCC will determine if there is a risk that the neonate has inherited a platelet function disorder and will advise on a delivery plan in conjunction with the Obstetrician. The following are standard guidelines for the delivery of infants who may have an inherited bleeding disorder.

- Ultrasound should be performed to determine sex and position.
- There should be a low threshold for caesarean section.
- Foetal scalp sampling and electrodes should be avoided.
- The use of ventouse and/or mid-cavity forceps is contraindicated due to the increased risk of intracranial haemorrhage.
- Lift out forceps can be performed if deemed necessary by a Consultant Obstetrician.
- If delivery is instrumental, then an urgent cranial ultrasound should be undertaken.
- The use of intramuscular injections should be avoided.
- Vitamin K should be administered orally, not the intra-muscular route.
- The Bacillus Calmette-Guérin (BCG) vaccine can be administered without haemostatic support.
- A Heel-Prick test can be undertaken for Guthrie card analysis without haemostatic support.
- In the event a platelet function disorder is suspected the child should be referred to the Paediatric Haematologist on-call at Our Lady’s Children's Hospital, Crumlin or Cork University Hospital.
5.0: Rare Bleeding Disorders

5.1: General Information

Rare bleeding disorders (RBDs) include deficiencies of factors I (Fibrinogen), II, V, VII, X, XI and XIII. These deficiencies can be severe or mild. Severe deficiencies may present with bleeding symptoms similar to haemophilia. Not all mild deficiencies are associated with bleeding but the bleeding tendency may be variable in some RBDs. Expert advice from a CCC is always required.

5.2: Disease Severity

Disease severity relates to the baseline level of the deficient factor but in some deficiencies, the patient’s personal bleeding history may need to be considered. The patient’s CCC will be able to advise on the bleeding severity for an individual patient.

<table>
<thead>
<tr>
<th>Deficient Factor</th>
<th>Normal Reference Interval (NCHCD, St James’s Hospital)</th>
<th>Severe Deficiency</th>
<th>Mild Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen</td>
<td>1.9-3.5 g/L</td>
<td>Undetectable</td>
<td>&lt;1.5g/L</td>
</tr>
<tr>
<td>Prothrombin</td>
<td>0.72-1.31 IU/ml</td>
<td>&lt; 0.10 IU/ml</td>
<td>0.10-0.71 IU/ml</td>
</tr>
<tr>
<td>V</td>
<td>0.63-1.33 IU/ml</td>
<td>&lt;0.10 IU/ml</td>
<td>0.10-0.62 IU/ml</td>
</tr>
<tr>
<td>VII</td>
<td>0.51-1.54 IU/ml</td>
<td>&lt;0.10 IU/ml</td>
<td>0.10-0.50 IU/ml</td>
</tr>
<tr>
<td>X</td>
<td>0.64-1.50 IU/ml</td>
<td>&lt;0.01 IU/ml</td>
<td>0.06-0.63 IU/ml</td>
</tr>
<tr>
<td>XI</td>
<td>0.72-1.53 IU/ml</td>
<td>&lt;0.20 IU/ml</td>
<td>0.20-0.70 IU/ml</td>
</tr>
<tr>
<td>XIII</td>
<td>0.73-1.60 IU/ml</td>
<td>&lt;0.10 IU/ml</td>
<td>0.10-0.73 IU/ml</td>
</tr>
</tbody>
</table>

Table 5.0: Factor VIII Disease Severity Categories

5.3: Bleeding Episode Management

In the event a person with Rare Bleeding Disorders (RBDs) presents with a bleed / potential bleed the Clinician should take the following steps:

Step 1: Patient Assessment

- Perform initial evaluation and assessment.
- Identify the site of the suspected bleed
- Assess for compression of vital structures e.g. airway, nerves or blood vessels, and manage accordingly.
- Undertake pain assessment and treat accordingly- Refer to Pain Management Guidelines (refer to appendix).
- Where possible, obtain details from patient or relative regarding bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Check patient registration card
- Weigh the patient or estimate weight where necessary
- Undertake initial blood testing to include: FBC, Biochemistry, Group and Cross-match, Coagulation and Factor Levels
- Arrange appropriate imaging but **DO NOT DELAY** haemostatic treatment if a bleed is suspected. Treat first, image after.
- If in doubt manage as a bleed, but consider alternative diagnosis and investigate accordingly.

### Step 2: Communication to CCC

- Contact the patient’s CCC **IMMEDIATELY** following the initial assessment
- Confirm the patient’s bleeding disorder diagnosis, factor level, inhibitor status and treatment of choice
- Agree a management plan and follow up with the CCC

### Step 3: Treatment Administration

- **Prescribers must ensure that they prescribe the correct clotting factor concentrate if indicated (See Table 5B)**

- **In doing so the Prescriber must note that not all patients with mild rare bleeding disorders require clotting factor concentrate and the use of alternative treatments may be indicated e.g. Tranexamic Acid**

- **The patient’s treatment of choice must be confirmed with the relevant CCC.**

The deficiency type will determine the appropriate Clotting Factor Concentration to be used – As in Table 5B below.

**Table 5B: RBD – CFC Indications**

<table>
<thead>
<tr>
<th>Deficiency</th>
<th>Clotting Factor Concentrate (If indicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen</td>
<td>Fibrinogen concentrate</td>
</tr>
<tr>
<td>Factor II</td>
<td>Prothromplex (Prothrombin complex concentrate)</td>
</tr>
<tr>
<td>Factor V</td>
<td>Octaplas (Solvent detergent treated frozen plasma)</td>
</tr>
<tr>
<td>Factor VII</td>
<td>Recombinant factor VIIa</td>
</tr>
<tr>
<td>Factor X</td>
<td>Prothromplex (prothrombin complex concentrate)</td>
</tr>
<tr>
<td>Factor XI</td>
<td>FXI Concentrate or Octaplas.</td>
</tr>
<tr>
<td>Factor XIII</td>
<td>Fibrogammin P (FXIII concentrate)</td>
</tr>
</tbody>
</table>

- **The Clinician should establish the treatment of choice, prepare and administer as follows:**
  
  - The required dose must be determined by calculating the patients weight and the required post treatment factor level which is determined by the severity and location of the bleed. Please discuss with the CCC or the Haematologist on-call in St. James’s hospital.
  
  - Clotting Factor Concentrate must be reconstituted for use using an aseptic technique (Refer to Factor Reconstitution Procedure (see Appendix)
Administration
- Factor concentrate should be administered as a slow intravenous push over 5 minutes
- A post treatment factor level should be drawn 20 minutes post administration (two coagulation samples, send to local laboratory for forwarding to the CCC for analysis)
- Liaise with CCC regarding the post treatment level result in case further treatment is required.

Reactions
In the event of a reaction or suspected reaction the Clinician should undertake the following:
- Discontinue the Factor Concentrate
- Assess the patient
- Contact the relevant CCC for advice on alternative treatments.

In the event of **mild to moderate reaction** the Clinician should undertake the following:
- Administer Chlorpheniramine 10-20 mg IM or slow IV (at least over one minute)
- If required, add Hydrocortisone 100 - 200mg slow IV (over three minutes)

In the event of **severe allergic or anaphylactic reaction** local hospital resuscitation / response protocols should be followed. The use of the following medications is recommended:
- Adrenaline (Epinephrine) should be given by the intramuscular (IM) route at a dose of 500micrograms (0.5mg) for example 0.5ml of 1:1000 adrenaline.
- Chlorpheniramine 10mg IV or IM and Hydrocortisone 200mg IV or IM should also be given.
- Oxygen should be administered as soon as possible (15 litres/min) using a mask with an oxygen reservoir
- Bronchodilators: Consider salbutamol (inhaled), or ipratropium (inhaled).

Tranexamic Acid (Cyklokapron)
- Tranexamic Acid is an antifibrinolytic agent indicated in patients with haemophilia for short-term use (two to eight days) to reduce or prevent haemorrhage
- Tranexamic acid should not be used in combination with either FEIBA or factor XI concentrate (risk of thrombosis).
- Tranexamic Acid is available in tablet and Intravenous Injection form
  - **Oral / Tablet form** (500 mg Tranexamic Acid)
    - Recommended dose 15-25 mg/kg TDS or QDS (usually 1g TDS or QDS)
  - **Intravenous Injection** (500mg in 5ml ampoule)
    - Recommended dose 10 mg/kg TDS
    - Bolus injection – The required dose can be administered undiluted slowly i.e. at a rate of 100mg/min
- Intravenous Infusion – The required dose can be diluted in 100mls normal saline and given as an infusion over 30 minutes.

### Contraindications
Should not be used in the following circumstances
- Patients with a history of thromboembolic disease
- Patient with Disseminated Intravascular Coagulation (DIC)
- Persons with bleeding from the upper urinary tract (risk of ureteric clot colic and obstruction)

### Adverse effects
- Nausea, vomiting, and diarrhoea
- Rapid intravenous injection may cause dizziness and hypotension (do not administer faster than 100 mg/min).

### Step 4: Documentation
- In addition to routine prescribing and recording, the dose and batch number of all Factor Concentrates administered must be recorded in the patient’s medical notes and as per local hospital/laboratory policy.

### Step 5: Initiate ‘PRICE’ for all Joint Bleeds
- **Protection:** Reduce weight bearing or stress on the affected joint or muscle by providing crutches or other supports such as a ‘collar and cuff’ for the arm. Avoid putting weight on the affected side completely for the first 48 hours; and possibly longer if it is a severe bleed.
- **Rest:** The affected arm or leg should be gently placed on a pillow or in a sling or bandage. The individual should not move the bleeding joint.
- **Ice:** Wrap an ice pack in a damp towel and place over bleed. After 5 minutes, remove ice for 10 minutes. Repeat this step for as long as the joint feels hot. This may help decrease pain and bleeding.
- **Compression:** Gentle pressure from a tensor bandage (e.g. Tubigrip, size appropriate for the patient’s limb) can help to limit bleeding and support the joint. Use compression carefully with muscle bleeds if a nerve injury is suspected.
- **Elevation:** Raise the affected area above the heart. This may slow blood loss by lowering pressure in the area of the bleed.
- **Ensure that the patient is referred to a physiotherapist for assessment and treatment.**
5.4: Surgery Management

- Patients with bleeding disorders should ideally have surgery in a hospital where there is a Haemophilia Comprehensive Care Centre and haemostatic management should be supervised by the CCC Team

- In rare circumstances surgery may need to be performed in a hospital without a CCC, such as in emergencies or where the person needs to avail of specialist surgical services.

- In these circumstances, haemostatic management must be determined by the patient’s CCC and it is recommended that the local Haematology service provides on-site consultation.

In the event a person with a bleeding disorder is undergoing surgery in a non-specialist CCC the Clinical staff should ensure the following steps are undertaken:

- **Pre-Operative**
  - Confirm the patient’s known bleeding diagnosis, baseline levels, inhibitor status and treatment of choice with the patient and the relevant CCC.
  - Confirm the patient’s virology (i.e. Hepatitis A, B, C and HIV) and TSE at-risk status with the CCC.
  - Obtain a written management plan from the CCC.
  - Liaise with local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate.
  - Ensure a ‘No NSAIDS, No Aspirin, No Heparin and No IM injections’ note is communicated and recorded clearly in the drug idiosyncrasies section of the patient’s prescription form, the front cover of their medical chart and in all other relevant healthcare records e.g. Nursing Care Plans etc.
  - Ensure that the local Anaesthetic Department / Team are informed that epidural and spinal anaesthesia are contra-indicated in patients with bleeding disorders. This must be clearly documented in the patient’s healthcare record.

- **Post-Operative**
  - Liaise with the relevant CCC to determine the requirement for ongoing haemostatic treatment and factor levels.
  - Ensure that the patient is provided with adequate haemostatic cover for all invasive procedures e.g. placement of central lines or removal of sutures, clips, drains etc. As theses procedures are likely to occur some days after the surgery the patient’s CCC should be contacted to advise regarding additional treatment requirements.
5.5: Pregnancy Management

- Women who have Rare Bleeding Disorders (RBD) should have an individual management plan for the pregnancy, labour and delivery determined collaboratively by the woman, her CCC and the woman’s Obstetrician. This plan should be made available to the patient, the woman’s Obstetrical Department / Provider, the local Haematologist and the woman’s GP.

- Some women with RBDs may need haemostatic treatment peripartum. The woman’s CCC will determine this.

- The woman’s Obstetrical Department / Provider should liaise with their local Blood Transfusion Laboratory to ensure availability of adequate clotting factor concentrate, if indicated.

Maternal Labour, Delivery and Postpartum Period Management

- Some patients with RBDs will require treatment at the time of delivery to maintain their levels within the normal range. The CCC should be contacted to advise on the appropriate treatment, dose and required blood testing.

- Some women with rare bleeding disorders may be managed with a “watch and wait” approach or with Tranexamic acid. If there is a clinical suspicion of excessive bleeding, the clinical team should contact the CCC for advice.

- **Epidural Anaesthesia**
  The use of Epidural Anaesthesia is contra-indicated in patients with RBDs.

- **Analgesia**
  - The use of Intramuscular injections e.g. Pethidine are contra-indicated in patients with RBDs
  - Alternative analgesia such as inhaled nitrous oxide and oxygen or intravenous Remifentanil is acceptable for patients with RBDs.
  - For women with RBDs, appropriate options for analgesia MUST be discussed with the local Maternity unit Anaesthetic service in advance.

- **Post Partum Management**
  - Normal factor levels should be maintained for 3 days following vaginal delivery and for 5 days after caesarean section.
  - In the event the patient has received haemostatic treatment to cover the delivery, it will be necessary to send factor levels daily for 3 days following vaginal delivery and for 5 days following caesarean section.
  - Postpartum, factor levels can fall quickly in women who have low baseline levels but who have had a pregnancy-induced rise in levels and therefore have not needed treatment for labour. If
a patient with a RBD has excessive bleeding post-partum, factor levels should be sent and advice obtained from the CCC in addition to usual obstetrical management.

- Delayed post-partum haemorrhage is a feature of inherited bleeding disorders and affected women should be provided with emergency contact numbers for their CCC and Obstetric Unit / Provider following discharge.

**Management of the infant During Labour and Delivery**

The CCC in conjunction with the Obstetrician determines the delivery plan but the following standard guidelines should be followed:

- Ultrasound should be performed to determine position
- There should be a low threshold for caesarean section
- Foetal scalp sampling and electrodes should be avoided
- The use of ventouse and/or mid cavity forceps is contraindicated due to the increased risk of intracranial haemorrhage
- Lift out forceps can be performed if deemed necessary by a Consultant Obstetrician
- If delivery is instrumental, then an urgent cranial ultrasound should be undertaken
- The specific factor level should be measured on a cord blood sample from all potentially affected infants
- The cord blood sample should be sent in a 2.5 mls citrate tube via the local laboratory to the laboratory at Our Lady's Hospital, Crumlin
- The sex of the baby and specific factor deficiency should be clearly documented on the laboratory request form
- In the event the child is delivered using a ventouse or forceps delivery the factor level analysis should be undertaken as an emergency. The receiving laboratory must be informed that the factor level is required urgently
- The use of intramuscular injections should be avoided
- Vitamin K should be administered by the oral and not the intramuscular route
- The Bacillus Calmette-Guérin (BCG) vaccine can be administered without haemostatic support
- A Heel-Prick test can be undertaken for Guthrie card analysis without haemostatic support
- In the event the factor level is found to be reduced, the child should be referred to the Paediatric Haematologist on-call at Our Lady's Children’s Hospital, Crumlin or Cork University Hospital.
References


Bibliography

1. BNF 68, September 2014 – March 2015, BMA, RPSGB, Pharmaceutical Press

2. Child Pugh; Oxford Textbook of Medicine, 3rd edition, p2094


4. NAPP medicines information unit


10. St. James’s Hospital Prescriber’s Guide

**VIII Deficiency Treatment - Clotting Factor Concentrate (Advate™) - Dose Calculations**

### 1.0 Bolus Dosing in FVIII Deficiency CFC i.e. Advate

Rise required = desired level of factor concentrate (%) - baseline factor level (%)

Dose required Calculation = \[ \text{Rise Required (%) \times \text{Weight(kgs)}} \div k \]

**Example** -

A 50kg patient with a FVIII:C <0.01 IU/ml (<1%) who needs a post factor level of 1.0 IU/ml (100%) will require 2500 units FVIII concentrate

100% (1.0 IU/ml) – 0 % (<0.01 IU/ml) x 50kg = 2500 units

### 2.0 Desired Post Treatment Factor Levels for Bleeds Types in Persons with FVIII deficiency

<table>
<thead>
<tr>
<th>Bleeding Site</th>
<th>Target post treatment FVIII and FIX Factor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleed</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>CNS or bleed involving peripheral nerve</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Ileopsoas /retroperitoneal</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Tongue/neck/retropharyngeal</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Haemarthrosis</td>
<td>0.5 – 0.7 (50 - 70%) IU/ml</td>
</tr>
<tr>
<td>Minor bleed</td>
<td>0.5 IU/ml (50%)</td>
</tr>
<tr>
<td>Laceration requiring sutures</td>
<td>0.4 IU/ml (40%) until sutures removed</td>
</tr>
<tr>
<td>Haematuria</td>
<td>High fluid intake +/- rise to 0.3-0.5 IU/ml (30-50%)</td>
</tr>
<tr>
<td>Minor surgery (angiogram, lumbar puncture)</td>
<td>1.0 IU/ml (100%) with further dosing if required</td>
</tr>
<tr>
<td>Liver biopsy or central venous catheter</td>
<td>1.0 IU/ml (100%) + commence CI* x 3 days</td>
</tr>
<tr>
<td>Major surgery</td>
<td>1.0IU/ml (100%) + commence CI * Consider treatment x 5-14 days (usually switch to bolus dosing by day 5-7)</td>
</tr>
</tbody>
</table>

**CI = continuous infusion**

Continuous infusion should only be used in severe haemophilia as may increase risk of inhibitor formation in mild haemophilia (especially in persons with Factor VIII Deficiency)
3.0 Continuous Infusion in FVIII Deficiency CFC i.e. Advate

- Continuous Infusion should **only** be used for the management of surgery or severe bleeding episodes in persons with FVIII Deficiency.

- A bolus dose should be administered to bring the patient’s factor level up to 100%. This should be administered approximately 60 minutes before the planned operation time, and pre and 20 mins post factor levels taken.

- The continuous infusion (C I) should then be set up in a mechanical syringe driver pump.

- Factor VIII concentrate infusions should begin at **4 iu/kg/hr** and should be calculated for a period of **no longer than 24hr**.

- It must be noted that the syringe can only hold up to a maximum of 50mls of reconstituted factor.

- Water for injection must **not** be added to the reconstituted solution in order to bring the syringe to 50mls.

**Calculation** - Using FVIII product **Advate** 1000iu - each reconstituted vial contains **5mls** of solution to infuse at 4iu/kg/hr

- Calculate total dose per hour by multiplying the required 4iu x the patients weight in Kg
  
  For Example  Patient’s Wgt 70kgs = 4iu x 70 =280iu per hour

- To calculate the **total dosage for the syringe**, multiply the total numbers of units per hour by the number of hours you want the infusion to continue for.
  
  i.e. 280iu x 24hrs = 6,720iu  round up to 7,000iu

- To calculate the **volume of the syringe** divide the total number of units by the vial size available.

  i.e.  
  
  \[
  \frac{7000iu}{1000iu \text{ (vials)}} = 7 \text{ vials}
  \]

- As each reconstituted vial has 5mls of solution the **Total volume of syringe** = 7 x 5mls = 35mls

- The concentration of factor in the syringe is the total dose of factor divided by the total volume in the syringe

  i.e.  
  
  \[
  \frac{7,000iu}{35mls} =200iu/ml
  \]

- The rate per hour is the desired units/hour divided by the concentration of factor in the syringe

  i.e.  
  
  \[
  \frac{280iu/hour}{200iu/ml} =1.4mls/hour
  \]
4.0 Continuous Infusions Requirements

- A ‘fall off’ level should be taken four hours after the bolus. The rate of the continuous infusion must be adjusted according to this and the daily factor level.

- All infusion giving sets / IV lines must be changed **every 24hrs**. Each new IV line must be flushed using the factor concentrate solutions.

- Sodium Chloride 0.9% should be infused through the same cannula via a Y port at a rate of 20mls/hr to prevent phlebitis.

- Nursing should record hourly observations of the cannula site, syringe rate and volume on a Continuous Infusion Observation Sheet or local equivalent (Available on SJH H&H ward)

- The syringe can only hold up to a maximum of 50mls of reconstituted factor. Water for injection must not be added to the reconstituted solution in order to bring the syringe volume to 50mls.

**Dose Adjustments Guidelines in patients receiving Factor VIII or IX concentrate by Continuous Infusion.**

- The Consultant Haematologist on call must be consulted before adjusting the Continuous Infusion.

- The following guidance are based on using 1000iu vials of Factor VIII and IX when reconstituting product for continuous infusion

<table>
<thead>
<tr>
<th>Factor VIII or IX Level</th>
<th>Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5 IU/ml (&lt;50 %)</td>
<td>Administer Bolus dose to 1.0 IU/ml (100%) and increase the rate of infusion by 1.0iu/kg/hr</td>
</tr>
<tr>
<td>0.5-0.9 IU/ml (50-90%)</td>
<td>Increase Rate of Infusion by 0.5iu/kg/hr</td>
</tr>
<tr>
<td>0.9-1.1 IU/ml (90-110%)</td>
<td>No Change</td>
</tr>
<tr>
<td>&gt;1.1 IU/ml</td>
<td>Decrease rate by 0.5iu/kg/hr</td>
</tr>
</tbody>
</table>
Calculating and Adjusting Factor VIII CFC Dose for Continuous Infusion

4iu/kg/hr using **1000iu** vials of FVIII only

1ml = 200iu/ml

<table>
<thead>
<tr>
<th>Weight (Kgs)</th>
<th>Total dosage of Syringe (IU) for 24 hours</th>
<th>Total volume of Syringe (MLs)</th>
<th>Starting rate mls/hour (4 units/kg/hour)</th>
<th>&lt;0.5iu/ml (&lt;50%) Bolus dose to increase to 1.0iu/ml (100%) and increase rate to</th>
<th>0.5-0.9 (50-90%) Increase rate to</th>
<th>0.9-1.1iu/ml (90-100%) No change</th>
<th>&gt; 1.1iu/ml Decrease rate to</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>5,000iu</td>
<td>25mls</td>
<td>1.0mls/hr</td>
<td>1.25mls/hr</td>
<td>1.13mls/hr</td>
<td>No change</td>
<td>0.88mls/hr</td>
</tr>
<tr>
<td>60</td>
<td>6,000iu</td>
<td>30mls</td>
<td>1.2mls/hr</td>
<td>1.5mls/hr</td>
<td>1.35mls/hr</td>
<td>No change</td>
<td>1.05mls/hr</td>
</tr>
<tr>
<td>70</td>
<td>7,000iu</td>
<td>35mls</td>
<td>1.4mls/hr</td>
<td>1.75mls/hr</td>
<td>1.58mls/hr</td>
<td>No change</td>
<td>1.23mls/hr</td>
</tr>
<tr>
<td>80</td>
<td>8,000iu</td>
<td>40mls</td>
<td>1.6mls/hr</td>
<td>2.0mls/hr</td>
<td>1.8mls/hr</td>
<td>No change</td>
<td>1.4mls/hr</td>
</tr>
<tr>
<td>90</td>
<td>9,000iu</td>
<td>45mls</td>
<td>1.8mls/hr</td>
<td>2.25mls/hr</td>
<td>2.03mls/hr</td>
<td>No change</td>
<td>1.58mls/hr</td>
</tr>
<tr>
<td>100</td>
<td>10,000iu</td>
<td>50mls</td>
<td>2.0mls/hr</td>
<td>2.5mls/hr</td>
<td>2.25mls/hr</td>
<td>No change</td>
<td>1.75mls/hr</td>
</tr>
</tbody>
</table>

Please note all calculations are based on 24 hour pump
## FIX Deficiency Treatment - Clotting Factor Concentrate (BeneFIX ™) - Dose Calculations

### 5.0 Bolus Dosing in FIX Deficiency CFC i.e. Benefix

### 6.0 Desired Post Treatment Factor Levels for Bleeds Types in Persons with FVIII deficiency

<table>
<thead>
<tr>
<th>Bleeding Site</th>
<th>Target post treatment FVIII and FIX Factor levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major bleed</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>CNS or bleed involving peripheral nerve</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Ileopsoas /retroperitoneal</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Tongue/neck/retropharyngeal</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1.0 IU/ml (100%) + commence CI*</td>
</tr>
<tr>
<td>Haemarthrosis</td>
<td>0.5 – 0.7 (50 - 70%) IU/ml</td>
</tr>
<tr>
<td>Minor bleed</td>
<td>0.5 IU/ml (50%)</td>
</tr>
<tr>
<td>Laceration requiring sutures</td>
<td>0.4 IU/ml (40%) until sutures removed</td>
</tr>
<tr>
<td>Haematuria</td>
<td>High fluid intake +/- rise to 0.3-0.5 IU/ml (30-50%)</td>
</tr>
<tr>
<td>Minor surgery (angiogram, lumbar puncture)</td>
<td>1.0 IU/ml (100%) with further dosing if required</td>
</tr>
<tr>
<td>Liver biopsy or central venous catheter</td>
<td>1.0 IU/ml (100%) + commence CI* x 3 days</td>
</tr>
<tr>
<td>Major surgery</td>
<td>1.0 IU/ml (100%) + commence CI * Consider treatment x 5-14 days (usually switch to bolus dosing by day 5-7)</td>
</tr>
</tbody>
</table>

*CI = continuous infusion

Continuous infusion should only be used in severe haemophilia as may increase risk of inhibitor formation in mild haemophilia (especially in persons with Factor VIII Deficiency).

### 7.0 Continuous Infusion in FIX Deficiency CFC i.e. Benefix

- Continuous Infusion should **only** be used for the management of surgery or severe bleeding episodes in persons with FIX Deficiency.

- A bolus dose should be administered to bring the patient’s factor level up to 100%. This should be administered approximately 60 minutes before the planned operation time, and pre and 20 mins post factor levels taken.

- The continuous infusion (CI) should then be set up in a mechanical syringe driver pump.
- Factor concentrate infusions should begin at a rate of 6iu/kg/hr and should be calculated for a period of no longer than 12hrs. This is mainly due to the larger volume of reconstituted solution in the Benefix vials.

- It must be noted that the syringe can only hold up to a maximum of 50mls of reconstituted factor.

- Water for injection must not be added to the reconstituted solution in order to bring the syringe to 50mls.

- **Calculation** - Using FIX product Benefix 1000iu - Each reconstituted vial contains 5mls of solution to infuse at 6iu/kg/hr
  
  - Calculate total dose per hour by multiplying the required 6iu x the patients weight in Kg
  
  For Example Patient’s Wgt 70kgs = 6iu x 70 =420iu per hour

  - To calculate the total dosage for the syringe, multiply the total numbers of units per hour by the number of hours you want the infusion to continue for.
  
  i.e. 420iu x 12hrs = 5,040iu round to 5,000iu

  - To calculate the volume of the syringe divide the total number of units by the vial size available.
  
  i.e. 
  
  \[
  \frac{5000\text{iu}}{1000\text{iu (vials)}} = 5 \text{ vials}
  \]

  - As each reconstituted vial has 5mls of solution the **Total volume of syringe** = 5 x 5mls = 25mls

**Concentration of factor in syringe** is dose of factor divided by the volume of the syringe.

i.e 

\[
\frac{5000\text{iu}}{25 \text{ mls}} = 200\text{iu/ml}
\]

**Rate per hour** is desired units/hr divided by concentration of factor in syringe

i.e 

\[
\frac{420\text{iu per hour}}{200\text{iu/ml}} = 2.1\text{mls per hour}
\]

**8.0 Continuous Infusions Requirements**

- A ‘fall off’ level should be taken four hours after the bolus. The rate of the continuous infusion must be adjusted according to this and the daily factor level.

- All infusion giving sets / IV lines must be changed every **24hrs**. Each new IV line must be flushed using the factor concentrate solutions.

- Sodium Chloride 0.9% should be infused through the same cannula via a Y port at a rate of 20mls/hr to prevent phlebitis.
- Nursing should record hourly observations of the cannula site, syringe rate and volume on a Continuous Infusion Observation Sheet or local equivalent (Available on SJH H&H ward).

- The syringe can only hold up to a maximum of 50mls of reconstituted factor. Water for injection must not be added to the reconstituted solution in order to bring the syringe volume to 50mls.

### Dose Adjustments Guidelines in patients receiving Factor VIII or IX concentrate by Continuous Infusion.

- The Consultant Haematologist on call must be consulted before adjusting the Continuous Infusion.

- The following guidance are based on using 1000iu vials of Factor VIII and IX when reconstituting product for continuous infusion

<table>
<thead>
<tr>
<th>Factor VIII or IX Level</th>
<th>Dose Adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.5 IU/ml (&lt;50 %)</td>
<td>Administer Bolus dose to 1.0 IU/ml (100%) and increase the rate of infusion by 1.0iu/kg/hr</td>
</tr>
<tr>
<td>0.5-0.9 IU/ml (50-90%)</td>
<td>Increase Rate of Infusion by 0.5iu/kg/hr</td>
</tr>
<tr>
<td>0.9-1.1 IU/ml (90-110%)</td>
<td>No Change</td>
</tr>
<tr>
<td>&gt;1.1 IU/ml</td>
<td>Decrease rate by 0.5iu/kg/hr</td>
</tr>
</tbody>
</table>
Calculating and Adjusting Factor IX CFC Dose for Continuous Infusion

6iu/kg/hr using 1000iu vials of FIX (Benefix) only
1ml = 200iu/ml

<table>
<thead>
<tr>
<th>Weight (Kgs)</th>
<th>Total dosage of Syringe (IU) per 12 hours</th>
<th>Total volume of Syringe (MLS)</th>
<th>Starting rate mls/hour (units /kg/hr)</th>
<th>&lt;0.5iu/ml (&lt;50%) Bolus dose to increase to 1.0u/ml (100%) and increase rate to</th>
<th>0.5-0.9 (50-90%) Increase rate to</th>
<th>0.9-1.1iu/ml (90-100%) No change</th>
<th>1.1iu/ml Decrease rate to</th>
</tr>
</thead>
<tbody>
<tr>
<td>50</td>
<td>3,000iu</td>
<td>15mls</td>
<td>1.5 mls/hour</td>
<td>1.75 mls/hour</td>
<td>1.63 mls/hour</td>
<td>No change</td>
<td>1.38 mls/hour</td>
</tr>
<tr>
<td>60</td>
<td>4,000iu</td>
<td>20mls</td>
<td>1.8 mls/hour</td>
<td>2.1 mls/hour</td>
<td>1.95 mls/hour</td>
<td>No change</td>
<td>1.65 mls/hour</td>
</tr>
<tr>
<td>70</td>
<td>5,000iu</td>
<td>25mls</td>
<td>2.1 mls/hour</td>
<td>2.45 mls/hour</td>
<td>2.28 mls/hour</td>
<td>No change</td>
<td>1.93 mls/hour</td>
</tr>
<tr>
<td>80</td>
<td>5,000iu</td>
<td>25mls</td>
<td>2.4 mls/hour</td>
<td>2.8 mls/hour</td>
<td>2.6 mls/hour</td>
<td>No change</td>
<td>2.2 mls/hour</td>
</tr>
<tr>
<td>90</td>
<td>6,000iu</td>
<td>30mls</td>
<td>2.7 mls/hour</td>
<td>3.15 mls/hour</td>
<td>2.93 mls/hour</td>
<td>No change</td>
<td>2.48 mls/hour</td>
</tr>
<tr>
<td>100</td>
<td>7,000iu</td>
<td>35mls</td>
<td>3.0 mls/hour</td>
<td>3.5 mls/hour</td>
<td>3.25 mls/hour</td>
<td>No change</td>
<td>2.75 mls/hour</td>
</tr>
</tbody>
</table>

Please note all calculations are based on 12 hour pump.