# Haemophilia - Suspected Bleed - Full Clinical Guideline

Reference no.: CG-HAEM/2023/013

## 1. Introduction

Haemophilia is an X-linked congenital bleeding disorder caused by a deficiency of coagulation factor VIII (FVIII) (in haemophilia A) or factor IX (FIX) (in haemophilia B). The deficiency is the result of mutations of the respective clotting factor genes.

Both haemophilia A and B are inherited in an X-linked recessive manner and, therefore, males almost exclusively have the phenotype. Homozygosity and lyonisation may lead to haemophilia in females.

Haemophilia A affects approximately 1 in 5000 males, whereas haemophilia B is much less common.

The severity of bleeding in haemophilia is generally correlated with the clotting factor level.

| Severity | Clotting factor level | Bleeding phenotype |
|---|---|---|
| Severe | < 1 IU/dl (< 0.01 IU/ml) or < 1 % of normal | Spontaneous bleeding into joints or muscles, predominantly in the absence of identifiable haemostatic challenge |
| Moderate | 1-5 IU/dl (0.01-0.05 IU/ml) or 1-5% of normal | Occasional spontaneous bleeding; prolonged bleeding with minor trauma or surgery. Many with lower levels have a phenotype very similar to severe patients. |
| Mild | 5-40 IU/dl (0.05-0.40 IU/ml) or 5-<40% of normal | Severe bleeding with major trauma or surgery. Spontaneous bleeding is rare. |

While the history of bleeding is usually life-long, people with severe haemophilia often do not have bleeding symptoms until they begin walking or running.

People with mild haemophilia may not bleed excessively until they experience trauma or surgery.

Typical sites of bleeding in haemophilia are joints (haemarthrosis); muscles; especially deep compartments (iliopsoas, calf, and forearm); mucous membranes in the mouth, gums, nose, and genitourinary tract; life threatening intracranial bleeding; neck/throat bleeding and gastrointestinal bleeding.

Any unexplained symptoms in a person with haemophilia should be assumed to be due to bleeding until proved otherwise. Prompt treatment to restore normal coagulation should be administered promptly pending further investigation.

## 2. Aim and Purpose

To enable the timely, safe and effective treatment of bleeds in people with haemophilia.

## 3. Definitions, Keywords

Haemophilia A - Congenital deficiency of clotting factor VIII; Haemophilia B - Congenital deficiency of clotting factor IX. Severe haemophilia is associated with spontaneous bleeding into joints, muscles and organs e.g. the brain. Even minor interventions can cause bleeding if the bleeding disorder is not treated beforehand.

Clotting Factor Concentrate – this is given therapeutically to replace the clotting factor that is missing or low. CFC's come as vials of lyophiliyzed powder with diluent and a transfer mechanism to transfer the diluent into the vial of CFC. All CFC's are on the Medusa database used by the Trust.

Desmopressin. This is a medication which stimulates the release of Factor VIII and von Willebrands factor from their stores in the endothelial cells of blood vessels. Desmopressin can be used to treat mild haemophilia A and von Willebrands disease.

Inhibitor: an antibody against factor VIII or IX which reduces the efficacy of clotting factor treatment.

## 4. Main body of Guidelines

### Treatment of haemophilia

The mainstay of treatment in haemophilia is the administration of haemostatic therapy to control bleeding.

In more severely affected people, administration of clotting factor concentrates is usually required following a bleeding episode. Children with severe haemophilia will almost always be treated with prophylactic factor concentrate with the aim of zero bleeds. Treatment is usually started around the age of 1 year. However breakthrough bleeding may occur. Many young adults and middle aged haemophiliacs may be on prophylaxis also.

Mildly affected patients may be treated with desmopressin or clotting factor concentrates. Please see https://derby.koha-ptfs.co.uk/cgi-bin/koha/opac-detail.pl?biblionumber=1050&query_desc=kw%2Cwrdl%3A%20haemophilia for

guidance on the use of desmopressin. Desmopressin is not advised in children less than 2 years of age.

Adjunctive treatment with tranexamic acid should be used in most cases (except haematuria – see below.

Non-drug treatments such as protection, rest, ice and elevation are important following joint and muscle bleeding. Physiotherapy is a vital part of rehabilitation following musculoskeletal bleeding episodes.

**Inhibitors in haemophilia**

A serious and significant complication of the treatment of haemophilia is the development of an inhibitor (antibody) to FVIII or FIX. Most inhibitors occur in severe haemophilia, however, inhibitors can also occur in mild/moderate haemophilia. The highest risk period for the development of an inhibitor in severe haemophilia is during the first 20 exposures to factor concentrate. Inhibitor risk in mild haemophilia is not related to the number of exposures. The development of an inhibitor results in loss of efficacy to factor concentrate and should be suspected in a person with haemophilia who presents with bleeding despite adequate factor treatment. Inhibitors in haemophilia B may cause anaphylaxis following treatment with FIX concentrate.

Certain patients may have already been identified as being high risk for inhibitors eg known to carry a high risk genetic variant, or because of treatment related factors. These patients should always be discussed with a paediatric haematology consultant.

Further information about inhibitor surveillance and treatment can be found in the inhibitor guideline.

**Route of presentation**

Emergencies in children with bleeding disorders will be assessed in the Childrens Emergency Department. Alternative arrangements may be made in some circumstances to assess children with non-urgent conditions on Puffin ward.

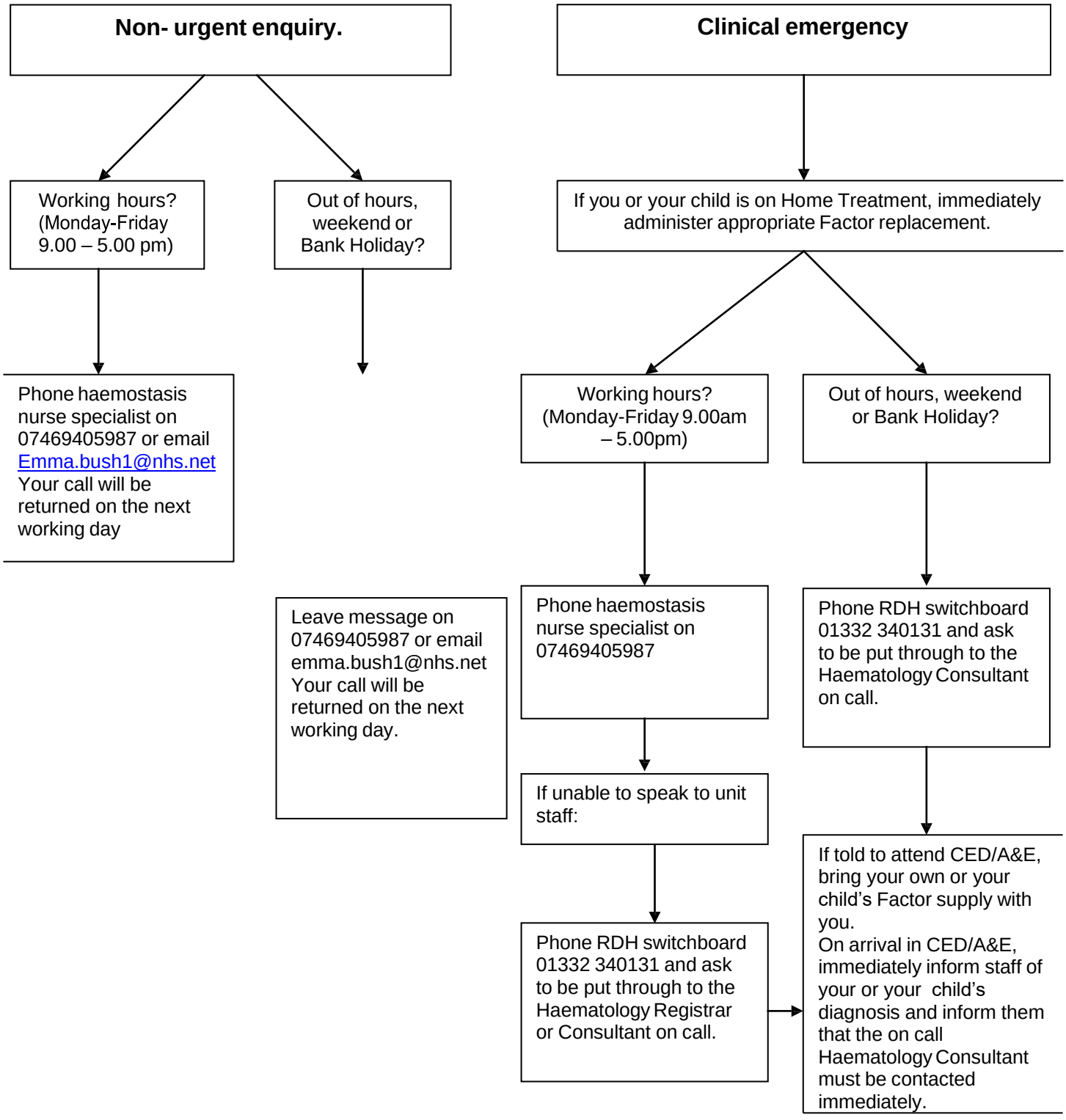
All parents/carers will be provided with written information about how to access advice and care for bleeding episodes.

Emergencies in Adults will be assessed in the Emergency Department, non-urgent conditions may be assessed in the Combined Day Unit.

Persons with haemophilia and Parents are advised to follow the pathway below.

In the event that a person with haemophilia needs to attend the Emergency Department or any other hospital department without the person/parent/carer having first spoken with a member of the Haemophilia team, the person/parent/carer must always immediately inform the nurse/doctor

who sees the child that they have a bleeding disorder. During normal working hours the Haemostasis Clinical Nurse Specialist must be contacted. Out of hours, patients should be discussed with the on-call Haematology Consultant or Registrar.




In the event that you need to attend the CED/Accident & Emergency Department or any other hospital department without having first spoken with a member of the Haemophilia team, **always** immediately inform the nurse/doctor who sees your child

**On arrival in the Emergency Department**

1. ***It is essential that people with haemophilia are managed as high priority and assessed and treated as soon as possible after arrival.***
   Do not send a haemophiliac patient home without treatment OR admit them unless this has been discussed with senior haematology staff (Registrar or Consultant).
   During normal working hours, the patient's management should be discussed with the the haemostasis consultant (Dr A McKernan or Dr M Rupparellia) or the on-call haematology consultant.
   Out of hours, patients should be discussed with the on-call haematology consultant.
2. The person/parent/carer must immediately inform staff that they have a bleeding disorder. All people with haemophilia should have a haemorrhagic risk card with details of their diagnosis and baseline Factor levels.
3. On arrival in the assessment area the maximum time to assessment should not exceed 15 minutes. The haematology consultant must be contacted at the point of triage.
4. The person with haemophilia should be assessed, investigated and treated by appropriately trained staff in consultation with haematology colleagues. Always listen to the person/child and their parent(s)/carer(s), as they will be very familiar with their condition and treatment, and will often be able to help you.
5. Any previously untreated child/person must be discussed with the haematology consultant.
6. All patients with inhibitors must be discussed with the haematology consultant.
7. If treatment is required, the maximum time to delivery of treatment should not exceed 30 minutes. In the event of communications difficulty with haematology staff, treatment should not be delayed.
8. If the person/ child is on home treatment, the person/parent/carer will have been instructed to bring factor concentrate with them.
9. If the haemophiliac's own product is not available, or they are not on home treatment, the product can be obtained from the blood issue fridge room next door to blood bank, or a fridge in CED resus:
   **Pharmacy keep the main stock but for emergency use a small amount is kept in 2 places around the Trust:**

   1. **Blood issue fridge room on the 5th Floor**, next door to blood bank: combination for fridge is 2244.
   Refacto (recombinant factor 8 for haemophilia A): 5000 units
   Advate, (recombinant factor 8 for haemophilia A): 5000 units
   Benefix (recombinant factor 9 for haemophilia B): 10,000 units
   Wilate (von Willebrand and Factor 8, plasma derived, for type 2 VWD): 5000 units
   FEIBA: 5000 units

   2. **Childrens emergency dept** - in a fridge in the room at the back of children's' resus:
   Refacto and advate - 5000 units each
   Wilate 2000 units.

10. If stock is removed from either fridge , the record sheet must be filled in (available on top of the fridge).
11. Desmopressin is available from Pharmacy.
12. Details of the person with haemophilia's usual treatment should be available in their electronic record and alert card.
    Other information about treatment can be found from the medical notes or the clinic letters.
    Patients from outside the Derbyshire area should carry a card detailing their treatment and usual centre. If this is not available, the patient/carer must be asked for information about their usual treatment centre and usual treatment. It is advised that their usual treatment centre should be contacted to confirm the information supplied.

13. If admission is required, children should be admitted to Puffin ward, adults to ward 301 or 302. However, it may be clinically appropriate to admit to another specialty ward in which case haematology will have shared care.
14. The haemophilia team must be notified of the person/child's presentation on the next working day (whether or not admission is required).

**Management of specific bleeding episodes**

The table below shows target levels for treating bleeding episodes.

Factor levels post-treatment are not always required. This will be guided by the haematologist.

| **Type of bleed** | **Target activity**<br><br>**(Factor VIII or IX)** |
|---|---|
| Early haemarthrosis<br><br>Early muscle bleed<br><br>Most cutaneous / soft tissue bleeds | Target 50-60% =<br><br>FVIII: 25 – 30 u/kg<br><br>FIX: 40 – 60 u/kg |
| Significant haemarthrosis<br><br>Significant muscle bleed<br><br>Oral bleeds | Target 60 – 80% =<br><br>FVIII: 30 – 40 u/kg<br><br>FIX: 60 – 80 u/kg |
| Gastro-intestinal, intracranial, intra-abdominal, intra-thoracic or bleeds involving airway | Target 100%<br><br>FVIII: 50 u/kg<br><br>FIX: 100 -120 u/kg |

*Head injury*
Any person with haemophilia who presents with anything other than a trivial bump to the head should be treated immediately aiming to achieve factor levels of 100%. The patient should be admitted and observed appropriately. There should be a lower threshold for requesting a CT head compared to people without haemophilia as there is an increased risk of intracranial haemorrhage in haemophilia.

*Haemarthrosis*
Children (and some adults) with severe (and moderate) haemophilia (without inhibitors) will be treated with prophylactic factor concentrate with the aim of preventing haemarthrosis altogether. The aim is zero joint bleeds.
Presentation with haemarthrosis therefore should be unusual, but if it does occur, it is essential that treatment is delivered as soon as possible to limit long term joint damage.
Haemarthrosis can occur after trauma in patients receiving prophylaxis and in patient with mild haemophilia.

The earliest clinical signs of a joint bleed are increased warmth over the area and discomfort with movement, particularly at the ends of range. Later symptoms and signs include pain at rest, swelling, tenderness, and extreme loss of motion.
Following a joint bleed, flexion is usually the most comfortable position, and any attempt to change this position causes more pain. Secondary muscle spasm follows as the patient tries to prevent motion and the joint appears “frozen”.
The goal of treatment of acute haemarthrosis is to stop the bleeding as soon as possible. This should ideally occur as soon as a bleed is suspected, rather than after the onset of overt swelling and pain.

Evaluate the patient clinically. Usually, X-rays are not indicated unless a fracture is suspected.

Factor concentrate should be administered according to the guidance above .

Adjunctive treatment to factor concentrate includes:

- Adequate analgesia (avoiding NSAIDs). NCA/PCA may be required. Pain team should be involved if needed.
- Ice/cold pack applied around the joint for 20min 3-4 times per day (not directly to skin)
- Rest and elevation (splinting may be considered)
- Admission for analgesia and rest may occasionally be required.
- Orthopaedic review if compartment syndrome is suspected.

Bleeding will often respond to one treatment. If symptoms fail to improve, a further dose of factor concentrate may be required. This needs to be discussed with the haematologist on call for haemophilia.

Most people with haemophilia will be able to go home. All attendances must be reported to the haemophilia unit as soon as possible either by phone: ext 87973 or email: dhft.haematologysecretaries@nhs.net.

*Muscle bleeds*
Muscle bleeds can occur in any muscle of the body, usually from a direct blow or a sudden stretch. Small children may develop muscle bleeding when first starting to weight bear and walk eg in the gluteal muscles.
Haemophiliacs receiving factor prophylaxis may still develop muscle bleeds after trauma or exercise. Muscle bleeds can be either diagnosed clinically and/or by imaging studies.

Symptoms of muscle bleeds are:

- aching in the muscle
- maintenance of the limb in a position of comfort severe pain if the muscle is stretched
- pain if the muscle is made to actively contract tension and tenderness upon palpation and possible swelling
- functional impairment eg limp

Early identification and proper management of muscle bleeds is important to prevent permanent contracture, re-bleeding, and formation of pseudotumours.

Sites of muscle bleeding that are associated with neurovascular compromise, such as the deep flexor muscle groups of the limbs, require immediate
management to prevent permanent damage and loss of function. These groups include:

- the iliopsoas muscle

- the superior-posterior and deep posterior compartments of the lower leg
- the flexor group of forearm muscles

Bleeding can also occur in more superficial muscles.

Factor treatment should be given as in the table above.

Minor bleeds are likely only to need one treatment and the person with haemophilia may safely be discharged.

Bleeds in significant areas such as ileo-psoas or if compartment syndrome is a risk, are likely to require inpatient treatment.

*Haematuria*
Mild haematuria may respond to simple increase in hydration.
MSU should be taken and infection treated as appropriate.
Significant haematuria will require haemostatic replacement therapy.
Admission may be required if the haemophiliac is unable to maintain an adequate oral intake of fluids.
Tranexamic acid is contra-indicated.

*Bleeding into the tongue or pharynx*
Significant bleeding in this area is a medical emergency.
Urgent factor replacement and tranexamic acid are required.
Admission for observation and protection of the airway will be required in significant bleeds.

*Epistaxis*
Usual ENT assessment for epistaxis should be given.
Systemic and/or topical tranexamic acid should be given.
In severe epistaxis, factor replacement may be required.

*Oral bleeding*
Mouth bleeding may occur in children after shedding of deciduous teeth, following dental extraction, and after trauma.
Topical or systemic tranexamic acid should be used.
Consultation with the oral surgery team is recommended.
Haemostatic replacement therapy may be required in significant bleeding.

*Superficial cuts*
If bleeding is not controlled with pressure and local treatment (glue/sutures etc), haemostatic replacement therapy may be required.
Tranexamic acid should be given and may be sufficient in many cases.

**Administration of desmopressin**

Information about dosing and administration of desmopressin can be found in the relevant guideline:

https://derby.koha-ptfs.co.uk/cgi-bin/koha/opac-detail.pl?biblionumber=1050&query_desc=kw%2Cwrdl%3A%20haemophilia

Treatment is given to raise the coagulation factor level to that required to achieve haemostasis. Target levels are given in the table above , but should always be discussed with a haematologist.

**Administration of clotting factor concentrates**

All patients on prophylaxis should have a personalised treatment plan with doses for types of bleeding specified. This will be available in the case notes and their electronic record.

*Dose calculation*

Haemophilia A (FVIII):

$$\text{Dose required} = \frac{(\text{target activity(iu/dL)} - \text{patient's baseline (iu/dL)}) \times \text{weight (kg)}}{2}$$

This assumes that 1 unit of infused factor VIII concentrate will raise the plasma level by 2iu/dL.

Haemophilia B (FIX)
The recovery of different factor IX concentrated varies. For example, one unit of standard half-life FIX concentrate (Benefix) will raise the factor activity by about 0.7iu/dL in children, whereas one unit of the extended half-life concentrate Alprolix will raise the factor level by 1iu/dL.

Dose of Benefix = (target activity (iu/dL) – patient's baseline(iu/dL)) x weight (kg) x 1.0 – 1.2
Dose of Alprolix= (target activity (iu/dL) – patient's baseline(iu/dL)) x weight (kg)

The dose of concentrate to be administered should always be discussed with a haematologist.

The dose should always be rounded up to the nearest vial size to avoid wastage.

*Product selection*
All patients should be treated wherever possible with their current product.
Patients on home treatment should have a supply of product at home and they/their parent/carer will have been instructed to bring the product to hospital with them.
If the haemophiliac's own product is not available, or they are not on home treatment, the product can be obtained from the blood issue fridge room next door to blood bank, or a fridge in CED resus:

Pharmacy keep the main stock but for emergency use a small amount is kept in 2 places around the Trust:

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requested from Blood Bank . A blood bank request form should be completed with details of the product name and vial sizes required.
If the clinician collects the product in person from the Blood Bank cold room (haematology staff only), the haemophilia unit factor collection form should be completed with all details – forms are to be found in the cold room fridge with the products.

Details of the patient's usual product are available from:

- the parent/carer
- the patient's bleeding disorders card
- The patient's personalized plan (in their clinical notes and their electronic record)
- Clinic letters and clinical notes in the patient's electronic record.

If the patient is registered at another Haemophilia Centre (not Derby), their centre should be contacted immediately to confirm information from the patient's parent/carer and/or alert card.

*How to and who can administer the concentrate?*
All clotting factor concentrates administered in hospital must be prescribed on the patient's prescription chart (this may be on iCM or Lorenzo).
**It is essential that the decision to prescribe, the batch number, the reason for giving and the dose calculation is recorded in the patient's notes.**
Family members who have received appropriate training can administer concentrates.
Older children and adults may have learned to administer their own treatment.
If the patient or carer is unable to administer the treatment, all hospital staff who have received training in the administration of intravenous drugs may administer clotting factor concentrates. Details can be found on Medusa.

# PROPHYLAXIS HOME TREATMENT REGIME

Date: ……. Name: ……

Date of Birth: …… NHS Number:

Diagnosis: …… Factor Baseline:

Weight: …… Factor Product:

## PROPHYLAXIS REGIME

| | | | |
|---|---|---|---|
| **Factor:** | | | |
| **Dose:** | | | |
| **Frequency:** | | | |
| **Comment:** | | | |
| **Desired Trough Level:** | | | |
| **Actual Trough Level:** | | **Date:** | |

## GUIDANCE TO MANAGEMENT OF A BLEED

| TYPE OF BLEED | TARGET FACTOR LEVEL | DOSE |
|---|---|---|
| **Superficial bleed, nose or gum bleed, early joint/muscle bleed:** | **50 – 60%** | |
| **Moderate joint or deep muscle bleed:** | **60 – 80%** | |
| **Major joint bleed, stomach/ bowel/head or airway bleed:** | **80 – 100%** | |

**! NOTE:** Dose is calculated according to your factor baseline level and your **weight**, therefore may need to be adjusted. In many circumstances a follow up dose of factor is required.

If you have any questions or are in any doubt about treating your bleed, please contact the Haemophilia Team.

Name:.. .. Signature: ……. Date:… ….

## 5. References (including any links to NICE Guidance etc.)

Emergency and out of hours care for patients with bleeding disorders – Standards of care for assessment and treatment. John Hanley, Mary Mathias, Emma Franklin, Chris Harrington,Oliver Chapman, Kate Talks and Stephanie Smith on behalf of the UK Haemophilia Centre Doctors Organisation (UKHCDO)

Guidelines for the management of acute joint bleeds and chronic synovitis in haemophilia

A United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) guideline

J. Hanley, A. Mckernan, M. D. Creagh, S Classey, P. Mclaughlin, N. Goddard, P. J. Briggs, S. Frostick, P. Giangrande, J. Wilde,J. Thachil and P. Chowdary on behalf of the Musculoskeletal Working Party of the UKHCDO. Haemophilia (2017), 1–10

Guidelines for the management of haemophilia. A. Srivastava, A. K. Brewer, E. P. Mauser-Bunschoten, N. S. Key, S. Kitchen, A. Llinas, C. A. Ludlam, J. N. Mahlangu, K. Mulder, M. C. Poon And A. Street; Treatment Guidelines Working Group On Behalf Of The World Federation Of Hemophilia. Hemophilia 2013, 19, e1–e47

## 6. Documentation Controls

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|---|---|
| Development of Guideline: | A McKernan Consultant Haematologist |
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| Approved By: | Thrombosis group 5/3/19<br>Reviewed A.McKernan Dec 23<br>CDCS Division - Dec 23 |
| Review Date: | Dec 2026 |
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