Haematology

Disease Treatment Algorithm:

Haemophilia and Related Bleeding Disorders Emergency Management

THIS IS A CONTROLLED DOCUMENT

The contents of this document must not be modified

This protocol is authorised for use at
Norfolk and Norwich University Hospital

This protocol may be authorised for use at different sites on a named patient basis

Document reference	H.MA.190 v10 Trust Doc 8782 v9		
Policy Name	Haemophilia and Related Bleeding Disorders Emergency Management		
Author (Name and Position)	Dr Hamish Lyall Consultant Haematologist, NNUH		
Approver (Name and Position)	Dr Suzanne Docherty Consultant Haematologist, NNUH		
Date of issue	26.11.2025	Review date	26.11.2027

HAEMATOLOGY: Disease Treatment Algorithm

H.MA.190 – Haemophilia and Related Bleeding Disorders – Emergency Management

1. Introduction

The Norfolk and Norwich University Hospital NHS Foundation Trust is a registered haemophilia centre. For adult patients this service is provided by the haematology department.
Children are registered with the comprehensive care centre at Addenbrookes hospital, Cambridge but may present to NNUHFT for emergency treatment. This document gives guidance on where to find information and management of an acute bleeding episode

The term haemophilia and related bleeding disorders includes:

- Haemophilia A (Factor VIII deficiency)
- Haemophilia B (Factor IX deficiency)
- Other coagulation factor deficiencies (e.g. Factor XI)
- Von Willebrand Disease (type 1, type 2, type 3)
- Platelet disorders (including Glanzmann thrombasthaenia)
- Acquired haemophilia A (Factor VIII deficiency)

2. Emergency sources of information

- Patients known to the Norfolk and Norwich haemophilia centre have been issued with an ‘alert card’. This should contain specific details of their condition. These individuals have been advised to contact the haematology department directly if they have an emergency bleeding problem.
- Paediatric patients may have an individualised protocol in the open access folder in childrens assessment unit (CAU)
- Adult patients with have a Haematology annotation (K:drive)
- Electronic template
- Patients not known to the Norfolk and Norwich Haemophilia centre may occasionally present to the hospital. This is usually temporary visitors (persons on holiday) or students from the UEA. They will usually be registered with a haemophilia centre at their local hospital in the UK and will have been issued with an alert card.

3. General points

- **The consultant haematologist or registrar on call must ALWAYS be contacted for advice**
- It is best to assume that a presenting problem could be related to bleeding until proven otherwise
- Some patients are considered at risk of vCJD for public heath purposes due to their exposure to UK sourced plasma products between 1990-2001. If known to NNUHFT these individuals will have an alert on PAS. Infection control should be notified on admission if a procedure needs to be performed to allow for a risk assessment of surgical instruments and safe disposal of equipment.

4. Treatment of a bleeding episode

- Patients should receive the correct factor concentrate without delay. The products available at NNUHFT and the dosing schedules are in Appendix A.
- Treatment should be discussed with a haematologist first
- NSAIDs and IM injections should be avoided
- For uncomplicated/non severe bleeds patients can usually be discharged home and do not necessarily need admission

- **Admissions Pathways**

- Adult patients have direct access to the haematology department by utilising the Acute Oncology Service (AOHS) pathway (01603 646753). See haematology handbook H006. **The nurse taking the phone call MUST seek advice from the on call haematology registrar or Consultant**.
- During the working day patients requiring review are assessed on the Hoveton day unit.
- When AOHS/Hoveton is not available patients are directed to ED as per the haematology admissions pathway.
- Patients contacting for advice with a potentially life threatening bleeding problem (e.g. head injury) should be advised to go directly to the emergency department (ED). The ED should be contacted in advance to advise on clotting factor replacement (call ED nurse coordinator ext 3312)
- Paediatric patients have direct access to CAU. Parents can contact CAU (01603 289774) requesting their child to be seen. The attending CAU doctor should discuss with Addenbrookes in the first instance. There may be a recent care plan or letter in the CAU open access folder to support management

5. Development and consultation process

This protocol has been developed by the author on behalf of the Haematology Department at the Norfolk and Norwich University Hospital. During its development it has been circulated to the Haematology Consultants. The childrens pathway has been agreed with the lead paediatrician for haematology Dr J Ponnampalam (Consultant Paediatrician).

Appendix A

Factor VIII replacement

Recombinant Factor VIII (Advate)		
Type of Haemorrhage	**Target Level**	**Regimen**
Early joint bleed or muscle bleed, oral bleed	>40%	Given 12 hourly. 1 – 2 doses usually satisfactory.
More extensive joint bleed or muscle bleed. Large haematoma	>60%	Give 12 hourly. May need treatment for >1 day.
Life threatening haemorrhage	>100%	Give 12 hourly. Frequency may need increasing to 8 hourly. Monitor levels to maintain satisfactory trough (pre) level. Will need treatment for several days.
Surgery (minor)	>60%	Give 12 hourly. Duration of treatment depends on type of surgery and risk of post operative bleeding.
Surgery (major)	>100%	Give 12 hourly. Frequency may need increasing to 8 hourly. Monitor levels to maintain satisfactory trough (pre) level. Will need treatment or several days.

Factor VIII dose = $\frac{\text{(target level – patients level) x Weight (kg)}}{2}$

e.g.

60kg patient with a head injury, historical Factor VIII level 7%.

Dose = $\frac{(100 - 7) \times 60}{2}$ = 2790units = 3000units (rounded up to nearest vial size)

Final factor VIII level must be greater than target level (see table above) and should not exceed 150%

N.B
Check previous doses and levels if available to guide dosing.
In an emergency if no details can be obtained give 50units/kg
Advate is available in 1000unit vials
For information on administration see Appendix B
For patients with mild haemophilia who do not have life threatening bleeding consider DDAVP (**Protocol H.T.C012.4**)

Factor IX replacement

Recombinant Factor IX (BeneFIX)		
Type of Haemorrhage	**Target Level**	**Regimen**
Early joint bleed or muscle bleed. Oral bleed	>40%	Give once daily. Single dose usually satisfactory.
More extensive joint bleed or muscle bleed. Large haematoma	>60%	Give once daily. May need treatment for >1 day.
Life threatening haemorrhage	>100%	Give daily. Monitor levels to maintain satisfactory trough (pre) level. Frequency of doses may need increasing to 12 hourly or 8 hourly. Will need treatment for several days
Surgery (minor)	>60%	Give daily for at least one day. Duration will depend on type of surgery and bleeding risk.
Surgery (major)	>100%	Give daily. Monitor levels to maintain satisfactory trough (pre) level. Frequency of doses may need increasing to 12 hourly or 8 hourly. Will need treatment for several days.

Factor IX dose = (target level – patients level) x Weight (kg) x 1.25

e.g.

60kg male with a head injury, historical Factor IX level 7%.

Dose = (100 – 7) x 60 x 1.25 = 6975units = 7000 units (rounded up to nearest vial size)

Final factor IX level must be greater than target level (see table above) and should not exceed 150%

Recombinant Factor IX (Alprolix)		
Type of Haemorrhage	**Target Level**	**Regimen**
Early joint bleed or muscle bleed. Oral bleed	>40%	Give once daily. Single dose usually satisfactory.
More extensive joint bleed or muscle bleed. Large haematoma	>60%	Give once daily. May need treatment for >1 day.
Life threatening haemorrhage	>100%	Give daily. Monitor levels to maintain satisfactory trough (pre) level. Frequency of doses may need increasing to 12 hourly or 8 hourly. Will need treatment for several days
Surgery (minor)	>60%	Give daily for at least one day. Duration will depend on type of surgery and bleeding risk.
Surgery (major)	>100%	Give daily. Monitor levels to maintain satisfactory trough (pre) level. Frequency of doses may need increasing to 12 hourly or 8 hourly. Will need treatment for several days.

Factor IX dose = (target level – patients level) x Weight (kg)

e.g.

60kg male with a head injury, historical Factor IX level 7%.

Dose = (100 – 7) x 60 = 5580 units = 6000 units (rounded up to nearest vial size)

Final factor IX level must be greater than target level (see table above) and should not exceed 150%

N.B.

Check previous doses and levels if available to guide dosing.
In an emergency if no details can be obtained give 100 units/kg
BeneFIX is available in 1000 unit vials
Alprolix is available in 1000 unit, 2000 unit and 3000 unit vials
DDAVP is not a treatment for FIX deficiency (Factor IX levels do not rise with DDAVP)
For information on administration see Appendix B

Von Willebrand Factor Replacement

- Factor VIII/Von Willebrand Factor concentrate (Voncento)
- Recombinant von Willebrand concentrate (Veyvondi)

Used for the treatment of Von Willebrands disease in persons with bleeding, or who are non-responsive to, or have a contraindication to DDAVP.

NB: VWF concentrates should be prescribed in VWF IU (not Factor VIII IU). To minimise the risk of dosing errors state VWF IU on prescription.

Voncento (ratio FVIII to VWF:RCo is 1 : 2.4)

Vial sizes
1200 VWF IU (contains 500 IU Factor VIII)
2400 VWF IU (contains 1000 IU Factor VIII)

In an emergency if VWF levels not known give Voncento 60 VWF IU/kg

To calculate dose use patient baseline VWF activity level. 1 VWF IU/kg increases the VWF:RCo by approximately 0.02iu/ml (2%)

e.g.

Known type 2 VWD. Historical levels: factor VIII 30%, VWF Antigen 28%, VWF activity 10%.
Weight 70kg.
Target VWF:RCo 100%

$\frac{(100 - 10) \times 70}{2}$ = 3150 units = 3600 units (rounded to 1x 2400 unit and 1 x 1200 unit vials)

Estimated final levels VWF:RCo 113%, FVIII 73%

Prescribe Voncento 3600 VWF units

Veyvondi

Veyvondi is a recombinant product and therefore not derived from blood products. It is licensed for treatment of patient with VWD age > 18 years for treatment of haemorrhage and surgical bleeding and prevention of surgical bleeding. It is not licensed for regular prophylaxis.
For 'off label' treatment of children with Veyvondi discuss with paediatric centre at Addenbrookes Hospital, Cambridge.

Veyvondi contains no factor VIII. 1IU/kg body weight raises VWF:RCo by 2%.

The first dose of Veyvondi should be 40-80 IU/kg body weight.

Patients with baseline Factor VIII < 0.4 IU/ml.

A factor VIII level > 0.4 IU/ml is needed to ensure haemostasis. Following administration of Veyvondi most patients will have a rise in factor VIII to above 0.4 iu/ml after 6 hours which is sustained for up to 72 hours. If immediate haemostasis is needed give a dose of recombinant factor VIII (Advate) within 10 mins following dose of Veyvondi.

N.B
Review previous records to guide treatment where possible
Many patients with VWD can be treated with DDAVP
Voncento is a blood product. Where possible patients should be made aware of this before treatment
Ensure final factor VIII level is predicted to be > 0.5iu/ml (50%).
For major haemorrhage ensure final factor VIII level and VWF:RCo level > 80-100%
VWF activity levels can be monitored in the laboratory similar to other coagulation factor levels using current VWF assay
Voncento is given once or twice daily in VWD
If patient is being treated for more than 1 day monitoring of levels is required as FVIII may start to accumulate
For information on administration see Appendix B

DDAVP - See protocol H.T.C012.4

Used for the treatment of mild haemophilia or VWD in patients who are known to, or who are likely to respond.

Dose: 0.3 mcg/kg by subcutaneous injection. Prescribe tranexamic acid 1g tds for 5-10 days in addition to DDAVP to support haemostasis.

N.B
1. DDAVP is obtained from pharmacy

2. DDAVP should not be given if the patient has uncontrolled hypertension or ischaemic heart disease, heart failure or significant hyponatraemia
3. DDAVP should not be used for children under 2 years old
4. Peak factor levels are achieved 60-90mins post injection
5. Variable duration of responses are seen. A second dose can be given after 12-24 hours if ongoing haemostatic cover is required.
6. Tranexamic acid is contraindicated in persons with haematuria.

FEIBA

Used for treatment of patients with haemophilia who have an inhibitor to Factor VIII or IX (including acquired haemophilia).
Do not use if patient is receiving emicuzimab. Discuss alternatives with haemophilia centre at Addenbrookes.

Dose 50units/kg twice daily

e.g. for 100kg patient. Dose = 50 x 100 = 5000units

N.B

- Review previous records to guide treatment
- Vial size is 1000units
- FEIBA is a blood product. Where possible patients should be made aware of this before treatment
- Frequency can be increased to tds in severe bleeding
- Dose may be increased to 100units/kg if clinically not responding to treatment
- Maximum dose 200units/kg day
- No laboratory monitoring is available
- For major bleeding problems seek specialist advice from Addenbrookes
- Limited supplies of FEIBA are held at NNUH. Always check stock with blood bank. In an emergency contact Addenbrookes haemophilia service to help with supply of FEIBA if NNUHFT stocks cannot be ordered in time

Recombinant factor VIIa (Novoseven)

Indications

- treatment of Glanzmanns thrombasthaenia in persons with platelet antibodies
- Persons with haemophilia who have inhibitors (including acquired haemophilia)
- Factor VII deficiency.

<u>Glanzmann Thrombasthaenia</u>

(HLA matched platelet transfusions and tranexamic acid may be given as well)

Dose: 90mcg/kg every 2 hours for 3 doses then reassess clinically.

<u>Acquired haemophilia or persons with congenital haemophilia and inhibitor</u>

Dose: 90mcg/kg every 2-3 hours. Give 2 doses and then reassess clinically.

Factor VII deficiency

Dose: 15-30 units/kg Give 4-6 hourly depending on clinical situation

N.B

- Vial size 1mg, 2mg, 5mg
- No monitoring is required
- For information on administration see Appendix B

Fibrinogen Concentrate (Fibryga)

Indication

- Hypofibrinogenaemia/Dysfibrinogenaemia

Dose: Use patient's fibrinogen (Clauss) level to dose. For major bleeding/critical haemostasis use target level of 1.5g/L. This is to achieve a level > 1g/L which is needed for haemostasis. Half life is 3-4 days. Measure levels if subsequent doses needed.

For patients > 12 years of age use formula below. For < 12 years of age see product literature

Dose in **milligrams/kg body weight** = $\frac{\text{target Level (g/L)} - \text{patients level (g/L)}}{0.018}$

e.g. 70 kg patient with known fibrinogen level 0.36g/L presenting with major haemorrhage

Dose = $\frac{1.5-0.36}{0.018} \times 70 = 63$ mg/kg = 4 grams (rounded to 1g vial size)

NB.

- Fibryga is available in 1 g vials
- For acquired hypofibrinogenaemia e.g. (major haemorrhage, DIC). The dose for adult patients is 1-2 grams initially with subsequent doses as required. In severe haemorrhage e.g major surgery larger doses 4-8 g may be required**.**
- For information on administration see Appendix B

Appendix B Administration

How to administer coagulation factor concentrates for haemophilia treatment

- Prescribe products using brand name on EPMA. If product is not registered on EPMA, prescribe on paper chart
- Collect medication from blood bank. If patient brings in own supply from home this may be used
- Some patients are trained in home therapy and are able to self-administer treatment. This is permissible, providing that their ability to administer treatment is not currently impaired. Observe treatment given and document.
- Obtain IV access by inserting an intravenous cannula. A 'blue' cannula is adequate for factor concentrate administration. Patients who are experienced in their haemophilia treatment will often know their veins very well and be a useful guide as to which vein is best.
- Check expiry date of products – important if using patients own supply
- Remove instructions from the packet and reconstitute the product as per package instructions. This will result in a syringe of factor concentrate ready for administration if followed correctly.
- Discard the butterfly cannula supplied with the product. This is used to enable patients who have been trained in home therapy to self-administer treatment at home.
- Reconstitute all the required vials before treating the patient. Label the syringes.
- Factor concentrates should be given by slow intravenous bolus injection directly into the cannula or via the 'octopus' extension set on the cannula. Do not give into a running drip. It is not necessary to give via an infusion pump, although this can be used for FEIBA which can have a long infusion time.
- Patients will vary in how they prefer the product to be given. Ask patient at what rate they prefer their treatment to be given, but do not exceed maximum permitted rate: see table below.
- Sit next to the patient and inject factor concentrate slowly, the procedure will usually take 10-15mins. Note for FEIBA this may take significantly longer.
- Record on EPMA or paper chart to confirm administration
- Coagulation factor concentrates are not always listed on Medusa. If any queries arise read package insert. If further advise needed discuss with haematology registrar or Consultant.

Infusion Rates

Coagulation Factor Concentrate	Recommended infusion rate
Advate	Infuse as per patient comfort level. Not to exceed 10 ml per minute.
Alprolix	Infuse as per patient comfort level. Not to exceed 10 ml per minute.
BeneFIX	Infuse as per patient comfort level. Not to exceed 4 ml per minute
FEIBA	Not to exceed 2 units / kg body weight / minute
Fibryga	Maximum rate congenital hypofibrinogenaemia 5 ml / min acquired fibrinogen deficiency 10 ml / min
Novoseven	Administer over 2-5 minutes
Veyvondi	Maximum rate 4 ml/min
Voncento	Maximum 6 ml/minute Infuse as per patient comfort level

AMENDMENT HISTORY

A record of changes in this document.

Date	Updated version number	Previous version number	Page Number/ Section (updated version)	Details
27.07.2012	2	1	All	Document has been split into 2 protocols this one remains for emergency use with additional information on the front 2 pages. **For outpatient management now new treatment algorithm H191**
07.01.15	3	2	All	Reviewed by Dr Lyall: - VCJD risk updated, Advate added, Wilate added, Riastap added Minor typographical changes
03.04.2017	4	3	All	Reviewed by Dr H Lyall. Dr Katy Rice replaces Dr G Turner as approver – no changes made Admissions pathway flow chart replaced with text. Minor changes to reflect H006
31.08.18	5	4	All	Helixate, Haemate P removed. Novoeight added. Administration appendix added. Admissions pathway approved at haematology quality meeting 08.10.18.
03.07.19	6	5	All	Voncento added “Mulbarton” changed to “haematology ward”
09.09.21 21.09.21	7	6	All	HDL review : Veyvondi added; AOS area added; Other minor changes for clarity. LL Added ‘A’ & ‘B’ to appendices, updating reference to each in the text. Added hyperlink to the SOP H.T.C012.4 DDAVP references.
24.10.23	8	7		Review by HDL Concentrates, vial sizes and infusion rate table updated; Emicuzimab caution added to FEIBA; Vial size rounding removed
12.03.25	9	8		DRS links updated following migration to IQM cloud. SWC.002 allows amendment to proceed without further approval in this instance. Review date remains unchanged
26.11.25	10	9		Alprolix added. Blood bank register removed. Other minor updates for clarification. Admissions pathway updated. Grammatical updates