North West Anglia
NHS Foundation Trust

Cryoprecipitate Transfusion – Guideline for Practice

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Target Audience	All staff involved in prescribing and administering blood components

North West Anglia NHS Foundation Trust

DOCUMENT VERSION CONTROL SCHEDULE					
Year and Version Number	**Author**	**Date Published on Document Library**	**Revisions from previous issue**	**Ratification Committee**	**Date of Ratification**
2009 Version 1	Dr Kanchan Rege	May 2009	Original version of document	Quality Governance Operational Committee	April 2009
2013 Version 2	Dr Kanchan Rege	February 2013	Review led by Hospital Transfusion Team. Re formatted into current trust procedural documents format	Quality Governance Operational Committee	27/02/2013
2015 Version 3	Dr M Sivakumaran	13/07/2016	Review led by Hospital Transfusion Team. NICE guidance on indications for use incorporated. Advice on Hepatitis E negative components included.	Quality Governance Operational Committee	12/07/2016
2019 Version 4	Dr M Sivakumaran Kaye Bowen Andy King Venables	14/10/2019	Advice on Hepatitis E negative components removed as all components now screened. Early use advised in major obstetric haemorrhage when fibrinogen is <2·0g/L. Revised NHSBT leaflet included.	Quality Governance Operational Committee	10/10/2019

Key Points

- Cryoprecipitate is the cryoglobulin fraction of plasma obtained by thawing a single donation of FFP at 4 +/- 2 ˚C.
- Cryoprecipitate is rich in Factor VIII, von Willebrand factor and Fibrinogen.
- The indications for its use are limited but are primarily to provide fibrinogen to prevent bleeding due to coagulopathy.
- Cryoprecipitate is stored frozen (-30°C) and is defrosted in preparation for patient use. At least 30 minutes should be allowed from the time of request to issue to permit appropriate thawing.
- Cryoprecipitate for patients born after 1st Jan 1996 is collected from non UK donors, to reduce the risk of transmission of variant CJD. It is virally inactivated by treatment with Methylene Blue or solvent detergent, to reduce the risk of transmission of pathogens

Contents

1. Introduction

Cryoprecipitate is manufactured by the UK Blood Transfusion Services (UKBTS) by slowly thawing FFP overnight at 4°C. This precipitates out cryoproteins: FVIII, von Willebrand factor (VWF), FXIII, fibronectin and fibrinogen. After centrifugation, the cryoproteins are resuspended in a reduced volume of plasma (20–60 ml).

UK Blood Transfusion Services (UKBTS) produce pooled cryoprecipitate prepared from five single donations which contain approximately 700 mg fibrinogen and 350 iu FVIII in a typical volume of 200–280 ml.

Cryoprecipitate is stored at a temperature of −30°C for a maximum of 36 months. When requesting cryoprecipitate from the Transfusion Laboratory, at least 30 minutes should be allowed from the time of request to issue to permit appropriate thawing.

Once thawed, cryoprecipitate must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4h.

The risks of transfusing cryoprecipitate are similar to those of other UK blood components. Of particular concern are allergic reactions and anaphylaxis, pulmonary complications and haemolysis from transfused antibodies to blood group antigens especially A and B.

Cryoprecipitate is produced from FFP from voluntary blood donations collected in the UK. However, cryoprecipitate for use in patients born after 1st Jan 1996 is produced from FFP donated by non UK donors, which is then treated with Methylene Blue to reduce the risk of transmission of pathogens. This measure is designed to reduce the slight possible risk of transmission of variant Creutzfeldt Jacob Disease (vCJD), as those born after 1 January 1996 are unlikely to have been exposed via the food chain.

There is no current clinical indication for cryoprecipitate-depleted plasma (the supernatant left after cryoprecipitate has been removed from plasma) in the UK; this product is no longer produced by the UKBTS.

2. Purpose

The purpose of this document is to give guidance to clinical staff who may be involved in the requesting, prescription or administration of Cryoprecipitate in North West Anglia NHS Foundation Trust. They aim to standardise use of cryoprecipitate across the trust in line with national guidelines.

3. Scope

These guidelines apply to all members of staff involved with the prescription, handling and administration of Cryoprecipitate.

4. Definition of terms

FFP – Fresh Frozen Plasma- Plasma produced from blood donations and stored at -30°C.

Cryoprecipitate – the cryoglobulin fraction of plasma obtained by thawing a single donation of Fresh Frozen Plasma (FFP) at 4˚C (+/- 2 ˚C).

DIC – Disseminated Intravascular Coagulation- An acquired syndrome characterised by activation of coagulation pathways, resulting in formation of intravascular thrombi and depletion of platelets and coagulation factors.

DDAVP – desmopressin acetate (1-deamino-8-D-arginine vasopressin).

5. Indications for use of cryoprecipitate

Disseminated Intravascular Coagulation (DIC) in the presence of haemorrhage when fibrinogen <1g/L.

Liver Disease with bleeding or pre surgery when fibrinogen <1g/L.

Bleeding associated with thrombolytic therapy causing hypofibrinogenaemia.

Major haemorrhage to maintain fibrinogen >1.5g/L. In major obstetric haemorrhage consideration should be given to the early use of fibrinogen supplementation when fibrinogen levels are <2·0g/L and there is on-going bleeding

Renal failure or liver failure with abnormal bleeding where DDAVP not appropriate.

Inherited hypofibrinogenaemia when concentrate not available.

Consider cryoprecipitate transfusions for patients without major haemorrhage who have clinically significant bleeding and a fibrinogen level below 1.5 g/L.

Do not offer cryoprecipitate transfusions to correct the fibrinogen level in patients who are not bleeding and are not having invasive procedures or surgery with a risk of clinically significant bleeding.

Consider prophylactic cryoprecipitate transfusions if fibrinogen is <1·0g/L, and other factors (i.e. personal/family bleeding history, drug history, bleeding risk associated with planned procedure) indicate a significant bleeding risk prior to a procedure.

6. Dose and Group

An adult therapeutic dose is 2 packs (of 5 donor pools), which contain 3-6g of fibrinogen in a volume of 200 to 500 ml, and will raise the plasma fibrinogen level by about 1g/L.

Paediatric packs are available and contain approximately 30mls. For children, the recommended dose is 5–10 ml/kg body weight, using the higher volume particularly in bleeding patients.

Patients born after 1st January 1996 should only receive pathogen reduced cryoprecipitate, this is Methylene blue treated FFP from non-UK donors.

Group compatible cryoprecipitate should be used where possible. Cryoprecipitate which is not of the same ABO group should only be used if it contains no high-titre anti A or anti B. Group O cryoprecipitate must only be given to Group O patients.

Cryoprecipitate of any RhD group may be transfused. If RhD positive cryoprecipitate is given to an RhD negative individual, no anti-D prophylaxis is required

Cryoprecipitate has no cellular content and therefore does not need to be irradiated or selected as Cytomegalovirus (CMV) sero-negative.

The prescription should ideally be made on the dedicated blood product prescription chart. For adults the prescription must indicate the number of packs to be administered (e.g.: 2 packs of 5 pools). In paediatrics, the prescription must be in mls/kg body weight.

Reassess the patient's clinical condition, repeat the fibrinogen level measurement and give further doses if needed.

7. Administration

Cryoprecipitate must be administered through a 170-200micron filter (a standard blood giving set). A 170-200micron filter is also required if giving cryoprecipitate via a syringe for neonatal transfusion.

The cryoprecipitate pack should be visually inspected for pack integrity and discolouration prior to transfusion. Check that packs do not appear grainy or more cloudy than usual. If in doubt, DO NOT TRANSFUSE and contact the transfusion laboratory for advice.

All patients receiving cryoprecipitate must wear a trust ID band. The patient’s identity must be checked by 2 members of staff (either a Doctor, Registered Nurse or Midwife or ODP) prior to commencement of the transfusion. The details on the tag attached to the pack must be checked against the details on the patient’s ID band. In addition, the patient should be asked to confirm their name and date of birth, if they are able to do so.

Cryoprecipitate takes approximately 20- 30 minutes to thaw and for maximum efficacy should be administered as soon as possible after thawing. Start the transfusion as soon as the pack is received from the laboratory. Cryoprecipitate is stored at **room temperature** when thawed and must be used within 4 hours of thawing- there will be a note to this effect on the compatibility form issued with the pack. **Cryoprecipitate must never be refrigerated**, as this will cause re-precipitation**.**

In adults each pack should be given over 30-60 minutes, though more rapid infusion may be required in major bleeding. In paediatrics, the recommended rate of transfusion is 10-20ml/kg/hr.

Inform the patient of possible complications of transfusion, and the importance of reporting any adverse effects. A number of reactions may follow cryoprecipitate transfusions. They are the same as those which can occur after the transfusion of red cell concentrates including:-

- Febrile Reactions.
- Urticarial Reactions.
- Anaphylactic Reactions.
- Pulmonary complications such as Transfusion Associated Circulatory Overload (TACO) and Transfusion Associated Dyspnoea (Transfusion Related Acute Lung Injury TRALI is rare since cryoprecipitate is now sourced from male UK donors)
- Reaction to a bacterially contaminated unit.

Follow the same baseline, 15 minute and post transfusion observation checks as for red cell transfusions. If a reaction is suspected, STOP THE TRANSFUSION, and inform medical staff and the transfusion laboratory immediately. An adverse event and transfusion reaction form must be completed.

8. Endorsement

This guideline will be approved by the Hospital Transfusion Committee & endorsed by the Quality Governance Operational Committee.

9. Distribution

This guideline will be available on the trust intranet.

10. References

British Society of Haematology (2018) Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding Available : https://onlinelibrary.wiley.com/doi/full/10.1111/bjh.15167 [Accessed 10/06/2019]

British Committee for Standards in Haematology (2015) A practical guideline for the haematological management of major haemorrhage. Available:- https://onlinelibrary.wiley.com/doi/10.1111/bjh.13580 [Accessed 10/06/2019].

British Committee for Standards in Haematology (2004) Guidelines for the use of Fresh Frozen Plasma, Cryoprecipitate and Cryosupernatant. Available: http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2004.04972.x/full [Accessed 10/06/2019].

National Institute for Health and Care Excellence (2015) Blood Transfusion Available; https://www.nice.org.uk/guidance/ng24 [Accessed 10/06/2019].

Norfolk, D (ed) (2013). Handbook of Transfusion Medicine, 5th edition. Norwich: TSO. Available: http://www.transfusionguidelines.org.uk/transfusion-handbook [Accessed 10/06/2019].

11. Associated documents

- Blood Transfusion Policy.
- Guideline for Management of Massive blood loss.
- Policy for Competency Assessment of Staff Handling Collecting and/or Administering Blood and Blood Components.

Appendix 1 NHS Blood and Transplant Factsheet- Cryoprecipitate

NHS
Blood and Transplant

FACTSHEET

Standard Cryoprecipitate and Methylene Blue treated Cryoprecipitate

Information for Healthcare Professionals

The indications for transfusing cryoprecipitate are limited and specific.

Please transfuse appropriately.

Standard Cryoprecipitate

Cryoprecipitate contains concentrated Factor VIII:C, von Willebrand factor, fibrinogen, Factor XIII, and fibronectin and is produced by further processing of Fresh Frozen Plasma (FFP). Clinically it is used to replace fibrinogen.

As with FFP, the plasma from which the cryoprecipitate was produced has been leucodepleted and was obtained from a male donor to reduce the risk of transfusion-related acute lung injury (TRALI). Cryoprecipitate should be stored at a core temperature of -25°C or below for up to 36 months.

Clinical indications for use of cryoprecipitate in adults*

- **Clinically significant bleeding and a fibrinogen level <1.5g/L (<2g/L in obstetric bleeding)**
- **Fibrinogen level is <1g/L and pre-procedure**
- **Bleeding associated with thrombolytic therapy**
- **Inherited hypofibrinogenaemia where fibrinogen concentrate is not available.**

(*National Blood Transfusion Committee Indication Codes for Transfusion, 2016.)

Presentation and dosage of cryoprecipitate

Cryoprecipitate is available as a single unit, or as a pooled product made up of five single units. Pooled units are more commonly used to treat adult patients.

The adult therapeutic dose is two pooled units, or one single unit per 5-10kg body weight, dependant on the degree of fibrinogen deficiency. Paediatric dosing is 5-10mL/kg.

Methylene Blue treated Cryoprecipitate (MB Cryoprecipitate)

MB Cryoprecipitate is made from non-UK sourced plasma and should be used for those born after 1st January 1996.

MB Cryoprecipitate is produced from donations from previously tested donors, either males, or females who have been screened for any Human Leucocyte Antigens in the last 2 years; they are leucodepleted and treated with methylene blue (MB) followed by exposure to visible light to inactivate viral pathogens. Any residual MB is then removed.

MB Cryoprecipitate is available as a single unit, or as a pooled product made up from six single units.

If MB Cryoprecipitate is not available, patients should be treated with standard Cryoprecipitate, when indicated, in an emergency.

Practical instructions for the use of Cryoprecipitate

Once thawed, Cryoprecipitate must not be refrozen and should be used immediately. If delay is unavoidable the component should be stored at ambient temperature (i.e. **not** in a fridge), to prevent re-precipitation, and must be transfused within four hours. Transfuse using a standard blood giving set with a 170-200 micron filter. The typical infusion rate is 10-20mL/kg/hr (30-60 min per five pool unit).

Compatibility

ABO group identical Cryoprecipitate should be given whenever possible; if not possible Cryoprecipitate of a different ABO group may be acceptable (this must be discussed with the hospital transfusion laboratory staff or haematologist).

ABO compatibility for plasma components is different to that of red cells and **Group O Cryoprecipitate MUST only be given to group O recipients**.

Standard Cryo selection for ABO group

Recipient Group	O	A	B	AB
1st Choice	O	A	B	AB**
2nd Choice	A	B*	A*	A*
3rd Choice	B	–	–	B*

**Pooled Group AB Cryo. is in limited supply and only available on a named patient basis.
*Suitable for use in adults if negative for high titre anti-A/anti-B (labelled HT-)

MB Cryoprecipitate selection for ABO group

Recipient Group	O	A	B	AB
1st Choice	O	A	B	AB
2nd Choice	A	AB	AB	A*
3rd Choice	B	B*	A*	B*

*MB Cryoprecipitate is not tested for HT antibodies. Group compatible plasma should be used wherever possible. Non-compatible groups should only be used in emergencies when compatible groups are not available.

Group AB cryoprecipitate is haemolysin free and suitable for patients of any ABO group but is in limited supply.

D group

Cryoprecipitate **does not need to be matched for D group**. D positive plasma components may be given to D negative recipients without the need for anti-D Ig prophylaxis. The EU Blood Directive currently requires that the D group is stated on the label.

If you are unsure about the compatibility of Cryoprecipitate for your patient always check with your hospital transfusion laboratory staff before transfusing.

Specific requirements

Cryoprecipitate has no cellular content and therefore **does not need** to be irradiated or selected as Cytomegalovirus (CMV) sero-negative.

The use of other frozen components produced is covered in a separate factsheet:

- Standard Fresh Frozen Plasma (FFP), Methylene Blue treated FFP, and Solvent Detergent treated FFP.

References:

Green, L *et al* on behalf of British Society of Haematology (2018) *Guidelines on the spectrum of fresh frozen plasma and cryoprecipitate products: their handling and use in various patient groups in the absence of major bleeding.* Available at: https://www.b-s-h.org.uk/guidelines/guidelines/spectrum-of-fresh-frozen-plasma-and-cryoprecipitate-products/

Hunt, B *et al* on behalf of British Committee for Standards in Haematology Transfusion Task Force (2015) *A practical guideline for the haematological management of major haemorrhage.* Available at: https://b-s-h.org.uk/guidelines/guidelines/haematological-management-of-major-haemorrhage/

Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services *Professional Advisory Committee Guidelines for blood transfusion services* (red Book). Available at: https://www.transfusionguidelines.org/red-book/chapter-7-specifications-for-blood-components/7-15-fresh-frozen-plasma-leucocyte-depleted

National Blood Transfusion Committee (2016) *Indication Codes for Transfusion – An audit tool.* Available at: http://www.transfusionguidelines.org.uk/

New, H *et al* on behalf of British Committee for Standards in Haematology (2016) *Guidelines on transfusion for fetuses, neonates and older children.* Available at: https://b-s-h.org.uk/guidelines/guidelines/transfusion-for-fetuses-neonates-and-older-children/

NHS Blood and Transplant (2016) *Portfolio of components and guidance for their clinical use* (specification SPN223/8). Available at: http://hospital.blood.co.uk/products/

Norfolk D. (Ed) (2013) *Handbook of Transfusion Medicine* 5th Edition, The Stationery Office

Robinson, S. *et al* on behalf of the British Society for Haematology (BSH) (2017) Administration of Blood Components. Available at: https://www.b-s-h.org.uk/guidelines/guidelines/administration-of-blood-components/

Further supplies of this factsheet can be ordered by accessing
https://hospital.nhsbtleaflets.co.uk

For further information please consult your Hospital Blood Transfusion Policy or contact a member of your Hospital Transfusion Team.

NHS Blood and Transplant

NHS Blood and Transplant (NHSBT) saves and improves lives by providing a safe and reliable supply of blood components, organs, stem cells, tissues, and related services to the NHS and other UK health services. We manage the UK-wide voluntary donation system for blood, tissues, organs, and stem cells and turn these donations into products that can be used safely to save lives or radically improve the quality of people's lives.

We rely on thousands of members of the public who voluntarily donate their blood, organs, tissues, and stem cells. Their generosity means each year we're able to supply around 2 million units of blood to hospitals in England and 7,500 organ and tissue donations within the UK, which save or improve thousands more people's lives.

The information in this factsheet has been sourced from NHSBT transfusion experts. NHSBT Customer Services Patient Blood Management Practitioner Team does not accept any legal liability for errors or omissions.

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Quality Assurance Checklist - Version Number: 3 **Appendix: 3**

		Y/N/n/a	COMMENTS (where necessary)
1	**Title of document** Cryoprecipitate Transfusion – Guideline for Practice (C0330)		
2	**Type of document (e.g. Policy, guidance)**	Guideline	
	Is it clear whether the document type is a policy, guideline, procedure?	Yes	
3	**Introduction**		
	Are reasons for the development of the document clearly stated?	Yes	
4	**Content**		
	Is there a standard front cover?	Yes	
	Are the key points identified? (Policies only)	N/A	
	Is the document in the correct format?	Yes	
	Is the purpose of the document clear?	Yes	
	Is the scope clearly stated?	Yes	
	Are the definitions clearly explained?	Yes	
	Are the roles and responsibility clearly explained? (policies only)	N/A	
5	**Evidence Base**		
	Is the type of evidence to support the document explicitly identified?	Yes	
	Are key references cited?	Yes	
	Are associated documents referenced?	Yes	
6	**Approval Route**		
	Does the document identify which committee/ group will approve it?	Yes	
7	**Process to Monitor Compliance and Effectiveness (policies only)**		
	Are there measurable standards or KPIs to support the monitoring of compliance with the effectiveness of the document?	Yes	
8	**Review date**		
	Is the review date identified?	Yes	
9	**Equality and Diversity (policies only)**		
	Is a completed Equality Impact Assessment	N/A	

If answers to any of the above questions is ‘no’, then this document is not ready for endorsement, it needs further review.

Compliance Team:		
1.	Date of Compliance Team approval	20/05/2019
2.	Comments to author for any amendments	
3.	Name of compliance lead	Stanley Balachander, Quality Governance and Policies Administrator.

Approval Committee: Hospital Transfusion Committee			
If the committee/group is happy to approve this document would the chair please sign below and send the document and the minutes from the approval committee to the author. To aid distribution all documentation should be sent electronically wherever possible.			
Name	LYNNADUNN	**Date**	18/9/19.
Signature			

Endorsing Committee: Quality Governance Operational Committee			
If the committee/group is happy to endorse this document would the chair please sign below and send the document and the minutes from the endorsing committee to the author. To aid distribution all documentation should be sent electronically wherever possible.			
Name	SUZANNE HAMILTON	**Date**	10·10·19
Signature			