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Policy for the use of recombinant factor VIIa (rVIIa) in the treatment of uncontrolled haemorrhage

Division	Family & Integrated Support Services Division
Department	Pathology
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Ratifying Committee	Quality Governance Operational Committee
Date Ratified	12/8/2021
Approval Committee	Hospital Transfusion Committee
Date Approved	1/7/2021
Author Name and Job Title	Kerry Winham-Whyte Haematology & Blood Transfusion Manager
Key Words (*for search purposes)*	Factor VIIa; NovoSeven; Haemorrhage; Transfusion
Date Published on Document Library	16/8/2021
Review Date	12/8/2024
Target Audience	All staff involved in prescribing or administering of recombinant factor VIIa in the treatment of uncontrolled haemorrhage

Equality Impact Assessment
North West Anglia NHS Foundation Trust (NWAngliaFT) strives to ensure quality of opportunity for all service users, local people and the workforce. As an employer and a provider of health care, NWAngliaFT aims to ensure that none are placed at a disadvantage as a result of its policies. This policy has therefore been equality impact assessed to ensure fairness and consistency for all those covered by it regardless of their individuality. The results are shown in the Equality Impact Tool at Appendix 6.

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DOCUMENT VERSION CONTROL SCHEDULE					
Year and Version Number	**Author**	**Date Published on Document Library**	**Revisions from previous issue**	**Ratifying Committee**	**Date of Ratification**
2007 Version 1	Kaye Bowen	December 2007	New Policy	Hospital Transfusion Committee	December 2007
2011 Version 2	Kanchan Rege	January 2011	Reviewed	Hospital Transfusion Committee	January 2011
2014 Version 3	Kaye Bowen	June 2014	Reviewed and formatted into new Trust format	Quality Governance Operational Committee	12/05/2014
2015 Version 3.1	Kaye Bowen	July 2015	Appendix 2 amended to reflect the details in the policy	Hospital Transfusion Committee	08/07/2015
2017 Version 4	Kaye Bowen, Andy King-Venables	28/06/2018	Combined document for NWA	Quality Governance Operational Committee	07/06/2018
2021 Version 5	Trust Transfusion Team	16/8/2021	Advice regarding stock holding and sharing between sites Flowchart amended to include dose authorised by the consultant haematologist to be given to lab on request for product.	Quality Governance Operational Committee	12/8/2021

Key Points

This document

- Applies to all staff with responsibility for prescribing and administering of recombinant factor VIIa.

- Gives guidance on when and how to request recombinant factor VIIa, including indications for use, relative contraindications, and recording use in the patient's notes for monitoring purposes.

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Contents

Policy for the use of recombinant factor VIIa (rVIIa) in the treatment of uncontrolled haemorrhage

1. Introduction

Recombinant Factor VIIa (rVIIa) is a freeze-dried concentrate which is currently only licensed for treatment prophylaxis of haemorrhage in patients with haemophilia A or B with inhibitors to factors VIII or IX, acquired haemophilia, factor VII deficiency, or Glanzmann's thrombasthenia. Recently however, there have been many positive case reports about the efficacious off-label use of rVIIa in uncontrolled post-operative bleeding.

2. Purpose

The purpose of this policy is to give guidance on the prescription and use of recombinant Factor VIIa.

3. Scope

The policy is to be used by all members of staff involved in the prescription and administration of the product.

4. Indications for use

rVIIa is only indicated for patients not responsive to standard transfusion support measures (see below) nor attempts at surgical haemostasis.

As first line therapy in uncontrollable haemorrhage in Jehovah's Witnesses who have definitively refused all products derived from human blood.

5. Relative contra-indications

Theoretically, rVIIa may predispose to arterial and venous thrombosis. There is limited data about such sequelae in the literature but caution should be exercised in those patients deemed to be at risk.

There may be increased risk of thrombosis when a period of time has elapsed after surgery e.g. 24 – 48 hours, before rVIIa is given.

6. Clinical Use

Surgical bleeding must be eliminated, therefore a return to theatre for exploration must be considered if appropriate. Additionally, the following criteria must have been met:

- Fresh Frozen Plasma (FFP) must be given to maintain PT/APTT < 1.5 x normal control.
- Platelets must be > 75 x 10^9/L.

- Fibrinogen must be > 1.0 g/L.
- Temperature must be > 35°C.

If these criteria are ALL met then rVIIa should be considered, and the Consultant Haematologist informed before requesting the drug from the blood bank.

The request for factor rVIIa must be made by a Consultant.

7. Dose

Because of the paucity of information, the "correct" dose in different clinical settings is unknown. However, the standard dose offered is 90 micrograms/kg by slow intravenous infusion. This may be repeated, if needed, after 2 hours.

If the bleeding is still not controlled, further assessment of the situation will be necessary.

The prescription for rVIIa should always be on the patient's prescription chart.

8. Monitoring

The efficacy of rVIIa can only be judged clinically. There are no straightforward laboratory parameters by which to measure the action of rVIIa.

The checklist (Appendix 5) must be completed and filed in the patient's notes as a unified record of who has authorised the use of rVIIa and that all pre-requisites for use have been fulfilled.

9. Cost

1mg of NovoSeven currently costs £525. The dose of rVIIa for a 70kg patient is currently around £3500.

10. Storage

In the PCH Stock Fridge, there will be kept as minimum stock:
1 vial each of rVIIa (NovoSeven) 1mg and 2mg.
2x 5 mg vials of rVIIa (NovoSeven).

In the HH Stock Fridge, there will be kept as a minimum stock:
1x 1 mg vial of rVIIa (NovoSeven)
1x 2 mg vial of rVIIa (NovoSeven)
1x 5 mg vial of rVIIa (NovoSeven).

Further supplies are obtainable in an emergency. These may be by stock sharing between PCH and HH, or from the haemophilia centre at Addenbrookes, so delivery times may vary.

11. Implementation

The policy will be reviewed every three years or sooner if required in light of new evidence or statutory requirements.

The transfusion laboratory will maintain responsibility for ensuring rVIIa and will monitor each request to ensure it is requested and issued appropriately.

If there is any deviation from this policy, an incident form will be raised via DATIX. The incident will be investigated and corrective and preventative actions implemented. If appropriate, a report will be made to Serious Hazards of Transfusion (SHOT) and Serious Adverse Blood Reactions and Events (SABRE).

12. Ratification

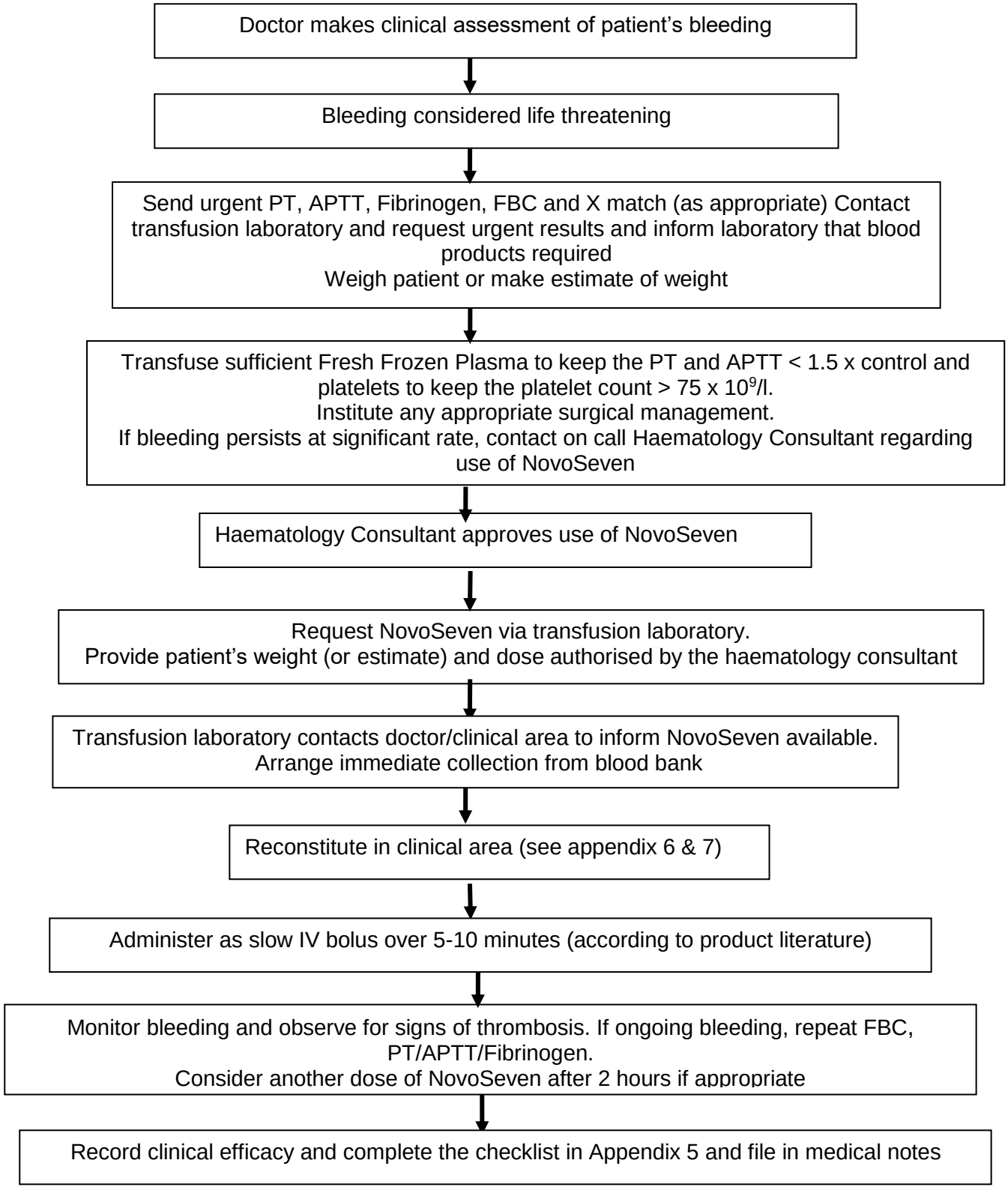
This policy will be approved by the Hospital Transfusion Committee and ratified by the Quality Governance Operational Committee.

13. Distribution

This policy will be available on the Trust Document Library.

Appendix 1

Flow Chart for Use of NovoSeven



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Appendix 2

Checklist for the use of recombinant factor VIIa

The issue of rVIIa is highly restricted.
Therefore, all criteria should be initialled to indicate that they have been met and then the form must be signed by/on behalf of a Consultant.

PLEASE RETAIN THIS DOCUMENT IN THE PATIENT'S NOTES.

Criteria	**Initial when met**
The Haematology Consultant on call should be contacted for confirmation	
Primary surgery (if at all) within the preceding 48 hours	
There has been surgical re-exploration (if appropriate) to ensure surgical haemostasis	
Fresh Frozen Plasma (FFP) has been be given to maintain PT/APTT < 1.5 x normal control	
Platelet count is > 75 x 10^9/L	
Fibrinogen > 1.0 g/L	
Acidosis has been treated (base excess > - 4)	
Temperature is > 35°C	

rVIIa approved by Consultant

Consultant Name _____

Contacted by (print Name) _____Signature_____

Date _____Time _____

rVIIa administered by

Print Name _____Signature_____

Date _____Time _____

Please write patient details below, or affix addressograph label

Patients Name_____

Date of Birth_____ **Hospital Number**_____

Appendix 3

Reconstitution of NovoSeven

Each NovoSeven package contains:
1 mg & 2 mg
– 1 vial (2 ml) with white powder for solution for injection.
– 1 vial (2 ml) with solvent for reconstitution.
5 mg
– 1 vial (12 ml) with white powder for solution for injection.
– 1 vial (12 ml) with solvent for reconstitution.

An infusion kit will also be issued, which contains all the equipment needed to prepare the NovoSeven for administration, including a luer lock syringe and vial adapters. It will also include the manufacturers written and visual instructions for reconstitution**.**

Always use an aseptic technique when preparing NovoSeven for administration.

1. Bring both vials, i.e. the NovoSeven (powder) and solvent (water), to room temperature by holding them in your hands. **Do not exceed 37°C.**

2. Remove the protective plastic caps from both vials, so that the central part of the rubber stopper is visible on each. **N.B. If the caps are loose or missing the vial must be discarded without use.**

3. Clean each of the rubber stoppers using an alcohol swab and allow to dry before proceeding.

4. Remove the protective paper from the vial adapter and click the vial adapter on to the solvent vial without taking it out of the protective cap. Take care not to touch the tip of the vial adapter. Once attached, remove the protective cap.

5. Remove the syringe from its packaging. Pull back the plunger, drawing up a volume of air equal to the amount of water required for injection (ml equals cc on the syringe). Screw the syringe onto the vial adapter attached to the solvent vial, ensuring that it is tightly fastened.

6. Inject air into the solvent vial by pushing the syringe plunger until a clear resistance is felt.

7. Hold the syringe so that the solvent vial is upside down and pull the plunger to draw the solvent into the syringe

8. Click the empty solvent vial from the vial adapter, by tipping the syringe and vial adapter forwards. Do not remove the vial adapter from the syringe.

9. Click the vial adapter, still attached to the syringe, onto the powder vial. Hold the syringe slightly tilted with the vial facing downwards. Push the plunger slowly to

inject the solvent into the powder vial. **Make sure not to aim the stream of solvent directly at the NovoSeven powder as this will cause foaming**.

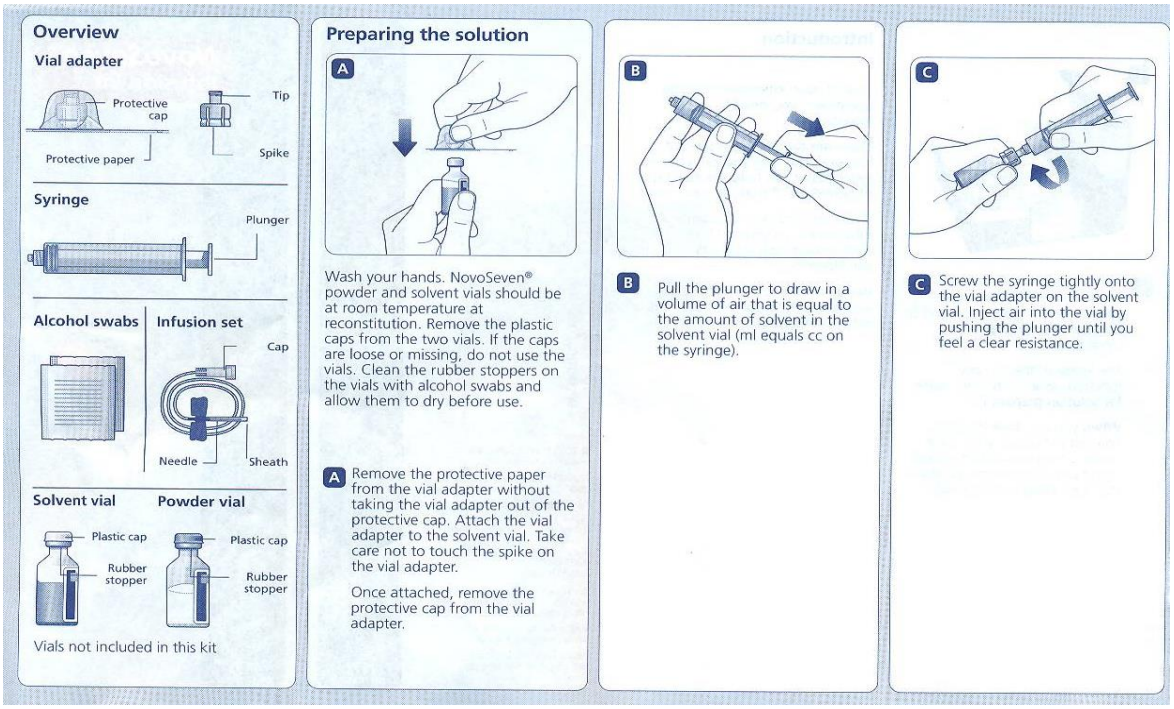
10. Gently swirl the vial until all the powder is dissolved. **Do not shake the vial as this will cause foaming**.

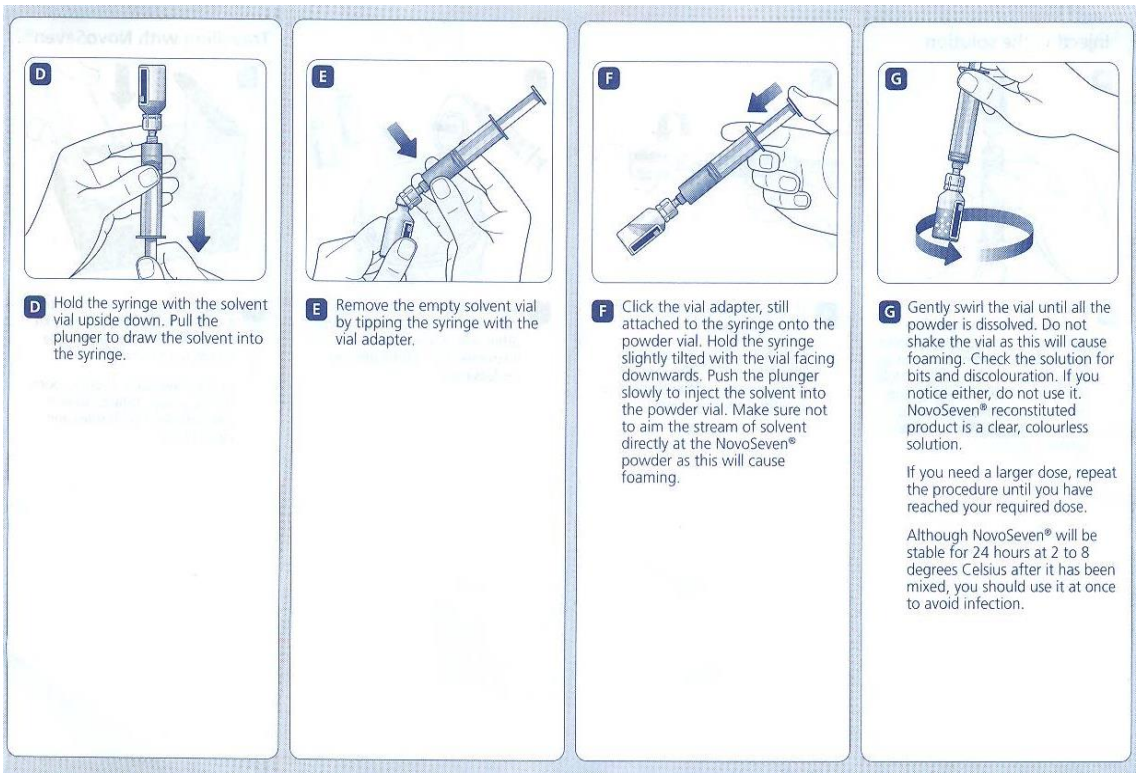
11. Check the solution is clear and colourless. **Do not use the solution if there is any discolouration or if any particles are present**. Draw all of the solution up into the syringe.

12. Unscrew the vial adapter with the empty vial attached from the syringe. Empty vials and adapters should be disposed of in the sharps waste.

Appendix 4

Manufacturer's instructions for reconstitution





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Appendix 5
Compliance Monitoring Table
Policy Title: Policy for the use of recombinant factor VIIa (rVIIa) in the treatment of uncontrolled haemorrhage
Author: Dr Kanchan Rege Consultant Haematologist, Kaye Bowen, Transfusion Practitioner PCH, Andy King-Venables, Transfusion Practitioner Hinchingbrooke Hospital

Document Section		Control	Checks to be carried out to confirm compliance with the policy	How often the check will be carried out	Responsible for carrying out the check	Results of check reported to: (Responsible for also ensuring actions are developed to address any areas of non-compliance)	Frequency of reporting
		WHAT?	**HOW?**	**WHEN?**	**WHO?**	**WHERE?**	**WHEN?**
6	Clinical Use	Appropriate requesting for issue of NovoSeven	Referral to Consultant Haematologist when NovoSeven requested	Each request	Biomedical scientist issuing product	Hospital Transfusion Team	Each request

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Equality Impact Assessment (EqIA) screening form Appendix:6

Policy name & Central Index number: Policy for the use of recombinant factor VIIa (rVIIa) in the treatment of uncontrolled haemorrhage C0255
Name of Principal author or Policy: Kerry Winham Whyte Haematology & Blood Transfusion Manager
Division: Family and Integrated Support Services **Date:** 4/6/2021

Equality Impact Assessment Stage 1
Indicate in the table below what kind of impact this policy will have upon the protected groups or how it is likely to influence the Trust's ability to comply with the Public Sector Equality Duty, which is to;

a) Eliminate discrimination, victimisation, harassment or other unlawful conduct that is prohibited under the Equality Act 2010 and/or;
b) Advance equality of opportunity between people who share a characteristic and those who do not and/or;
c) Foster good relations between people who share a relevant protected characteristic and those who do not.

Consider this in the context of the whole policy being updated. The easiest means of approaching this is to consider the following questions;

- **Would the adaptation meet my needs or ensure I had equal opportunities if I had any of the protected characteristics?**
- **Is there anything about the policy that would have a detrimental impact on me if I had one of the protected characteristics?**
- **Does it affect our ability to comply with the Public Sector Equality Duty?**

Please check the appropriate boxes relating to the impact of the policy or adaption:

Age	○ Positive	◉ None	○ Negative	○ Unknown
Disability	○ Positive	◉ None	○ Negative	○ Unknown
Gender Reassignment	○ Positive	◉ None	○ Negative	○ Unknown
Marriage/Civil Partnership	○ Positive	◉ None	○ Negative	○ Unknown
Pregnancy and Maternity	○ Positive	◉ None	○ Negative	○ Unknown
Race	○ Positive	◉ None	○ Negative	○ Unknown
Religion or Belief	○ Positive	◉ None	○ Negative	○ Unknown
Sex (Gender)	○ Positive	◉ None	○ Negative	○ Unknown
Sexual Orientation	○ Positive	◉ None	○ Negative	○ Unknown

If any boxes are checked as Negative, please escalate to a stage 2 assessment by emailing nwangliaft.qualitygovernance@nhs.net

If any boxes are checked as Unknown, please contact nwangliaft.edi@nhs.net

Agreement by	Signature	Date
Approving Panel Chair for Stage 1		**1/7/2021**
Ratifying Panel Chair (if required) for Stage 2		
Equality, Diversity and Inclusion Lead (if required) for Stage 2		

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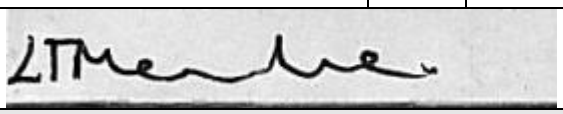
Quality Assurance Checklist - Version Number: 5 **Appendix: 7**

		Y/N/n/a	COMMENTS (where necessary)
1	**Title of document** Policy for the use of recombinant factor VIIa (rVIIa) in the treatment of uncontrolled haemorrhage(C0255)		
2	**Type of document (e.g. policy, guidance)**	Policy	
	Is it clear whether the document 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)	Yes	
	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 responsibilities clearly explained? (policies only)	Yes	
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 measureable 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 attached?	Yes	

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

Compliance Team:			
1.	Date of Compliance Team approval	4/6/2021	
2.	Comments to author for any amendments		
3.	Name of compliance lead	Stanley Balachander, Policies and Compliance Officer	
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	L Menadue	**Date**	**1/7/2021**
Signature			
Ratifying Committee: Quality Governance Operational Committee			
If the committee/group is happy to ratify this document would the chair please sign below and send the document and the minutes from the ratifying committee to the author. To aid distribution all documentation should be sent electronically wherever possible.			
Name	**Kanchan Rege**	**Date**	**12.08.21**
Signature