Group arrangements:
Salford Royal NHS Foundation Trust (SRFT)
Pennine Acute Hospitals NHS Trust (PAT)

Northern Care Alliance NHS Group

Thrombolysis in acute ischaemic stroke – management of acutely elevated blood pressure

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Division/ Department::	Manchester Centre for Clinical Neurosciences
Applies to: (Please delete)	Bury & Rochdale Care Organisation Salford Royal Care Organisation
Approving Committee	Medical Neurosciences Assurance and Risk Committee, Salford Royal
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Contents

1. Overview (What is this policy about?)

Thrombolysis with tissue plasminogen-activator (tPA) for acute ischaemic stroke in the setting of sustained elevated blood pressure (BP) may be associated with worse outcome

This document draws together available evidence and consensus to guide eligibility of tPA when there is sustained elevation of BP in hyperacute ischaemic stroke, and management of sustained hypertension for the 24 hour period after tPA

These guidelines will be used to determine eligibility for tPA based on BP parameters, and the specific approach to pharmacological lowering of pre-treatment and post-treatment BP where appropriate

2. Scope (Where will this document be used?)

This policy applies to:

1. All stroke medical and nursing staff; anaesthetic and critical care unit medical and nursing staff at the Salford Royal site

2. Adult patients in the emergency department (ED) or in-patients with suspected stroke being considered for thrombolysis on the Salford Royal site

3. Background (Why is this document important?)

The role of BP in determining outcome when thrombolysis is administered in acute ischaemic stroke remains unclear. Excessive elevation of BP may contribute to the risk of haemorrhagic transformation, but precipitous lowering of BP may worsen ischaemic injury. Data from the prospective Safe Implementation of Treatment in Stroke (SITS) registry suggest that pre-treatment BP, and BP upto 24 hours following initiation of tPA, are associated with symptomatic intracerebral haemorrhage (ICH) and adverse 3 month outcomes.[1] The National Institutes of Neurological Disorders and Stroke (NINDS) tPA trial [2,3] and European Collaborative Acute Stroke Study (ECASS) III[4] excluded patients with sustained systolic BP greater than 185 mm Hg or diastolic BP greater than 110 mm Hg at the time of randomisation, or where aggressive treatment was required to reduce BP to within these limits. Indeed, deviations from these BP criteria are associated with an increased risk of symptomatic ICH.[5] The NINDS study group proposed an algorithm for attempted pharmacological lowering of BP prior to randomisation, and guidelines for the management of BP in the 24 hours following treatment[3]. This algorithm has been recommended by expert consensus in European[6] and American[7] guidelines for the approach to BP management when tPA is considered for ischaemic stroke. A recent randomised trial of BP lowering in patients treated with tPA found that intensive BP lowering (target BP 130-140mmHg within 60 mins of randomisation) reduced the frequency of any intracranial haemorrhage) compared to guideline lowering (<180mmHg), but there was no overall difference in clinical outcomes.[8] This trial does not support the routine adoption of intensive BP lowering after administration of tPA.

This guideline is based on the NINDS algorithm and has been adapted for use in this Trust.

4. What is new in this version?

The recently published Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED) trial[8] comparing intensive versus guideline BP lowering has been reviewed and cited (in the introduction above), even though the results do not change the guidelines

5. Policy

5.1 Prior to considering thrombolysis with tPA

see FIGURE 1 and TABLE 1

- Check patient's medication and allergy history if possible.
- If initial **BP ≥ 185 (systolic) or ≥ 110mmHg (diastolic)** when considering thrombolysis, the BP should be repeated after 15 minutes prior to reconsidering thrombolysis
- If **BP remains ≥ 185 or ≥ 110mmHg**, treat with labetalol 10-20mg IV bolus over 1-2 minutes **or** IV glyceryl trinitrate (GTN) infusion starting at 1.5ml per hour, titrated gradually up to a maximum of 12ml per hour as required/ tolerated (see appendix 2) if labetalol contraindicated*
- If after a further 15 minutes **BP remains ≥ 185 or ≥ 110mmHg**, repeat labetalol bolus 10-20mg, if still no contraindications, or continue titrating IV GTN as tolerated
- If after a further 15 minutes **BP remains ≥ 185 or ≥ 110mmHg** do not proceed with thrombolysis
- **Note that labetalol is contraindicated in asthma, bradycardia <60/min (including second or third degree AV nodal block) and uncontrolled heart failure. Consult current BNF or SPC (Summary of Product Characteristics) for further cautions /contraindications*.

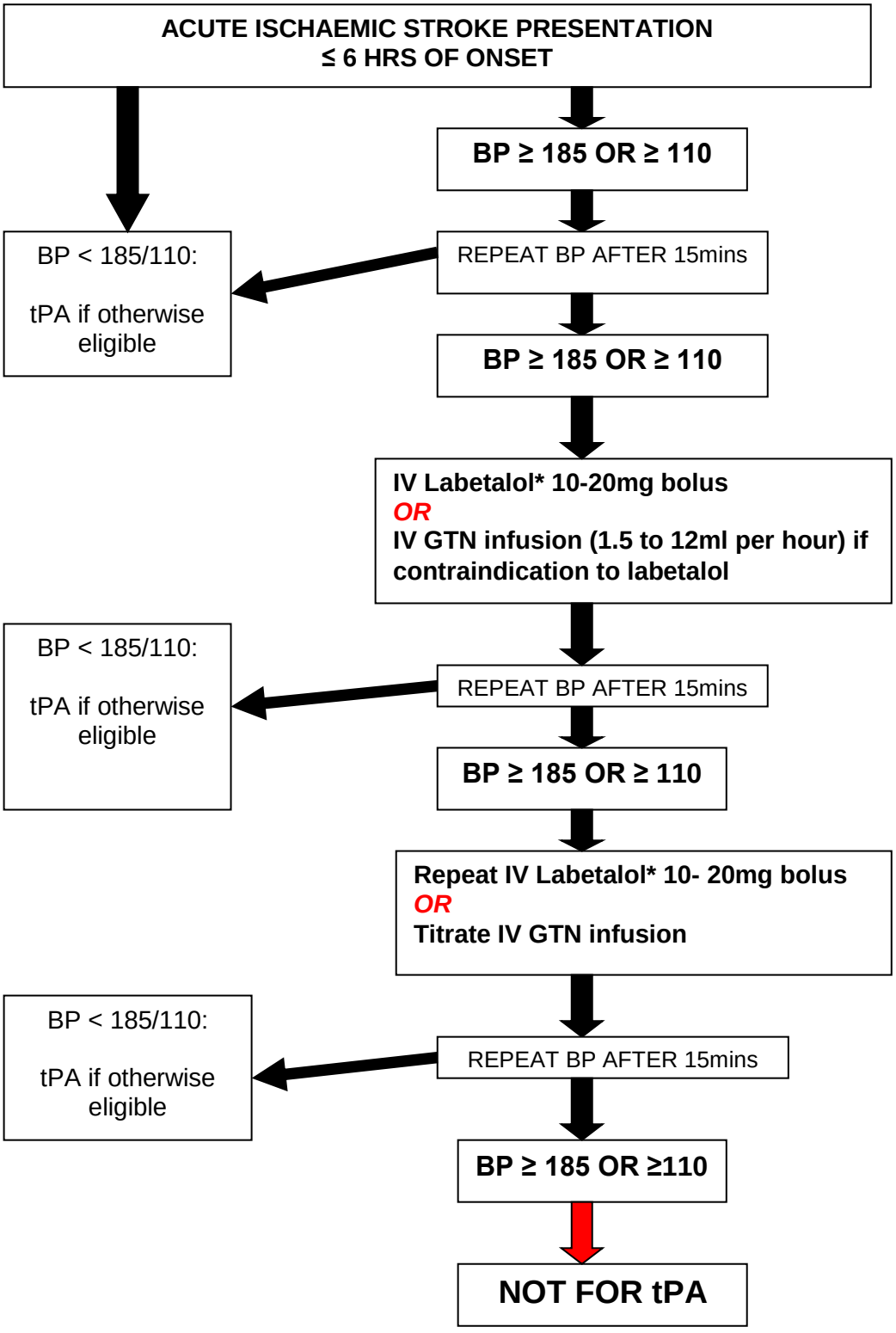
5.2 During and after tPA treatment (up to 24 hours)

see TABLE 1 and FIGURE 2

- Ensure patient is on a cardiac monitor, and record BP every 15mins for 2 hours, then every 30mins for 6 hours, then consider at least hourly BP monitoring thereafter up to 24 hours post tPA
- If **BP≥185 or 105mmHg** during the tPA infusion, the tPA should be stopped whilst the patient and BP are re-assessed. tPA may be re-started once the BP is within target levels if appropriate, on an individual basis
- Review antihypertensive therapy at 24 hours and consider switch to oral treatment if appropriate (consider restarting oral antihypertensive medication the patient was receiving prior to admission if suitable)

- Note that monitoring may vary for patients who require admission to Critical Care Unit.

FIGURE 1: Approach to BP prior to tPA treatment



** Labetalol is contraindicated in asthma, bradycardia <60/min (including 2nd/3rd degree heart block) and uncontrolled heart failure. Consult current BNF/SPC for further cautions / contraindications.*

TABLE 1

Refer to SPC or package insert for further details. If in doubt contact the prescriber, your ward pharmacist or the Medicines Information Centre.

IV Labetalol

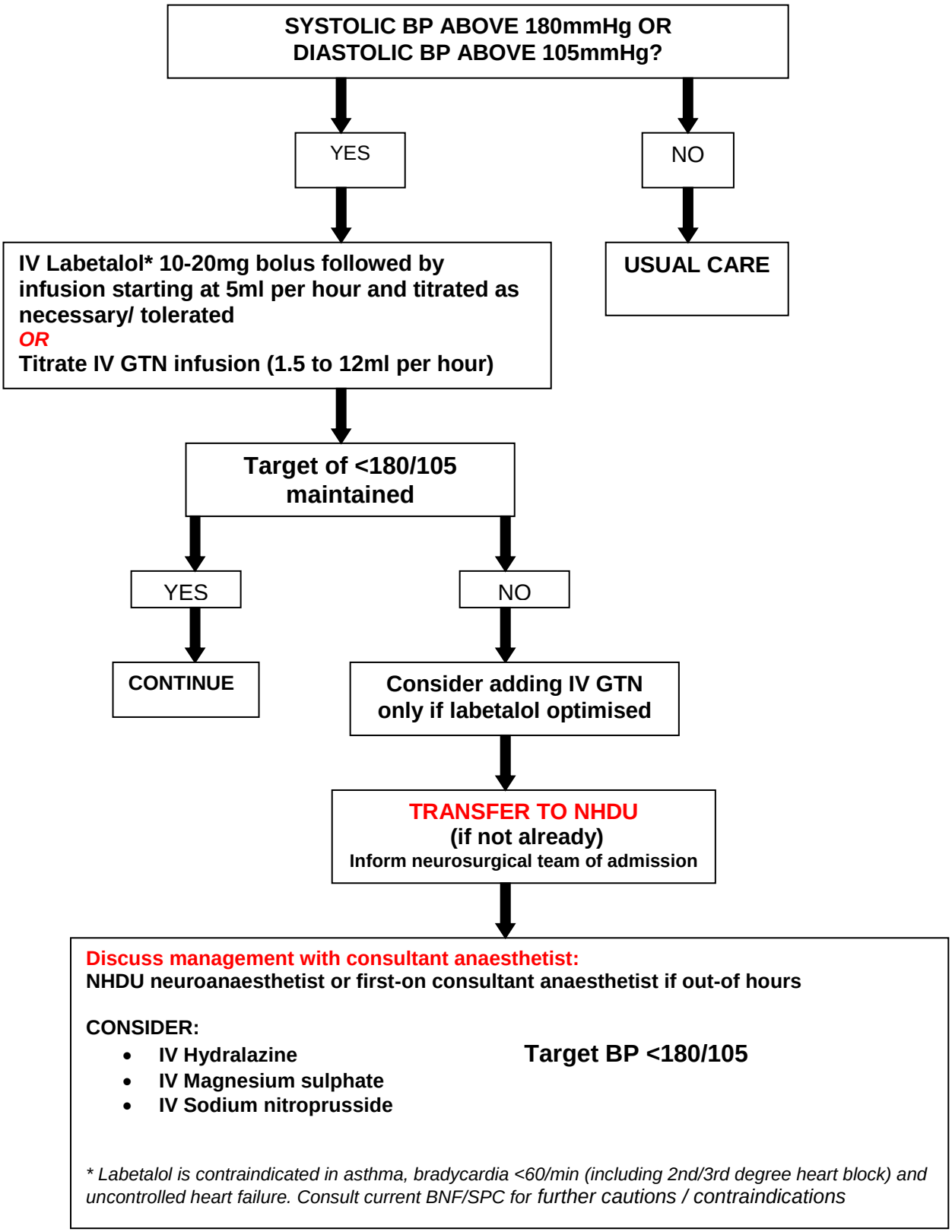
Dose	Start continuous IV infusion at 5ml (25mg) per hour and increase rate gradually as required/ tolerated
Form	Ampoules containing 100mg labetalol in 20ml (5mg per ml)
Dilution	Not required.
Administration	Draw up two ampoules (200mg /40ml) and administer through Braun syringe pump.
Flush	Before and after with sodium chloride 0.9%
Side-effects	May cause postural hypotension, rash, pruritus, tiredness, weakness, headache, scalp tingling, difficulty in micturition, epigastric pain, nausea, vomiting, nasal congestion, sweating and dyspnoea.
Cautions/ contraindications	Contraindicated in asthma, bradycardia <60/min (including second/third degree heart block) and uncontrolled heart failure. Consult current SPC/ BNF for further cautions /contraindications.
Monitoring	BP and pulse rate should be monitored throughout the infusion. Care must be taken to ensure BP is reduced gradually.

IV GTN (Glyceryl Trinitrate)

Dose	Start continuous IV infusion at 1.5ml per hour and increase rate gradually up to a maximum of 12ml per hour as required/ tolerated.
Form	Vials containing 50mg GTN in 50ml (1mg per ml)
Diluent/dilution	Not required.
Administration	Draw up contents of vial and administer through Braun syringe pump.
Flush	Before and after with sodium chloride 0.9%.
Side-effects	Headache, dizziness, flushing, hypotension and tachycardia may be encountered, particularly if the infusion is administered too rapidly.
Cautions	Caution necessary in severe liver or renal disease
Monitoring	BP should be monitored throughout the infusion. Titrate slowly to reduce BP gradually and note tolerance to nitrates may occur within 24 hours.

FIGURE 2: Management of BP during and 24hrs following tPA treatment

Ensure patient is on a cardiac monitor and record BP every 15mins for 2 hours, then every 30mins for 6 hours, then consider at least hourly BP monitoring thereafter up to 24 hours post tPA. Consider switch to oral antihypertensives when appropriate.



6. Roles & responsibilities

Stroke medical staff: to be aware of (1) Exclusion criteria for tPA based on BP parameters; (2) Role and limitations of pre-treatment BP lowering when considering eligibility for tPA; (3) Management of sustained hypertension in the 24 hours following treatment with tPA.

Stroke ward managers & nursing staff on the hyperacute stroke unit and acute stroke unit: to ensure awareness of (1) this document; (2) its implications for patient monitoring and safety; (3) indications for alerting senior medical staff.

Anaesthetic/ critical care unit medical staff: to be aware of this document and its implications for patients receiving tPA who may require management in a critical care environment.

7. Monitoring document effectiveness

- **Key standards:** 100% of patients being assessed for stroke thrombolysis with elevated BP will be managed according to this policy. 100% of patients receiving stroke thrombolysis with elevated BP during and within 24 h of thrombolysis will be managed according to this policy
- **Method(s)*:** Ongoing audit of thrombolysis standards for stroke M&M
- **Team responsible for monitoring:** Stroke clinical team
- **Frequency of monitoring:** Monthly
- **Process for reviewing results and ensuring improvements in performance:** Monthly M&M meetings with feedback to individual clinicians and teams; component of stroke team induction

8. Abbreviations and definitions

BP	Blood Pressure
BNF	British National Formulary
ECASS	European Cooperative Stroke Study
ED	Emergency Department
ENCHANTED	Enhanced Control of Hypertension and Thrombolysis Stroke Study
GTN	Glyceryl Trinitrate
IV	Intravenous
M&M	Mortality and Morbidity
mg	milligram
NINDS	National Institutes of Neurological Disorders and Stroke
NHDU	Neurological High-Dependency
SITS	Safe Implementation of Treatment in Stroke
SPC	Summary of Product Characteristics
tPA	Tissue plasminogen Activator

9. References

(1) Ahmed N, Wahlgren N, Brainin M, Castillo J, Ford GA, Kaste M, Lees KR, Toni D, for the SITS Investigators. Relationship of blood pressure, antihypertensive therapy, and outcome in ischemic stroke treated with intravenous thrombolysis. Retrospective analysis from safe

implementation of thrombolysis in stroke-international stroke thrombolysis register (SITS-ISTR). *Stroke* 2009; 40: 2442-2449.

(2) The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *New England Journal of Medicine* 1995; 333: 1581-1587

(3) Brott T, Lu M, Kothari R, et al. Hypertension and its treatment in the NINDS rt-PA stroke trial. *Stroke* 1998; 29: 1504-1509

(4) Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after ischemic stroke. *New England Journal of Medicine* 2008; 359: 1317-1329

(5) Tsivgoulis G, Frey JL, Flaster M, et al. Pre-tissue plasminogen activator blood pressure levels and risk of symptomatic intracerebral hemorrhage. Stroke 2009; 40: 3631-3634

(6) The European Stroke Organisation (ESO) Executive Committee and the ESO Writing Committee. Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovascular Diseases* 2008; 25: 457-507

(7) Powers WJ, Rabinstein A, Ackerson T, et al. 2018 Guidelines for the early management of adults with ischemic stroke. *Stroke* 2019; 49: e46-e99

(8) Anderson CS, Huang Y, Lindley RI, et al. Intensive blood pressure reduction with intravenous thrombolysis therapy for acute ischaemic stroke (ENCHANTED): an international, randomised, open-label, blinded-endpoint, phase 3 trial. *Lancet* 2019; 393: 877-888

11. Document Control Information

All sections must be completed by the author prior to submission for approval

Lead Author:	Professor Craig Smith, Professor of Stroke Medicine		
Lead author contact details:	extension 60623; craig.smith@srft.nhs.uk		
Consultation List the persons or groups who have contributed to this policy. (please state which Care Organisation)	**Name of person or group**	**Role / Department / Committee (Care Org)**	**Date**
	Dr Craig Carroll	Consultant Neuroanaesthetist, Salford Royal	January 2019
	Dr Jane Molloy	Consultant Neurologist, Salford Royal	January 2019
	Karen Hewitt	Pharmacist, Salford Royal	Contributor on original policy
Endorsement List the persons or groups who have seen given their support to this policy. (please state which Care Organisation)	**Name of person or group**	**Role / Department / Committee (Care Org)**	**Date**
	Dr Martin Punter	Stroke Clinical Governance Lead	April 2019
	Divisional Clinical Governance Committee	MCCN	July 2019
Keywords / phrases:	List the search terms and phrases you think that staff would use to search for this document. Add old reference/ID number if applicable – see section 4. Acute Ischaemic Stroke; Thrombolysis; tissue plasminogen activator; Blood Pressure		
Communication plan:	State below how the practice in this document will be rolled out across the organisation and embedded in practice The policy will be available under the Stroke Centre documents on the Salford Royal intranet. Stroke service medical and nursing staff will be made aware of the protocol through induction, in-service training and stroke study days. The Stroke Clinical Governance and M&M Group will review progress in implementation. Staff working within Stroke, Anaesthetics and Intensive Care will be made aware through their respective Clinical Governance frameworks. The policy will be implemented from the date of final ratification.		
Document review arrangements:	This document will be reviewed by the author, or a nominated person, at least once every three years or earlier should a change in legislation, best practice or other change in circumstance dictate.		

This section will be completed following committee approval

Policy Approval:	Name of Approving Committee: MCCN Divisional Clinical Governance Committee	
	Chairperson: Alison Dwyer	
	Approval date: 09/07/2019	
	Formal Committee decision (tick) x	Chairperson's approval (tick)

12. Equality Impact Assessment (EqIA) screening tool

Legislation requires that our documents consider the potential to affect groups differently, and eliminate or minimise this where possible. This process helps to reduce health inequalities by identifying where steps can be taken to ensure the same access, experience and outcomes are achieved across all groups of people. This may require you to do things differently for some groups to reduce any potential differences.

1a) Have you undertaken any consultation/ involvement with service users, staff or other groups in relation to this document?	No
1b) Have any amendments been made as a result?	No
2) Does this policy have the potential to affect any of the groups below differently or negatively?	

Protected Group	Yes	No	Unsure	Reasons for decision
Age *(e.g. are specific age groups excluded? Would the same process affect age groups in different ways?)*		X		
Sex *(e.g. is gender neutral language used in the way the policy or information leaflet is written?)*		X		
Race *(e.g. any specific needs identified for certain groups such as dress, diet, individual care needs? Are interpretation and translation services required and do staff know how to book these?)*		X		
Religion & Belief *(e.g. Jehovah Witness stance on blood transfusions; dietary needs that may conflict with medication offered.)*		X		
Sexual orientation *(e.g. is inclusive language used? Are there different access/prevalence rates?)*		X		
Pregnancy & Maternity *(e.g. are procedures suitable for pregnant and/or breastfeeding women?)*		X		If thrombolys is deemed otherwise suitable then the policy is applicable
Marital status/civil partnership *(e.g. would there be any difference because the individual is/is not married/in a civil partnership?)*		X		
Gender Reassignment *(e.g. are there particular tests related to gender? Is confidentiality of the patient or staff member maintained?)*		X		
Human Rights *(e.g. does it uphold the principles of Fairness, Respect, Equality, Dignity and Autonomy?)*		X		
Carers *(e.g. is sufficient notice built in so can take time off work to attend appointment?)*		X		
Socio/economic *(e.g. would there be any requirement or expectation that may not be able to be met by those on low or limited income, such as costs incurred?)*		X		
Disability *(e.g. are information/questionnaires/consent forms*		X		

available in different formats upon request? Are waiting areas suitable?) Includes hearing and/or visual impairments, physical disability, neurodevelopmental impairments e.g. autism, mental health conditions, and long term conditions e.g. cancer.				
Are there any adjustments that need to be made to ensure that people with disabilities have the same access to and outcomes from the service or employment activities as those without disabilities? *(e.g. allow extra time for appointments, allow advocates to be present in the room, having access to visual aids, removing requirement to wait in unsuitable environments, etc.)*		**X**		

3) Where you have identified that there are potential differences, what steps have you taken to mitigate these?

N/A

4) Where you have identified adjustments would need to be made for those with disabilities, what action has been taken?

N/A

5) Where the policy, procedure, guidelines, patient information leaflet or project impacts on patients how have you ensured that you have met the Accessible Information Standard – please state below:

N/A

……

EDI Team/Champion only*: does the above ensure compliance with Accessible Information Standard*

- Yes
- No

If no what additional mitigation is required:

Will this policy require a full impact assessment? No

Please state your rationale for the decision:

(*a full impact assessment will be required if you are unsure of the potential to affect a group differently, or if you believe there is a potential for it to affect a group differently and do not know how to mitigate against this - Please contact the Inclusion and Equality team for advice on* equality@pat.nhs.uk)

Author: Craig J Smith Date: 07/05/19

Sign off from Equality Champion: Date: