SCHEDULE 2 – THE SERVICES

Service Specifications

Service Specification No.	1668
Service	Thrombotic Thrombocytopenic Purpura (TTP), all ages
Commissioner Lead	*For local completion*
Provider Lead	*For local completion*

1. Scope

1.1 **Prescribed Specialised Service**

This service specification covers the provision of Thrombotic Thrombocytopenic Purpura (TTP) inpatient and outpatient services for all ages and for acute and chronic presentation and for acquired, congenital and other sub-group forms.

1.2 **Description**

TTP is a very rare, complex condition which can present as an acute life-threatening disorder that requires prompt diagnosis, early referral and effective immediate (and in the case of congenital TTP, ongoing) management in a centre with comprehensive provision and a multi-discipline approach. Specialist led co-ordinated care is key to improving outcomes for this patient group. This specification sets out the model of care for acute and congenital care.

1.3 **How the Service is Differentiated from Services Falling within the Responsibilities of Other Commissioners**

This service is for a very rare disease affecting a small number of patients. The service requires planning and coordination at national level, which is out with the remit of local commissioners.

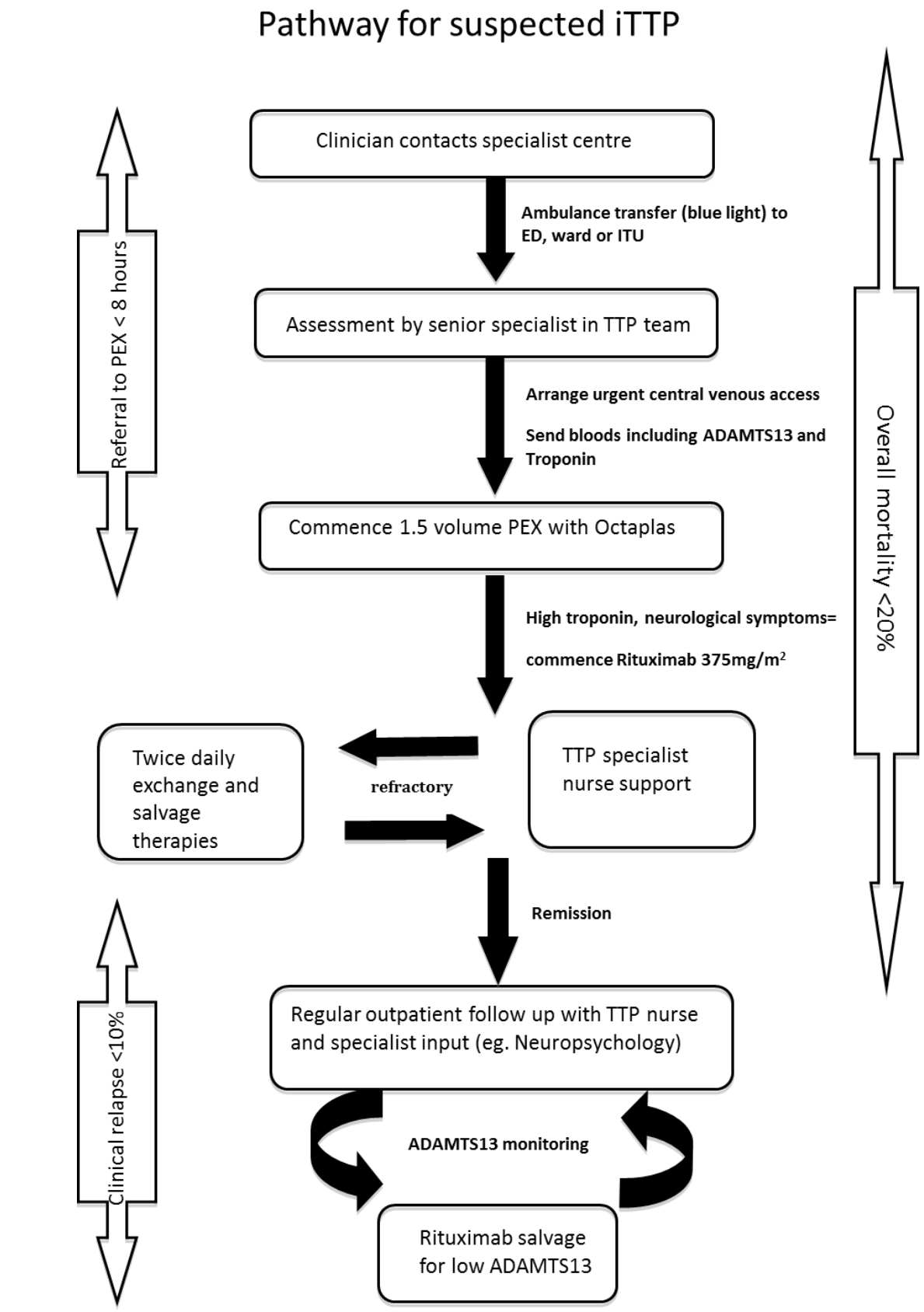
2. Care Pathway and Clinical Dependencies

2.1 **Care Pathway**

TTP is an acute life-threatening disorder; prognosis is directly related to prompt diagnosis and referral to a specialist centre with on-site apheresis, available 24/7. A summary of the pathway is set out below at Figure 1. The accepting centre (the Specialist TTP Centre (STTPC) must have an 'automatic acceptance' policy. Patients must not be refused admission due to non-availability of beds. However, in some circumstances, the service is expected to manage the patient's care remotely and arrange for treatment, if possible, at the referring hospital or another hospital in the Region as agreed with the STTPC and

arrange transfer as soon as possible. Automatic acceptance refers to STTPCs having capacity to accept the acute patients. However, all patients must be discussed with the STTPC to ensure they are appropriate for transfer and treatment.

Figure 1: Pathway for acute idiopathic TTP (iTTP) presentations:



Patients, including those on the maternity pathway, must be referred to the STTPC as soon as the diagnosis is suspected and transferred to the treating centre (which may be the STTPC or another hospital in the Region as agreed by the STTPC) urgently as delays in

treatment impact mortality. All patients must have started Plasma Exchange (PEX) ideally within four hours and within no longer than eight hours of referral to the STTPC**.** This includes securing a bed at the STTPC or another treating centre, transport time, central line insertion if applicable and defrosting of plasma for PEX. It is expected that patients will start on PEX within 90 minutes of admission to the STTPC.

2.2 Role of the Specialist TTP Centre and Interdependence with other services

2.2.1 Every STTPC (of which there are likely to be nine) sits within a defined geographical catchment area with a network of referring hospitals covered by the service. This information must be readily accessible to referring hospitals and the ambulance service covering the defined catchment area. Services must be accessible within a window transfer time of two hours to avoid delays in treatment.

2.2.2 There will be some areas of the country for whom the physical distance will be greater. STTPCs will make appropriate arrangements for either initial plasma exchange treatment (either at the referring hospital or at another hospital in the Region as agreed by the STTPC) or for expedited transfer to the STTPC; air transport can be considered in this context. Paediatric patients present in very small numbers and the expertise to care for this cohort is limited. STTPCs will develop a clinical partnership with expert paediatric haematologists. One STTPC will lead the network nationally.

All STTPCs must have:

- 24/7 access to therapeutic apheresis; where this is not directly provided but subcontracted, the clinical responsibility and decision making remains with the STTPC team
- Level 3 Critical Care Facilities
- Interventional Radiology/ IV Access Team with access 24/7 for urgent line insertion for patients not entering critical care
- Specialist Haematology Ward
- A dedicated TTP Consultant Team with 24/7 on call availability who are able to mobilise the ‘automatic acceptance’ policy
- A named paediatric haematologist for congenital TTP delivered through the clinical partnership with the paediatric specialist centre
- Intensive care specialists experienced in the management of this condition.
- Processes to support patient groups as part of the service development
- A specialist nursing team
- Trust approved patient pathways, Standard Operating Procedures (SOPs) and protocols will be based on national clinical guidelines
- Ability to carry out the appropriate diagnostics, including access to ADAMTS13 testing, which is used to identify activity indicative of TTP, 7 days a week
- Access to neurological, cardiac and other relevant services e.g. rheumatology, HIV, specialist obstetrics
- Access to clinical psychology
- Participation in national clinical fora and data entry onto the national registry
- Agreed ambulance and transport protocols for patients
- A list of the general hospitals with which they work

- A region-specific guideline for use in referring hospitals that sets out the specific arrangements for the care of TTP patients in that catchment area

2.2.3 Patients should be transferred as clinically appropriate, in consultation with a team led by level three critical care and admitted to a facility that can insert a central venous catheter and that has resuscitation facilities. Patients should be assessed by the TTP team as soon as they arrive at the STTPC. Plasma Exchange should be started ideally within 4 hours of referral to the STTPC and no longer than within 8 hours of referral. Patients should start on plasma exchange prior to a definitive confirmation of diagnosis. If the patient does not have TTP, they should be referred to another service such as atypical haemolytic uraemic syndrome and care should be continued as part of another service from that point. Patients are likely to require plasma exchange at least daily and often more frequently.

Diagnostics and drug therapy to be commenced in line with national clinical guidelines.

Octaplas (FFP) is the blood product to be used for plasma exchange (DHSC guidance). Drug therapy may include steroids, monoclonal antibodies and immunosuppressants. The drugs used in the pathway that are excluded from national tariff will be used in line with NHS England policies.

There will be a minimum of daily senior review. Senior cover needs to be in place for staff absence on leave, illness etc. It is expected that cover for specialist nursing will be provided by the wider specialist nursing team.

When the acute phase has improved, patients can be transferred to lower intensity of care but within designated specialist area e.eg within haematology and referred to other services based on the patient's clinical needs.

Patients and their families should have access to appropriate support from a specialist nursing team as soon as practicable.

The psychological impact of this disease is major, and patients should be referred for psychological support before discharge.

All STTPCs must contribute data to the TTP registry.

2.3 Discharge pathway

2.3.1 The discharge pathway for TTP is directed at the following:

a) Prevention and management of relapse
b) TTP-associated medical morbidity
c) long term psychosocial problems relating to the disorder and its treatment

2.3.2 Intensive follow up is required initially, preferably at the STTPC. Given the distance to travel, however, shared care with the local hospital can be arranged. The STTPC always retains the clinical responsibility for the patient's TTP care. Shared arrangements are developed in agreement with patients who may choose not to have all their care delivered by the STTPC. National shared care guidelines will be developed to support the balance between what needs to be delivered in the STTPC and what can be delivered more locally.

This may vary regionally in terms of implementation. Patients will be given information about the patient support groups as part of the patient discharge pathway.

2.3.3 Indicative follow up – some of which may be given under shared care arrangements – including ADAMTS 13 analysis (activity +/-IgG antibody) comprises:

1. Early: Weekly follow up in clinic for 4 weeks
2. Intermediate: 2-4 weekly for the following 3 months
3. Late: 3-monthly for 12 months
4. Long term: 3-6 monthly thereafter; long term follow up should continue in the majority of patients indefinitely as late relapses may occur
5. Participation in a biannual national forum to discuss difficult cases

ADAMTS 13 assessment enables detection of pre-clinical relapse, and allows its treatment without the need for admission to hospital and plasma exchange

2.3.4 Local referring hospitals:

1. A discharge summary and all correspondence must be shared with the referring hospital and the patient's GP
2. Organisation to undertake local routine laboratory testing
3. Organisation to take ADAMTS 13 samples for transfer to the STTPC if appropriate
4. STTPC will facilitate treatment, e.g. rituximab to prevent relapse, regular plasma or concentrate infusion for congenital TTPs, which may be charged through the STTPC or by the referring hospital
5. Direct access for patients if considered to have a relapse of TTP, before their transfer to the STTPC

2.4 Long term effects and the Multidisciplinary Team (MDT)

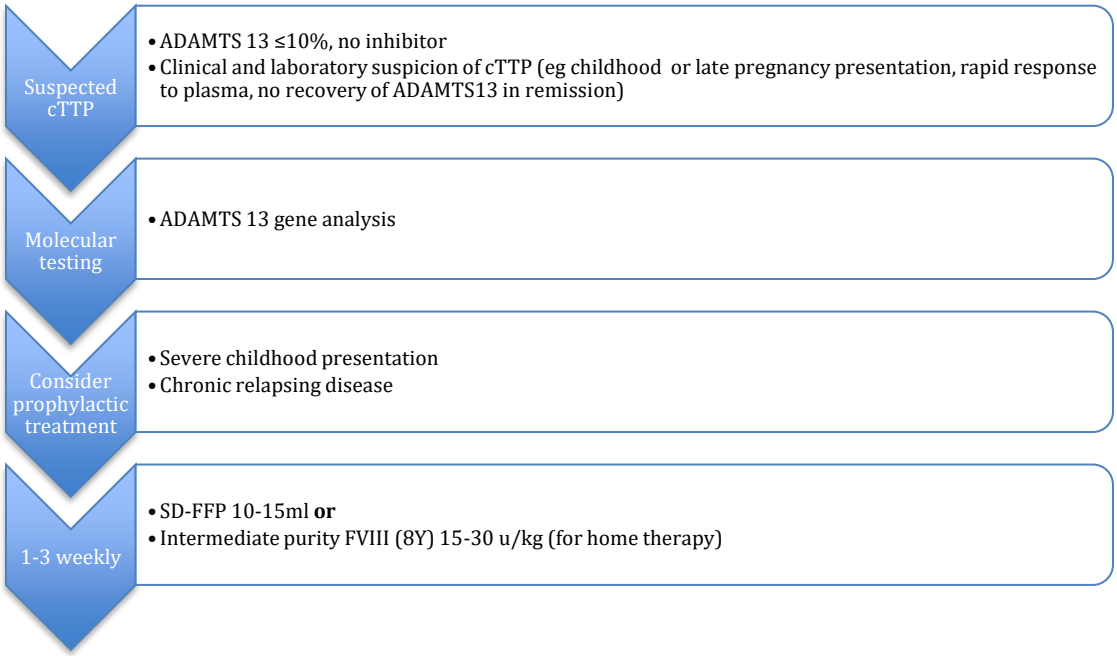
2.4.1 TTP patients may experience long term effects as a result of the condition and its treatment. Some of these will be obvious (e.g. hemiplegia secondary to thrombo-embolic stroke); whereas other may be more subtle (e.g. depression, reduced cognitive functioning, diabetes mellitus). The STTPC, with specialist colleagues and using appropriate diagnostics, has the role of identifying appropriate referral pathways for intervention. Poor memory and aphasia are reported problems which adversely impact on patients' ability and confidence in returning to work.

2.4.2 There is a requirement following the acute life-threatening nature of TTP and its organ involvement and therapy to have clinical psychologist input.

2.4.3 Elective rituximab/anti CD 20 therapy. The purpose of elective rituximab is to treat patients with sub-clinical relapse prior to the development of thrombotic microangiopathy and its more serious complications. Patients who are identified through screening as having low levels of ADAMTS13 activity (at least <15% with additional concerns, or <5%, +-detectable anti-ADAMTS13 antibody and a normal Full Blood Count) should be offered a course of (4 doses of weekly) rituximab. Patients should return to closer monitoring in line with early or intermediate follow up arrangements above.

2.5 Congenital pathway

2.5.1 Congenital TTP (cTTP) is a rare disorder associated with a severe deficiency of ADAMTS13 and is historically referred to as Upshaw-Schulman syndrome. There is likely to be an underestimate of the true frequency. It represents 3-5% of all TTP cases. The pathway is summarised in Figure 2



2.6 Maternity pathway

2.6.1 TTP occurring in pregnancy has been estimated to account for between 5-25% of all TTP presentations in published case series and registries. In addition to maternal morbidity and mortality, the risk of fetal loss can be >40% for TTP presenting in pregnancy. As there are a number of other causes of microangiopathic hemolytic anemia (MAHA) / Thrombotic Microangiopathy (TMA) in pregnancy, including haemolysis elevated liver enzymes low platelet count (HELLP) and atypical haemolytic uraemic syndrome (aHUS), it can be very difficult to distinguish between them in the short term. Thus, plasma exchange may often be commenced if there is uncertainty. Patients presenting for the first time with TTP in pregnancy should initially be treated as per acquired TTP unless a diagnosis of cTTP is made, in which case solvent/detergent plasma/fresh frozen plasma (SD-FFP) infusion may be an alternative to formal plasma exchange. Termination of pregnancy is not required in most cases however careful fetal monitoring with regular assessment of fetal growth and placental function is recommended. Aspirin and Low-molecular-weight heparin thromboprophylaxis should be considered. Ongoing antenatal management and delivery should take place in a tertiary specialist centre.

2.7 Paediatric pathway

2.7.1. Paediatric presentation is usually congenital TTP in the neonatal period and childhood and immune TTP in adolescence. These patients must be managed by expert paediatric haematologists. There must be close, regular liaison with the adult TTP team. Expertise in treating this cohort of patients is rare and it is expected to

develop through the commissioning of this service. As part of this partnership all parties will develop out-reach and education programmes to hospitals in their regional footprint, to support earlier diagnosis, appropriate intervention and improved outcomes.

2.7.2 It is the role of STTPCs to establish shared care pathways in local hospitals to ensure direct access in case of a relapse, for agreed local therapy using Factor VIII concentrate such as BPL 8Y, or routine laboratory blood tests. Congenital cases usually require regular therapy with factor concentrates e.g. BPL 8Y or plasma infusion (octaplas (FFP)). Immune cases will require therapy as described for adults e.g. plasma exchange and immune modulating therapy such as rituximab.

2.7.3 Paediatric patients presenting with an acute relapse should be admitted to the paediatric hospital coupled to their regional STTPC in order to be able to access the highest level of expertise.

2.7.4 Patients on maintenance therapy can receive this at their local hospital ensuring biannual multi-disciplinary team discussion with the adult regional STTPC. Follow-up care will require ongoing paediatric support with home and school visits, local hospital reviews, and tertiary appointments. Transfer of paediatric care to the adult STTPC should be undertaken in a joint manner ensuing smooth transition. It is expected that adolescents will have transitioned by 16 years of age and all will have transitioned by the age of 18 years at the latest.

2.7.5 In acute adolescent immune cases it may be necessary to transfer to the adult team to ensure optimal plasma exchange/immune suppressive therapy.

2.7.6 All paediatric congenital patients will be discussed biannually at a national forum, convened by one of the STTPCs, to ensure that they are being treated on the correct pathway, to support clinical learning and to improve outcomes.

Please note that access to treatment will be guided by any applicable NHS England national clinical commissioning policies.

2.8 Interdependence with other Services

Mandatory services on site: plasma apheresis, clinical haematology, level three critical care. Services that need to be available, with clear pathways and agreed response times, but not necessarily co-located: stroke rehabilitation, neurology, cardiology, renal, HIV, rheumatology and specialist obstetrics.

3. Population Covered and Population Needs

3.1 Population Covered by This Specification

The service outlined in this specification is for patients ordinarily resident in England*; or otherwise the commissioning responsibility of the NHS in England (as defined in Who Pays?: Establishing the responsible commissioner and other Department of Health guidance relating to patients entitled to NHS care or exempt from charges:

http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_127393

(*Note: for the purposes of commissioning health services, this EXCLUDES patients who, whilst resident in England, are registered with a GP Practice in Wales, but INCLUDES patients resident in Wales who are registered with a GP Practice in England).

This service is for adults and children. The paediatric level of activity is small. NHS England commissions the service for the population of England. Commissioning on behalf of other devolved administrations is reviewed annually, and a current list is available from NHS England commissioners. There may be some activity from Wales and Scotland, yet to be agreed. This is a new service and the funding of activity from devolved administrations has yet to be agreed. The funding for the NHS England service will be transferred from clinical commissioning groups.

3.2 Population Needs

The prevalence of this diseases is 330 people in England and there are approximately 150 patients who require acute admission every year. This cohort requires lifelong follow up and regular monitoring. Patients with congenital TTP require ongoing treatment also. The number of patients with congenital TTP is estimated to be 5-10% of all TTP cases. The number of children presenting per year approximately 2-5, these may be congenital or immune cases.

3.3 Expected Significant Future Demographic Changes

None.

3.4 Evidence Base

Although rare, TTP is a very aggressive acute condition which, unless treated promptly and appropriately, has high levels of mortality and morbidity. Outside of specialist centres the patient mortality is 50%. In specialist centres the survival rate is greater than 80%. There is also an appreciable acute morbidity, particularly in neurological disorders. The references below set out the clinical evidence for the diagnosis and treatment of this rare condition used by clinicians in England. The service specification is based on clinical consensus in England.

4. Outcomes and Applicable Quality Standards

4.1 Quality Statement – Aim of Service

TTP is a very rare thrombotic disorder with very acute onset and rapid morbidity and mortality if not identified and treated appropriately in a timely fashion. The rarity of the disease and the aggression of its progression require a nationally agreed approach to managing the disease in specialist centres.

This approach will:

- Improve the identification of patients with this disease

- Improve the time to treatment and management of the patients and improve their outcomes.
- Provide a specialist centre that can provide expert-led care
- Reduce the mortality from this disease
- Ensure patients have a positive experience of care
- Manage the ongoing long-term care and potential relapse
- Maintain and encourage patients own family/friend support (patient led)
- Improve times from diagnosis to treatment including bed availability, line insertion and start of apheresis
- Ensure infrastructure of staff to undertake this process e.g. consultant haematologists and a specialist nursing team
- Ensure referral to clinical psychologist support to capture depression/anxiety (in approximately 50% patients) and support return to normal activities pre TTP.
- Support patient groups who will also carry out independent patient satisfaction exercises and invite them to join the national annual Highly Specialised audit meeting to present this work to other services and commissioners.
- At the HSS annual clinical meeting, identify changes in the service based on patient feedback

NHS Outcomes Framework Domains

Domain 1	**Preventing people from dying prematurely**	**X**
Domain 2	**Enhancing quality of life for people with long-term conditions**	**X**
Domain 3	**Helping people to recover from episodes of ill-health or following injury**	**X**
Domain 4	**Ensuring people have a positive experience of care**	**X**
Domain 5	**Treating and caring for people in safe environment and protecting them from avoidable harm**	**X**

4.2 Indicators Include:

Domain 1 Preventing people from dying prematurely

A national service for TTP will improve the survival rate for this cohort of patients from a survival rate of 50% to a rate of above 80% throughout England.

Domain 2. Enhancing quality of life for people with long-term conditions

Patients with this disease need ongoing care and monitoring which expert centres will be able to provide This monitoring will lead to a reduction in acute admissions mortality and neurological and cardiac morbidity associated with this disease. All STTPCs will keep a register of patients and will offer 6 monthly ADMAMTS13 testing and other routine monitoring. Morbidity in terms of neurological, cardiological and renal deficits will be monitored.

Domain 3 Helping people to recover from episodes of ill-health or following injury

This disease can cause significant cardiac and neurological problems which affect the patients' recovery and ongoing prognosis. The TTP service will link closely with these other specialities to identify and treat these issues to improve outcomes and help patients manage their long-term effects. Morbidity will be monitored against a post discharge baseline and their progress against this baseline will be monitored and assessed to advise on future pathway modifications.

Domain 4 Ensuring **people have a positive experience of care**
National and local patient groups will engage with the service to advise on quality, patient satisfaction and service improvements. As a Highly Specialised Service all STTPCs will participate in national audit meetings to which patient and carer groups are invited. All STTPCs will conduct patient satisfaction surveys. All STTPCs must contribute to the national TTP registry.

Domain 5 Treating and caring for people in safe environment and protecting them from avoidable harm
Treatment in a specialist centre will provide a high-quality service delivered by clinical teams with appropriate expertise. Staff in the STTPCs will comprise as a minimum two consultants with a special interest, one the clinical lead. Each STTPC will have a specialist nursing team.

The service will undertake regular audits and share these as part of the UK TTP registry. Each TTPC will undertake annual outreach/study days/education sessions in their catchment area to ensure that TTP patients are identified appropriately and to support and manage effective shared care arrangements.

Laboratories used will be appropriately accredited and able to undertake testing in the required time intervals.

Number	Indicator	Data Source	Outcome Framework Domain	CQC Key question
Clinical Outcomes				
101	% of emergency admissions receiving a specialist consultant review within 14 hours.	Trust to provide	1, 3, 4	effective, caring, responsive
102	% of patients starting PEX within 4 hours of referral to the specialist centre	Trust to provide	1, 3, 4	effective, caring, responsive
103	% of patients starting PEX within 6 hours of referral to the specialist centre	Trust to provide	1, 3, 4	effective, caring, responsive

104	% of patients starting PEX within 8 hours of referral to the specialist centre	Trust to provide	1, 3, 4	effective, caring, responsive
105	% of patients surviving for a year from the point of diagnosis. Expected level 80%	Trust to provide	1, 3, 4	Effective
106	% of patients will have a central line inserted within 1 hour of admission	Trust to provide	1, 3, 4	effective, caring, responsive
107	Clinical relapse	Trust to provide	1, 3, 4	effective, caring
108	Critical care availability	Trust to provide	1, 3, 4, 5	safe, effective, responsive
Patient Experience				
201	Patient feedback	Trust to provide	4	effective, caring, responsive
202	Review of complaints	Trust to provide	4	effective, caring, responsive
203	Support for patients	Trust to provide	4	effective, caring, responsive
Structure and Process				
301	Clinical lead	Self-declaration	4	well-led
302	Service requirements	Self-declaration	1, 3, 4	Safe, effective, caring, responsive
303	Infrastructure and facilities	Self-declaration	1, 3, 4, 5	Safe, effective, caring, responsive
304	24/7 access to therapeutic apheresis	Self-declaration	1, 3, 4, 5	Safe, effective, caring, responsive
305	Inpatient access to expert advice	Self-declaration	1, 3, 4, 5	Safe, effective, caring, responsive
306	TTP follow-up.	Self-declaration	1, 3, 4, 5	Safe, effective, caring, responsive
307	ADAMTS13 testing is available 24/7	Self-declaration	1, 3, 4, 5	Safe, effective, caring, responsive
308	Data collection	Self-declaration	1, 3	Safe, effective, caring, responsive
309	Clinical guidelines	Self-declaration	1, 2, 3, 4, 5	Safe, effective, caring, responsive
310	Patient pathways	Self-declaration	1, 2, 3, 4, 5	Safe, effective, caring, responsive

311	Patients referred to another centre	Self-declaration	1,2,3,4,5	Safe, effective, caring and responsive

Detailed definitions of indicators, setting out how they will be measured, are included in Schedule 6 of the national contract.

4.3 Commissioned providers are required to participate in annual quality assurance and collect and submit data to support the assessment of compliance with the service specification as set out in Schedule 4A-C.

4.4 Applicable CQUIN goals are set out in Schedule 4D.

4.5 This is a highly specialised service. All providers commissioned to deliver this service are required to comply with the highly specialised commissioning team's annual clinical meeting, audit and information requirements.

5. Applicable Service Standards

5.1 Children and young people must only receive a service from a provider who takes steps to prevent abuse and does not tolerate any abusive practice should it occur (Outcome 7 Essential Standards of Quality and Safety, Care Quality Commission, London 2010 defines the standards and evidence required from providers in this regard).

5.2 All hospital settings should meet the standards for Children and Young People in emergency settings http://www.rcpch.ac.uk/emergencycare

5.3 All hospital settings should meet the Standards for the Care of Critically Ill Children (Paediatric Intensive Care Society, London 2010).

5.4 There should be age specific arrangements for meeting Regulation 14 of the Health and Social Care Act 2008 (Regulated Activities) Regulations 2010.

hTTP://www.b-s-h.org.uk/guidelines/

6. Designated Providers (if applicable)

To be advised

7. Abbreviation and Acronyms Explained

The following abbreviations and acronyms have been used in this document:

- Specialist Thrombotic Thrombocytopenic Purpura Centre (STTPC)
- Commissioning for Quality and Innovation (CQUIN)
- Thrombotic means clotting of the blood
- Thrombocytopenic means a reduction in the number of platelets in the blood
- Purpura means bleeding in the skin causing purple spots / rash
- ADAMTS 13, is an enzyme in the body that works with a substance called the von Willebrand Factor, to stop blood platelets clotting. Patients with TTP have a

deficiency of ADAMTS 13 in an acute episode which means that the platelets form blood clots which can affect any organ in the body.

- Thrombotic Microangiopathy (often known simply as TMA) is a rare but serious medical disease. It is a pattern of damage that can occur in the smallest blood vessels inside many of the body's vital organs – most commonly the kidney and brain.
- Plasma Exchange (PEX) or apheresis, is the removal, treatment, and return or exchange of blood plasma or components thereof from and to the blood circulation. It is an extracorporeal therapy.

Date published: ***<insert publication date>***

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