

SCHEDULE 2 – THE SERVICES

A. Service Specifications

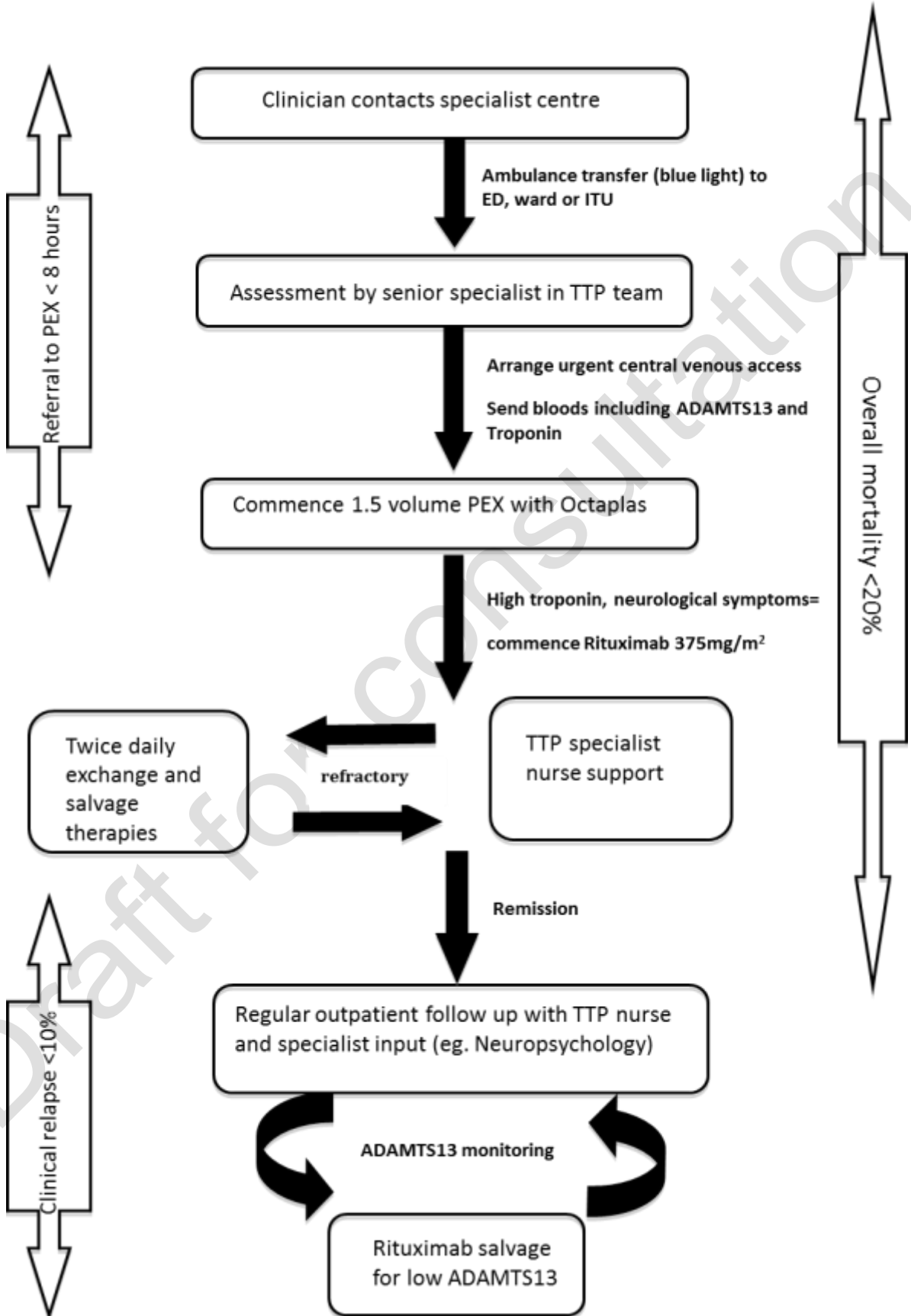
Service Specification No.	1668
Service	Thrombotic Thrombocytopenic Purpura (TTP), all ages
Commissioner Lead	<i>For local completion</i>
Provider Lead	<i>For local completion</i>

<p>1. Scope</p> <p>1.1 Prescribed Specialised Service</p> <p>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.</p> <p>1.2 Description</p> <p>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.</p> <p>1.3 How the Service is Differentiated from Services Falling within the Responsibilities of Other Commissioners</p> <p>This service is for a very rare disease affecting a small number of patients. This service is accessible to patients of the English NHS whom are thought to have TTP. The service requires planning and coordination at national level, which is out with the remit of CCGs.</p>
<p>2. Care Pathway and Clinical Dependencies</p> <p>2.1 Care Pathway</p> <p>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 (specialised centre) must have an 'automatic acceptance' policy. Patients must not be refused admission due to non-availability of beds. However, in extreme circumstances, the service is expected to manage the patient's care remotely and arrange for treatment, if possible, at the referring site and transfer as soon as possible.</p>

Figure 1 Pathway for acute TTP presentations

Draft for consultation

Pathway for suspected iTTP



Patients must be referred to the Regional Specialist Centre as soon as the diagnosis is suspected and transferred to a treating centre urgently as delays in treatment impact mortality. All patients must have started Plasma Exchange ideally within four hours and no longer than eight hours of referral to the specialist TTP centre. This includes securing a bed at the specialist centre, transport time, central line insertion if applicable and defrosting of plasma for PEX.

2.2 Role of Regional Specialist Centre

2.2.1 Every TTP specialist centre sits within a defined geographical site/Trusts covered by the service. This information must be readily accessible by referring Trusts and the ambulance service covering the defined area. Regional Services must be accessible within a window transfer time of 2 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. Specialist regional centres will make appropriate arrangements for either initial plasma exchange treatment or for expedited transfer to the regional centre; 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. Regional centres will develop a clinical partnership with expert paediatric haematologists.

All Specialist regional centres 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 regional specialist TTP team.
- Level 3 Critical Care Facilities
- Interventional Radiology/ IV Access Team access 24/7 for urgent line insertion for patients not entering critical care
- Specialist Haematology Ward
- Dedicated TTP Consultant Team with 24/7 on call availability
- A named paediatric haematologist for congenital TTP delivered through the clinical partnership with the paediatric specialist centre
- Intensive care specialists with experienced in the management of this condition.
- Support patient groups as part of the service development
- Clinical Nurse Specialist, whose role is summarised in Appendix 1
- Trust Approved Patient Pathways, SOPs and Protocols will be based on the Clinical guideline that accompanies this service specification.
- Ability to carry out the appropriate diagnostics, including access to ADAMTS13 testing 7 days a week.
- Access to neurological, cardiac and other relevant services e.g. rheumatology, HIV, specialist obstetrics
- Access to a dedicated clinical psychologist.
- Participate in national clinical forum and enter data onto the national registry

2.2.3 Patients should be transferred as clinically appropriate, in consultation with a team led by level three critical care as appropriate, 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 specialist centre. PEX should be started within 4 hours ideally of referral to the specialist TTP centre and no

longer than a within of 8 hours of referral. Patients should start on plasma exchange prior to a definitive confirmation of diagnosis. If the patient does not have TTP, their 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 the clinical guideline. Octaplas(FPP) is the blood product to be used for plasma exchange (DoH 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 and cover for the clinical nurse specialist need to be in place for staff absence on leave, illness etc.

When the acute phase has improved, patients can be transferred to lower intensity of care but within designated specialist area e.g 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 clinical nurse specialists as soon as practicable.

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

All specialist regional centres 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 On discharge the patient must be closely monitored, preferably at the specialist regional TTP centre. Given the distance to travel, shared care with the local hospital can be arranged. The specialist regional centre always retains the clinical responsibility for the patients TTP care. Shared arrangements are developed in agreement with patients' who may choose to have all their care delivered by the specialist centre. Patients will be given information about the patient support groups as part of the patient discharge pathway.

2.3.3 The TTP centre follow up, including ADAMTS 13 analysis (activity +/-IgG antibody)

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
5. Long term follow up should continue in the majority of patients indefinitely as late relapses may occur
6. Participate in a biannual national forum to discuss difficult cases
7. ADAMTS 13 assessment enables detection of pre-clinical relapse, and allow 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 patients GP
2. Organisation to undertake local routine laboratory testing
3. Organise to take ADAMTS 13 samples for transfer to the regional unit if appropriate
4. Regional centres will facilitate e.g. rituximab to prevent relapse, regular plasma or concentrate infusion for congenital TTPs, which may be charged through the regional centre or by the spoke trust.
5. Direct access for patients if considered to have a relapse of TTP, pre transfer to regional site.

2.4 Long term effects and the MDT

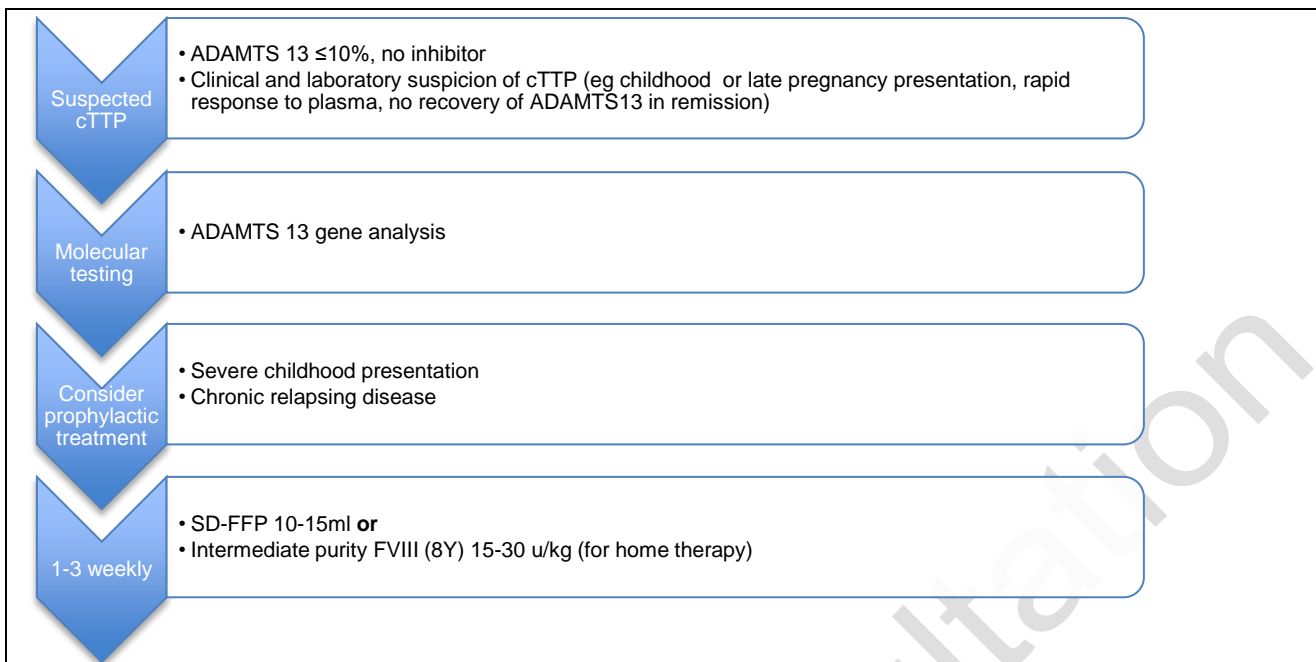
2.4.1 TTP patients may experience long term effects as a result of the condition and its treatment. Some of these will be obvious (e.g. hemiplegia secondary to thrombo-embolic stroke); whereas other may be more subtle (e.g. depression, reduced cognitive functioning, diabetes mellitus). The TTP centre, 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 as part of the inpatient and outpatient care of patients.

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 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 FBC) should be offered a course of (4 doses of weekly) rituximab. Patients should return to closer monitoring in line with early or intermediate follow arrangement 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 detailed care of these patients is set out as part of the clinical guideline. 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 MAHA/TMA in pregnancy, including HELLP and 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 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 LMWH 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 regional centres to establish shared care pathways in local hospitals to ensure direct access in case of a relapse, for agreed local therapy eg BPL 8Y or routine laboratory blood tests. Congenital cases usually require regular therapy with factor concentrates e.g. BPL 8Y or plasma infusion (octaplas(FPP)). 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 trust coupled to the regional adult centre 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 trust ensuring biannual multi-disciplinary team discussion with the adult regional centre. 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 centres should be undertaken in a joint manner ensuing smooth transition. It is expected that adolescents will have transitioned by 16 and all will have transitioned by the age of 18 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 TTP provider Trusts, 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 are stroke rehabilitation, neurology, cardiology renal, HIV, rheumatology and specialist obstetrics.

3. Population Covered and Population Needs

3.1 Population Covered By This Specification

This service is for the whole of 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

There are approximately 100-150 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 specialised 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. See Appendix 1

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 specialised regional 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 specialised 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 CNS
- Ensure dedicated PAs by a clinical psychologist to support in patient care and outpatient follow up 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 centres will keep a register of patients and will offer 6 monthly ADMAMTS13 testing and other routine monitoring as set out in Appendix 1. 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 centres will participate in national audit meetings to which patient and carer groups are invited. All centres will conduct patient satisfaction surveys. All centres 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 specialist TTP centres will comprise as a minimum two consultants with a special interest, one the clinical lead. Each centre will have one clinical nurse specialist.

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

All staff will undertake regular documented CPD.

Labs 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 regional centre	Trust to provide	1, 3, 4	effective, caring, responsive
103	% of patients starting PEX within 6 hours of referral to the regional centre	Trust to provide	1, 3, 4	effective, caring, responsive
104	% of patients starting PEX within 8 hours of referral to the regional centre	Trust to provide	1, 3, 4	effective, caring, responsive
105	% of patients achieving an 80% survival from the point of diagnosis.	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	Access to diagnostics	Self declaration	1, 3, 4, 5	Safe, effective, caring, responsive
307	TTP follow-up.	Self-declaration	1, 2, 3, 4, 5	Safe, effective, caring, responsive
308	ADAMTS13 testing is available 24/7	Self-declaration	1, 3, 4, 5	Safe, effective, caring, responsive
309	Data collection	Self-declaration	1, 3	Safe, effective, caring, responsive
310	Clinical guidelines	Self-declaration	1, 2, 3, 4, 5	Safe, effective, caring, responsive
311	Patient pathways	Self-declaration	1, 2, 3, 4, 5	Safe, effective, caring, responsive
312	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.

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:

CPD, Continuous Professional Development

CQUIN , Commissioning for Quality and Innovation

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.

Date published:

Appendix 1 **Role of the TTP CNS**

- a) Communicating the treatment plan(s) to colleagues in Apheresis, Chemotherapy and Pharmacy.
- b) Teaching and support to the patient and family on the acuity of TTP and associated treatment(s).
- c) Acting as the patient's advocate at all times.
- d) Acting as a point of contact for suspected relapse.
- e) On-going guidance and support to ensure that the patients, post their acute presentation of their TTP, return to as close to their quality of life pre the acute episode.
- f) Support TTP outpatient clinics.
- g) Be the link with the patient support group and the service.
- h) Educational sessions delivered both internally and externally to the organization.
- i) There must be appropriate cover for this post during absence.
- j) For paediatric services there needs to be CNS time made available to provide this service for paediatric patients.

References

1. Scully M et al. Regional UK TTP registry: correlation with laboratory ADAMTS 13 analysis and clinical features. *Br J Haematol* 2008;142:819–26.
2. Galbusera M et al. Thrombotic thrombocytopenic purpura—then and now. *Seminars in Thrombosis and Hemostasis* 2006, 32, 81–89.
3. Scully M et al. Guidelines on the diagnosis and management of thrombotic thrombocytopenic purpura and other thrombotic microangiopathies. *British Journal of Haematol*, 2012, 158, 323–335.
4. Hassan et al. The utility of ADAMTS13 in differentiating TTP from other acute thrombotic microangiopathies: results from the UK TTP Registry. *British Journal of Haematol*, 2015, 171, 830–835.
5. Benhamou et al. Cardiac troponin-I on diagnosis predicts early death and refractoriness in acquired thrombotic thrombocytopenic purpura. Experience of the French Thrombotic Microangiopathies Reference Center. *J Thromb Haemost* 2015; 13: 293–302.
6. Scully M et al. Thrombotic thrombocytopenic purpura and pregnancy: presentation, management, and subsequent pregnancy outcomes. *Blood*. 2014;124(2):211-219.
7. The International Consensus Group for Hematology Review. Suggested Criteria for Action Following Automated CBC and WBC Differential Analysis. International Society for Laboratory Hematology. Accessed 22/09/2016.
http://www.islh.org/web/consensus_rules.php
8. Gulati et al Purpose and Criteria for Blood Smear Scan, Blood Smear Examination, and Blood Smear Review. *Ann Lab Med* 2013;33:1-7.
9. A proposal: the need for thrombotic thrombocytopenic purpura Specialist Centres-- providing better outcomes. Dutt T and Scully M, *Br J Haematol*. 2015 Sep;170(5):737-42. doi: 10.1111/bjh.13568. Epub 2015 Jun 24.
10. Thrombotic thrombocytopenic purpura specialist centres: providing better outcomes for patients with rare but life-threatening conditions. Dutt et al., *Clin Med* June 1, 2015 vol. 15 no. Suppl 3 s21.