RITUXIMAB FOR IMMUNE-MEDIATED THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

INDICATIONS

- Acute TTP with plasma exchange with a baseline ADAMTS13 level of ≤10%
- TTP ADAMTS13 relapse and either:
  - ADAMTS13 activity 20 iu/dL or less
  - ADAMTS13 activity reduced below baseline and symptomatic

A BlueTeq form must be completed (there are separate forms for acute and chronic TTP).

This is an unlicensed (off-label) indication for rituximab. Ensure trust processes for off-label medication are followed.

TREATMENT INTENT

Acute TTP: improvement in time to remission (seven days faster on average) and reduced risk of relapse (10% relapse risk at 2 years compared to 68% without rituximab)

TTP ADAMTS13 relapse: 96% patients will achieve at least a partial remission

PRE-ASSESSMENT

1. Blood tests - FBC, U&Es, LFTs, hepatitis B core antibody, hepatitis B surface Antigen, hepatitis C IgG, HIV antigen/antibody
2. Urine pregnancy test - before first dose for women of child-bearing age unless they are post-menopausal, have been sterilised or undergone a hysterectomy.
3. Record height and weight.
4. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment. If patient is having concurrent treatment of caplacizumab for acute TTP, these should be recorded on the same consent form.
5. Advise dental check is carried out by patient's own dental practitioner before treatment starts.
6. Treatment should be agreed with a consultant experienced in the management of TTP from the regional TTP centre.

DRUG REGIMEN

	Intravenous
Pre-medication (30 minutes prior to rituximab infusion):	Chlorphenamine 10mg IV Hydrocortisone 100mg IV Paracetamol 1g PO

RITUXIMAB	375 mg/m^2 IV infusion in 500 mL sodium chloride 0.9%

CYCLE FREQUENCY

- Administer first dose as early as possible (particularly for patients with cardiac or neurological involvement) and always within 72 hours of diagnosis of acute TTP.
- For acute TTP treated with plasma exchange, give once every 3 days after plasma exchange for four to eight doses. Treatment should be given after plasma exchange. Ideally give rituximab after plasma exchange, or ensure infusion has completed 4 hours before starting plasma exchange
- For ADAMTS13 relapse or for acute TTP no longer on plasma exchange, give once a week for 4 to 8 weeks
  For both indications, Review rituximab after 4 doses – if there is no normalization of ADAMTS13 activity > 50%, continue rituximab for a total maximum of 8 doses. The majority of patients respond to 4 doses.
- Consider repeating course of rituximab for subsequent relapses, with a minimum interval between treatment episodes of 3 months

SPECIAL PRECAUTIONS

- Angina pectoris, or cardiac arrhythmias such as atrial flutter and fibrillation, heart failure or myocardial infarction have occurred in patient treated with rituximab. Patients with a history of cardiac disease and/or cardiotoxic chemotherapy should be monitored closely.
- 10% of patients experience hypotension with the first dose of rituximab, therefore consideration should be given to withholding anti-hypertensive medications 12 hours prior to the rituximab infusion.
- Patients with positive hepatitis B serology should be considered for treatment following trust protocols

STOPPING CRITERIA

- Normalisation of ADAMTS13 activity at ≥ 50 iu/dL OR
- Maximum 8 doses of rituximab at 375mg/m2 OR
- Acute or delayed serum sickness considered to be caused by rituximab

INVESTIGATIONS

All Doses	For outpatient rituximab, FBC, reticulocytes, U&E, LFTs, LDH and ADAMTS13 activity before each dose of rituximab

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

Severe cytokine release syndrome is characterised by severe dyspnoea, often accompanied by bronchospasm and hypoxia, in addition to fever, chills, rigors, urticaria, and angioedema. Hepatitis B reactivation – see pathway for treatment and management of HBV positive patient

REFERENCES

1. Scully *et al.* A phase 2 study of the safety and efficacy of rituximab with plasma exchange in acute acquired thrombotic thrombocytopenic purpura. Blood 2011;18:1746-53
2. Westwood *et al*. Rituximab prophylaxis to prevent thrombotic thrombocytopenic purpura relapse: outcome and evaluation of dosing regimens. Blood Adv 2017;1:1159-66
3. Doyle *et al*. Long-term risk of relapse in immune-mediated Thrombotic Thrombocytopenic Purpura and the role of anti-CD20 therapy. *Blood* 2023;141(3):285-94
4. NHS England (2022). Clinical Commissioning Policy: Rituximab for the treatment in acute Thrombotic Thrombocytopenic Purpura (TTP) and elective therapy to prevent TTP relapse (adults and children aged 2 years and above).

REVIEW

Name	Revision	Date	Version	Review date
Michael Desborough, Consultant Haematologist. Yen Lim, Haematology Pharmacist.	New protocol	Jan 2023	V1.0	Jan 2025
NSSG meeting	Reference update	Jul 2023	V1.1	Jul 2026