Tocilizumab

PROTOCOL FOR PAEDIATRIC RHEUMATOLOGY

1. Background and indications

Tocilizumab is a biologic drug which is an interleukin-6 receptor (IL-6R) monoclonal antibody. Tocilizumab is used in the treatment of Juvenile Idiopathic Arthritis (JIA) and other severe inflammatory diseases.

The use of tocilizumab is considered when a patient has had an insufficient response to one or more DMARD or anti-TNF drug. It can be used on its own or in combination with methotrexate. Tocilizumab is NICE approved for systemic JIA (sJIA) and polyarticular JIA (poly JIA) in children over 2 years of age.

2. Dose and frequency

- **Systemic JIA** – every 2 weeks
  - Patients weighing less than 30kg – 12mg/kg/dose
  - Patients weighing 30kg or over – 8mg/kg/dose

- **Poly JIA** – every 4 weeks
  - Patients weighing less than 30kg – 10mg/kg/dose
  - Patients weighing 30kg or over – 8mg/kg/dose

3. Procedures

3.1. Pre-treatment tests

Prior to the first infusion, all patients should have had the following (unless reason for deviation recorded by Consultant in the medical notes):

- TB Elispot (within the last 6 months or sooner if recent travel to a TB-endemic area) +/- CXR
- The dates of these tests should be completed on the biologics checklist (scanned and filed in EPR records)

3.2. Cannulation and bloods on the day

- Cannulation is usually undertaken by one of the day ward ANPs. If they are not available it should be undertaken by a member of the medical team.
- Routine bloods should be sent (FBC, ESR, U&Es, LFTs, CRP)
- No need to wait for results prior to infusion unless abnormal results from previous admission.

3.3. Clerking

- Clinicians or specialist nurses trained in clerking for tocilizumab infusions should complete the biologics clerking form and ensure that patients are documented ‘fit for infusion’ prior to administration
In the following circumstances it may be necessary to withhold the tocilizumab:

- **Abnormal blood results:**
  - If latest blood results show any of the following, repeat bloods urgently and review results prior to infusion. If results remain abnormal contact paediatric rheumatology team for advice:
    - Hb less than 100, platelets less than 150 (or symptoms and signs which may include bruising, bleeding, pallor)
    - Neutrophils less than 1.5
  - If latest or repeat blood results show any of the following, withhold infusion and inform paediatric rheumatology team:
    - Hb less than 90
    - Neutrophils less than 1
    - Liver Function - ALT more than 120

- If patient has a temperature of 38°C or above.

- Evidence of an infection or contact with an infectious disease. The infection could be an open cut or sore, a chest infection or an infection that affects the whole body (such as the flu or chicken pox). When assessing for infection, it is important to be aware that Tocilizumab is an IL-6 inhibitor and can therefore mask fevers and CRP response.

- The patient has heart failure or other heart conditions, multiple sclerosis, or Guillain-Barré syndrome, or if the patient has experienced numbness, tingling, or had a seizure.

- Lived in or visited an area of the country where an infection called histoplasmosis or coccidioidomycosis (an infection caused by a fungus that affects the lungs) is common.

- The patient has recently received any live vaccinations:
  - **Live vaccines** such as oral polio, rubella, MMR, chicken pox, BCG and yellow fever **should not be given** whilst patient is on tocilizumab.
  - Annual flu vaccines (IM or SC only) are safe, recommended and should be given annually.

**Tocilizumab SHOULD NOT BE GIVEN if:**

- Had a severe allergic reaction to Tocilizumab or any other product that was made with murine proteins.

- The patient has had tuberculosis (TB) (unless on ATT) or if there has been recent contact with someone who might have TB. TB screening must have been performed in all patients prior to commencing Tocilizumab therapy.

3.4. **Pre-medication**

- **No premedication is required.**
- **However, the following PRN drugs should ideally be prescribed prior to commencing infusion:**
3.5. Drug storage & preparation

- Store vials in a refrigerator (2°C–8°C). Do not freeze.
- Keep the vial(s) in the outer carton in order to protect from light.
- Vials contain 20mg/ml concentrated solution for infusion in the following sizes:
  - 80mg
  - 200mg
  - 400mg

**TOCILIZUMAB MUST BE DILUTED PRIOR TO ADMINISTRATION**
- ANTT should be used as per Trust policy for IV medications.
- Calculate dose of tocilizumab and fluid volume to be withdrawn

**Patient’s weight less than 30 kg**
- Withdraw a volume of sodium chloride 0.9% solution for injection from a 50ml infusion bag equal to the volume of tocilizumab concentrate required. The required amount of tocilizumab concentrate should be withdrawn from the vial and placed in the 50ml infusion bag to make a final volume of 50mls. Gently invert to mix.

**Patient’s weight 30 kg or over**
- Withdraw a volume of sodium chloride 0.9% solution for injection from a 100ml infusion bag equal to the volume of tocilizumab concentrate required. The required amount of tocilizumab concentrate should be withdrawn from the vial and placed in the 100ml infusion bag to make a final volume of 100mls. Gently invert to mix.
- Prior to administration solution should be inspected for particulate matter or discolouration. If this is present discard the solution.
- After preparation solution must be administered immediately, or within 4 hours if stored in fridge.

3.6. Administration rate and monitoring

- **A PHYSICIAN MUST BE CLOSE BY FOR ALL INFUSIONS**
- Infuse prescribed dose, diluted as above, over 1 hour
- Observations:
  - Baseline TPR and BP
  - TPR and BP after 15 minutes
  - TPR and BP every 30 minutes until flush finished
- If TPR and BP are outside normal limits or child has had a previous reaction, check observations every 15 minutes throughout infusion
- Upon completion, flush with 20ml 0.9% sodium chloride at the same infusion rate and monitor observations for at least 1 hour post infusion.
4. Side effects and infusion reactions

Most patients do not have side effects, but the potential side effects include;

1) **Infusion Reactions**: This is very rare but the patient should be monitored for this (TPR and BP). If there are any concerns a doctor should review the patient and the infusion could be slowed down or stopped.

2) **Skin rashes**: Itchy skin rashes may rarely occur around 24 - 48 hours after the second or third infusion and can last for several days. Anti-histamine or pre-medication with hydrocortisone might be needed.

3) **Increased risk of infection**: As with all biologics there is an increased risk of infection.

4) Other side effects can include conjunctivitis, abdominal pain or non-specific symptoms such as headaches

**Allergic Reaction**

If the following should occur STOP THE INFUSION AND INFORM A DOCTOR on the ward and the paediatric rheumatology team (see contact details at bottom of document)

- Swelling of the lips
- Hives (red, raised, itchy patches of skin)
- Difficulty breathing
- Chest pain
- The presence of high or low blood pressure (change by more than 20mmHg). Symptoms of light-headedness, dizziness or headache may alert to the presence of a marked change in blood pressure.

If in doubt, prioritise safety at all times: stop the infusion and call for help.

**Contacts for Paediatric Rheumatology Team**

1. Paediatric Rheumatology Nurse Specialists 01865 (7)37341 cnspaedrheum@ouh.nhs.uk
2. Paediatric Rheumatology consultant on-call via switchboard
3. Out of hours – contact can be made with the on-call Paediatric Rheumatology consultant via switchboard

**References**

- SPC for Tocilizumab found at [www.medicines.org.uk](http://www.medicines.org.uk)
- **NICE (2015)** Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis
- 2013 BSR/BHPR guideline for the use of IV Tocilizumab in the treatment of adult patients with RA.
- Modified from OxPARC Tocilizumab (RoActemra) PROTOCOL FOR PAEDIATRIC RHEUMATOLOGY UNIT E.Inness./E.Kendall/N.Wilkinson (Feb 2012)