Tocilizumab (RoActemra)
PROTOCOL FOR PAEDIATRIC RHEUMATOLOGY UNIT.

Tocilizumab is a drug used that works by blocking the interleukin-6 receptor (IL-6R). This protein is involved in inflammation, passing messages to other cells in the immune system and telling them to attack the body’s joints. Tocilizumab is used in the treatment of Juvenile Idiopathic Arthritis (JIA) and other inflammatory disease.

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.

Possible side effects during the infusion
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. The patient should be encouraged to report and adverse feelings.

2) **Skin rashes**: Itchy skin rashes have occurred in a few people usually around 24 - 48 hours after the second or third infusion and can last for several days. Anti Histamine can be prescribed to reduce this. No-one has stopped the drug due to itching, the rashes usually go away after a few more doses.

3) **Increased risk of infection**: As with all arthritis treatment there is an increased risk of infection. Blood test should be monitored regularly to check for immune suppression.

4) Other side effects can include conjunctivitis, abdominal pain and more non-specific symptoms such as headaches or temporary changes to blood results including WCC and ALT.

Previous experience of this drug in children, suggests side effects are generally mild and reversible. If these symptoms or any other unusual symptoms occur please contact the Clinical Nurse Specialists. Dr Wilkinson or Dr David should also be informed as well as the GP.

**Allergic Reaction**
If the following should occur STOP THE INFUSION AND INFORM A DOCTOR on the ward and Dr Wilkinson 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 lightheadedness, dizziness or headache may alert to the presence of a marked change in blood pressure.

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 TB (tuberculosis), unless suitable antibiotics are being given to treat TB, or if there has been recent contact with someone who might have TB. A CXR must have been performed in all patients (+/- mantoux/Elispot if considered high risk).

In the following circumstances please discuss with Dr Wilkinson or one of the paediatric rheumatology CNS team as it may be necessary to withhold the tocilizumab.

- 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).
- 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.

**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 are safe and recommended.

**Bloods are required prior to each dose. No need to wait for results from day of dose. Please inform & discuss with Rheumatology team if:**

Low blood cell count (Hb <9, platelets <150), symptoms and signs of which may include bruising or bleeding, pallor, or if patient has a temperature above 37.5°C.

**Neutrophils**

- >1 but <1.5 $10^9$/l - Give tocilizumab, but inform Rheumatology team
- < 1 $10^9$/l - Do not give tocilizumab.

**Liver Function - If ALT >120 inform Rheumatology team**

A PHYSICIAN MUST BE CLOSE BY FOR ALL INFUSIONS

<table>
<thead>
<tr>
<th>Rationale and funding for Tocilizumab treatment established</th>
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<tbody>
<tr>
<td>Patient and parents have received and understand information on Tocilizumab</td>
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Prescribe Tocilizumab

**Patients Weight < 30 kg 12mg/kg commencing two weekly.**

**Patients Weight ≥ 30 kg 8mg/kg commencing two weekly.**

Ensure drugs prescribed PRN incase required. No premed required.

<table>
<thead>
<tr>
<th>IV Hydrocortisone: child aged</th>
<th>1–5 years</th>
<th>6–12 years</th>
<th>12 years +</th>
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<tr>
<td></td>
<td>50 mg</td>
<td>100 mg</td>
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<tr>
<th>IV Chlorphenamine</th>
<th>1–5 years</th>
<th>6–12 Years</th>
<th>12 years +</th>
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<td>2.5 mg</td>
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</table>
Identify allergic history – inform paediatric rheumatology team if previous allergic reaction to Tocilizumab or other drugs that have murine proteins.

Identify presence of infections or contact with infectious disease (eg chicken pox, measles) and record vital sign.

Insert peripheral cannula or check existing central line is patent

Storage & preparation of infusion of RoActemra (Tocilizumab)
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 concentrate for solution for infusion
Each vial contains 80 mg of tocilizumab in 4 ml (20 mg/ml).
Each vial contains 200 mg of tocilizumab in 10 ml (20 mg/ml).
Each vial contains 400 mg of tocilizumab in 20 ml (20 mg/ml).

ANTT should be used. Calculate dose of tocilizumab and fluid volume to be withdrawn

Dilution of RoActemra (Tocilizumab)

Patients Weight ≥ 30 kg
Slowly add calculated volume (dose) of Tocilizumab to 0.9% Sodium Chloride to make a final volume of 100mls. Gently invert to mix.

Patients Weight < 30 kg
Slowly add calculated volume (dose) of Tocilizumab to 0.9% Sodium Chloride to make a final volume of 50mls. Gently invert to mix.

Prior to administration solution should be inspected for particulate matter or discolouration. If this is present discard.

After preparation solution must be administered immediately, or within 4 hours if stored in fridge.

Infuse over 1 hour

Baseline observations, then monitor vital signs after 15mins, then every 30 minutes until flush finished, If vital signs outside normal limits or child has had previous reaction check every 15min

Upon completion flush with 20ml 0.9% sodium chloride @ same infusion rate and monitor vital signs for at least 1 hour post infusion.

Contacts for Paediatric Rheumatology Team
Paediatric rheumatology nurse specialists 01865 737341 / 737317 cnspaedrheum@ouh.nhs.uk
Dr Wilkinson (Consultant Paediatrician & Rheumatologist) ext 01865 738049 via Hannah Trendell (Mobile 07944 723273 (emergencies only) Nick.wilkinson@ouh.nhs.uk
Dr David (Consultant Rheumatologist) ext 01865 738107

Out of hours – Contact can be made with the on-call Doctor for rheumatology via switchboard at the NOC 01865 741155.
References

- SPC for Tocilizumab found at www.medicines.org.uk