INFLIXIMAB (Remicade)
PROTOCOL FOR PAEDIATRIC RHEUMATOLOGY UNIT.

Infliximab is a drug that blocks a key protein of all inflammatory processes called Tumour Necrosis Factor (or TNF). TNF is a signalling protein that increases the activity of cells involved in inflammation and in patients with arthritis its concentration is particularly high. It has been shown in arthritis patients that persistently high levels contribute to tissue damage. Infliximab stops TNF from binding to cells, thereby reducing inflammation. Infliximab should only be used in patients who do not respond to other treatments. Patients receiving infliximab should continue to receive methotrexate or a similar type of drug.

Infliximab is not currently licenced for used in JIA. However it has been used for over 15 years for this indication and is approved for children with crohns disease aged 6-17 years. It is widely used for Rheumatoid arthritis and other inflammatory conditions. Approval from the Medicines Advisory Committee for use in Juvenile Arthritis (JIA), vasculitis, juvenile dermatomyositis (JDM) has been agreed.

Possible side effects during the infusion
Most patients do not experience side effects, but possible infusion related reactions include headache, fever, facial flushing, pruritus, myalgia, nausea, chest tightness, dyspnoea, vomiting, erythema, abdominal discomfort, shivers, hypertension, light headedness, hypotension and palpitations. For many patients these reactions resolve with slowing the infusion rate. From previous studies it has been shown that infusion reactions experienced were generally mild to moderate and they decreased in frequency with repeated dosing.

Some patients have had allergic reactions 3 to 12 days after receiving Infliximab. The symptoms of this type of delayed reaction may include fever, rash, headache, and muscle or joint pain. If these symptoms or any other unusual symptoms occur Dr Wilkinson or Dr David should 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.

Other medicines including steroids and adrenaline should be available if they need to be given to treat the allergic reaction.

Infliximab SHOULD NOT BE GIVEN if:

- Had a severe allergic reaction to Infliximab or any other product that was made with murine (mouse) 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 (+/- mantoux/Elispot if considered high risk) must have been performed in all patients.

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 infliximab.

- 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 infliximab.
- Annual flu vaccines are safe and recommended.

**Bloods 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, bleeding, pallor, or if patient has a temperature above 37.5°C.
- Neutrophils < 1.5 cells x 10⁹/l
- Liver Function - ALT >120

**A PHYSICIAN MUST BE CLOSE BY FOR ALL INFUSIONS**

1. Rationale and funding for Infliximab treatment established
2. Patient and parents have received and understand information on Infliximab
   - Consent obtained
3. Infliximab is prescribed at a dose of 6mg/kg
   - (Doses will be rounded to the nearest vial size and may go to a max of 10mg/kg)
   - Frequency of infusions can vary, but usually given on weeks 0, 2 or 4 and then 8 weekly
4. Record weight and height.
   - Drug chart to go to pharmacy.
5. Identify allergic history – inform paediatric rheumatology team if previous allergic reaction to infliximab or other drugs that have murine proteins.
6. Identify presence of infections or contact with infectious disease (eg chicken pox, measles) and record vital signs
7. Insert peripheral cannula or check existing central line is patent
**Contacts for Paediatric Rheumatology Team**

1. Paediatric rheumatology nurse specialists 01865 737341 / 737317 [cnspaedorheum@ouh.nhs.uk](mailto:cnspaedorheum@ouh.nhs.uk)
2. Dr David (Consultant Rheumatologist) 01865 738049 via Hannah Trendell

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

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**Premedicate with IV Hydrocortisone:**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–5 years</td>
<td>50 mg</td>
</tr>
<tr>
<td>6–12 years</td>
<td>100 mg</td>
</tr>
<tr>
<td>12 years+</td>
<td>200 mg</td>
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</tbody>
</table>

**Storage & preparation of Remicade (Infliximab)**

Store in a refrigerator (2°C - 8°C).

Each vial of Remicade contains 100mg of infliximab.

Reconstitute each vial with 10mls of sterile water for injection, gently swirl the vial, DO NOT SHAKE, and allow to dissolve over 5 minutes.

Solution must be yellow, opalescent and not cloudy.

Calculate dose of infliximab and fluid volume to be withdrawn.

**Dilution of Remicade (Infliximab)**

From 250ml bag of 0.9% sodium chloride, withdraw the volume equal to the volume of the reconstituted vial(s) and then slowly add the infliximab. Gently mix.

Therefore making a final volume of 250mls.

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

- A 1.2 microns filter MUST be used
- The IV line must not be used for any other medications or fluids.

**If there is a history of infusion related reactions:**

- In the presence of medical staff give an intravenous test dose of 3ml filtered medication over 15minutes.
- If a reaction occurs stop infusion and treat
- If no reaction occurs, continue as recommended infusion schedule.

**Infusion Schedule:**

Infuse at: 60ml/hr for the first 30 minutes, 80ml/hr for the next 30 minutes.

Then increase: 120ml/hr until completion of the infusion volume

Stop any infusion if any suspected reaction. If mild or reaction improves immediately, recommence the infusion at 10mls/hr and increase infusion at hourly intervals as tolerated.

**Monitor vital signs every 30 minutes,**

If vital signs outside normal limits or child has had previous reaction check every 15min

Upon completion flush with 20ml 0.9% sodium chloride @ 120mls/hr and monitor vital signs for at least 1 hour post infusion.
References

- SPC for Infliximab found at [www.medicines.org.uk](http://www.medicines.org.uk)

Modified from the Paediatric Gastroenterology Infliximab Protocol. Oxford Children's Hospital. OUH Trust.