Background
Infliximab is one of a group of anti-inflammatory agents that work by blocking the action of the pro-inflammatory cytokine, Tumour Necrosis Factor-alpha (TNF-α). TNF-α is a signalling protein that increases the activity of cells involved in inflammation. Infliximab stops TNF-α from binding to cells, thereby reducing inflammation.

Gastroenterology

Indications
Infliximab is used for treatment of patients with moderately to severely active Crohn’s disease and patients with fistulising Crohn’s disease, who have had an inadequate response to conventional therapy. It is also increasingly used in patients with severe ulcerative colitis, most commonly as “rescue therapy” in acute severe colitis to avoid or defer the need for colectomy.

Staging of the disease by endoscopy and/or small bowel/pelvic imaging must be carried out within 3 months prior to starting infliximab to confirm severe disease.

Regime

i) Induction - Infusions at 0, 2 and 6 weeks.

ii) Maintenance therapy
Clinical review should be carried out 4-6 weeks after the third induction dose in order to determine:
- Clinical response to treatment (including clinician assessment, height, weight, repeat PCDAI/PUCDAI)
- Whether maintenance therapy is appropriate

8 weekly maintenance infusions should be continued if appropriate.
When there is loss of effect after a clear initial response to infliximab, several strategies have been employed, including increasing the dose to 10mg/kg, decreasing the dosing interval and switching to other biologic therapy. These decisions need to be taken on an individual patient basis.
INFLIXIMAB

**Review and follow-up**

Patients on maintenance infliximab therapy should be reviewed a minimum of every 6 months by consultant paediatric gastroenterologist. Exit strategy documented by gastroenterology team in medical notes at each review. Co-immunosuppression with a thiopurine or methotrexate should normally be given in conjunction with infliximab.

In accordance with expert guidelines and consensus on good practice, patients on infliximab should have disease reassessment at least annually to inform decisions about the need for ongoing treatment.

---

**Rheumatology**

**Indications**

Infliximab is used in the treatment of a number of rheumatological conditions, including Juvenile Idiopathic Arthritis (JIA) and uveitis. In patients with active disease, TNF-α level is elevated. In arthritis patients, a persistently high TNF-α level contributes to tissue damage. Infliximab is used in patients who do not respond to standard treatments.

**Regime**

The treatment regime usually consists of intravenous infusions at 0, 2 and 6 weeks. Subsequent infusions are given 4, 6 or 8 weekly thereafter, depending on clinical response. Another regime is monthly infusions.

**Review and follow-up**

Rheumatology review at each infusion visit with documentation of Core Set Variables. Clinic review at minimum of 6 monthly intervals. When there is loss of effect after a clear initial response to infliximab, several strategies have been employed, including increasing the dose to 10mg/kg, decreasing the dosing interval and switching to other biologic therapy. These decisions need to be taken on an individual patient basis.
Contra-indications

Absolute contra-indications:
- Untreated chronic infection, such as tuberculosis
- Presence of undrained abscesses (including perianal)
- Patients with moderate to severe congestive heart failure
- Known hypersensitivity to murine proteins or any other component of the product

Relative contraindications/cautions:
- Intercurrent febrile illness (see below)
- Chronic hepatitis B carriage
- History of Guillain-Barré Syndrome, optic neuritis or Multiple Sclerosis
- Pregnancy
- Strictureing disease

Prior to First Treatment

Once the decision has been made that a patient requires infliximab,
- A written patient information leaflet should be provided and the patient and/or carer given the opportunity to discuss the treatment with the medical team.
- This must be fully discussed with the patient and/or carer.
- Responsible consultant to document discussion regarding risks/benefits of treatment (including serious risks) in full, either in patient case notes or on consent form.
- Responsible consultant to obtain written consent before first dose.

Direct questioning is required regarding:
- Recent/current infections
- Personal/family history and/or risk factors for TB
- Personal/family history of Guillain-Barré Syndrome, optic neuritis or multiple sclerosis
- Possibility of pregnancy and advice re use of contraception during treatment

Before commencing infliximab, it is important to exclude the possibility of TB.
Children under 5 years should have:
- CXR
- Mantoux
Discuss with Infectious Diseases if Mantoux is positive.

Children over 5 years should have:
- CXR
- Quantiferon Gold test
Pre-treatment bloods:
- ESR or CRP
- FBC, U&E, LFT, albumin
- ANA, dsDNA (if not performed within 3 months)
- Varicella Zoster serology (if not already documented)
- Measles serology (if not already documented)
- Hep B serology (HBsAg, AntiHBCab, Anti-HBsAb)
- Hep A serology (consider immunisation if non-immune)
- Hep C serology
- Urinalysis
- Consider pregnancy testing in females of childbearing age

Disease activity scores at baseline
- PCDAI (Crohn’s patients) – see Appendix
- PUCAI (Ulcerative colitis patients) – see Appendix
- Core set variables (JIA)

Dosage and Administration

Regime - See under specialty notes above.

On admission and prior to infusion
- Prior to each infusion, interval symptoms should be enquired about.
- Ask about recent infections (colds, URTIs, temps etc). If these are present and severe, discuss with consultant prior to commencing infusion. It may be prudent to defer the infusion for a week to allow recovery from the infection.
- Nurse to take baseline TPR, BP and facilitate IV access.
- Obtain bloods for ESR, CRP, FBC, electrolytes, urea and creatinine, LFT’s, albumin. Consider yearly ANA. Consider repeating screening for TB e.g. TB quantiferon gold if new risk factors.
- Medical review, particularly if patient febrile
- Disease activity score (PCDAI/PUCAI/Core set variables) as per specific indication

Premedication – please chart
1. Loratadine (Claratyne) or cetirizine – dose 0.5mg/kg PO (max 25mg) 30-60 minutes prior to the infusion. Loratadine comes as 5 and 10 mg tablets. Give dose to the nearest 5mg.
2. Hydrocortisone - 4mg/kg IV (max 200mgs) 15-30 minutes prior to infusion.
   - for all gastroenterology patients
   - for rheumatology patients if previous infusion reaction
3. Paracetamol - 15mg/kg PO (max dose 1gm) 15-30 minutes prior to infusion.

Anaphylaxis medication – please chart Adrenaline (see Anaphylaxis guideline for dose)
INFLIXIMAB

Infusion
- The Infliximab dose is usually 5mg/kg iv (dose range 3-10mg/kg). Any variation from standard dosage should be under advice from the responsible Consultant
- Dilute infliximab in 250ml of 0.9% normal saline. (For children <35kg, consider dilution in 125ml 0.9% normal saline, especially if concerns about fluid overload)
- Infuse using intravenous giving set with an in-line low protein-binding filter pore (1.2 microns or less)
- When reconstituting medicine DO NOT SHAKE THE VIAL. A swirling action can be used.
- Infuse over 2 hours unless otherwise stated and documented by medical staff
- Flush line with 0.9% sodium chloride to complete infusion

Patient Monitoring
Temperature, Pulse, Respiratory rate and BP as follows:
- At baseline
- ¼ hourly for 1 hour
- ½ hourly thereafter until one hour post-infusion

Observe for signs of adverse drug reaction

The patient must remain on the ward for 2 hours post infusion as delayed reactions to the drug can occur.

Adverse Drug Reactions
If any reaction is suspected, stop infusion and obtain medical review.

Mild-moderate allergic reactions
Occur most frequently with first and second infusions
Symptoms include:
- flushing
- rash
- pruritus
- urticaria
- nausea
- fatigue
- headache
- fever/chills
- dizziness

Severe allergic reactions/Anaphylaxis
Signs and symptoms include

Respiratory:
- Difficulty/noisy breathing
- Swelling of tongue
- Swelling/tightness in throat
- Difficulty talking and/or hoarse voice
- Wheeze or persistent cough
INFLIXIMAB

Cardiovascular:
- Loss of consciousness
- Collapse
- Pallor and floppiness (in young children)
- Hypotension

Management of allergic reactions

Mild-moderate reaction
1. Stop infusion
2. Administer paracetamol 15mg/kg PO, if not received a dose within the previous 4 hours
3. Administer cetirizine/loratadine dose 0.5mg/kg PO (max 25mg)
4. Restart infusion after 30 minutes at halved rate if symptoms resolved

Severe allergic reaction/Anaphylaxis
1. Stop infusion
2. Call 777 immediately
3. Lie patient flat
4. Administer high flow oxygen
5. Administer resuscitation drugs
   - Adrenaline 1 in 1,000 dilution 0.01ml/kg IM (min dose 0.1ml to max dose of 0.5ml)
     Adrenaline may be repeated if no effect within 2 minutes.
   - Hydrocortisone 4mg/kg IV
6. Refer to Starship Anaphylaxis Guideline
7. Contact on-call consultant responsible for care

References


National Institute for Clinical Excellence (UK) TA187 Crohn's disease - infliximab (review) and adalimumab (review of TA40): guidance; 19 May 2010


Remicade Information leaflet (Janssen)
## Appendix 1 – PCDAI (Paediatric Crohn’s Disease Activity Index)

### Abdominal pain

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>Mild (brief episodes, not interfering with activities)</td>
</tr>
<tr>
<td>10</td>
<td>Moderate/severe (frequent or persistent, affecting with activities)</td>
</tr>
</tbody>
</table>

### Stools

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0-1 liquid stools, no blood</td>
</tr>
<tr>
<td>5</td>
<td>2-5 liquid or up to 2 semi-formed with small blood</td>
</tr>
<tr>
<td>10</td>
<td>Gross bleeding, &gt;6 liquid stools or nocturnal diarrhoea</td>
</tr>
</tbody>
</table>

### Patient functioning, general well-being (Recall, 1 week)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No limitation of activities, well</td>
</tr>
<tr>
<td>5</td>
<td>Occasional difficulties in maintaining age appropriate activities, below par</td>
</tr>
<tr>
<td>10</td>
<td>Frequent limitation of activities, very poor</td>
</tr>
</tbody>
</table>

### EXAMINATION

#### Weight

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Weight gain or voluntary weight loss</td>
</tr>
<tr>
<td>5</td>
<td>Involuntary weight loss 1-9%</td>
</tr>
<tr>
<td>10</td>
<td>Weight loss &gt;10%</td>
</tr>
</tbody>
</table>

#### Height

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&lt; 1 channel decrease (or height velocity &gt; -SD)</td>
</tr>
<tr>
<td>5</td>
<td>&gt; 1&lt;2 channel decrease (or height velocity &lt; -1SD&gt; -2SD)</td>
</tr>
<tr>
<td>10</td>
<td>&gt; 2 channel decrease (or height velocity &lt; -2SD)</td>
</tr>
</tbody>
</table>

#### Abdomen

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No tenderness, no mass</td>
</tr>
<tr>
<td>5</td>
<td>Tenderness, or mass without tenderness</td>
</tr>
<tr>
<td>10</td>
<td>Tenderness, involuntary guarding, definite mass</td>
</tr>
</tbody>
</table>

#### Peri-rectal disease

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>None, asymptomatic tags</td>
</tr>
<tr>
<td>5</td>
<td>1-2 indolent fistula, scant drainage, tenderness of abscess</td>
</tr>
<tr>
<td>10</td>
<td>Active fistula, drainage, tenderness or abscess</td>
</tr>
</tbody>
</table>

#### Extra-intestinal manifestations

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Fever &gt; 38.5 x 3 days in week, arthritis, uveitis, erythema nodosum, or pyoderma gangrenosum</td>
</tr>
<tr>
<td>5</td>
<td>One</td>
</tr>
<tr>
<td>10</td>
<td>Two</td>
</tr>
</tbody>
</table>

### LABORATORY

#### Hct (%)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 10yrs</td>
<td>11-14 (male)</td>
</tr>
<tr>
<td>&gt; 33</td>
<td>&gt; 35</td>
</tr>
<tr>
<td>28-33</td>
<td>30-34</td>
</tr>
<tr>
<td>&lt; 28</td>
<td>&lt; 30</td>
</tr>
</tbody>
</table>

#### ESR (mm/hr)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>0</td>
</tr>
<tr>
<td>20-50</td>
<td>2.5</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>5</td>
</tr>
</tbody>
</table>

#### Albumin (g/L)

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 35</td>
<td>0</td>
</tr>
<tr>
<td>31-34</td>
<td>5</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>10</td>
</tr>
</tbody>
</table>

TOTAL =

### Author:
Dr. Jon Bishop, Dr. Jackie Yan

### Editor:
Dr. Raewyn Gavin

### Services:
Paed Gastroenterology & Rheumatology

### Date Issued:
May 2013

### Inflimab Page:
7 of 11
### Appendix 2

**PUCDAI (Paediatric Ulcerative Colitis Activity Index)**

<table>
<thead>
<tr>
<th>ITEM</th>
<th>POINTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Abdominal pain</td>
<td></td>
</tr>
<tr>
<td>No pain</td>
<td>0</td>
</tr>
<tr>
<td>Pain can be ignored</td>
<td>5</td>
</tr>
<tr>
<td>Pain cannot be ignored</td>
<td>10</td>
</tr>
<tr>
<td>2. Rectal bleeding</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Small amount only, in less than 50% of stools</td>
<td>10</td>
</tr>
<tr>
<td>Small amount with most stools</td>
<td>20</td>
</tr>
<tr>
<td>Large amount (&gt;50% of the stool content)</td>
<td>30</td>
</tr>
<tr>
<td>3. Stool consistency of most stools</td>
<td></td>
</tr>
<tr>
<td>Formed</td>
<td>0</td>
</tr>
<tr>
<td>Partially formed</td>
<td>5</td>
</tr>
<tr>
<td>Completely unformed</td>
<td>10</td>
</tr>
<tr>
<td>4. Number of stools per 24 hours</td>
<td></td>
</tr>
<tr>
<td>0-2</td>
<td>0</td>
</tr>
<tr>
<td>3-5</td>
<td>5</td>
</tr>
<tr>
<td>6-8</td>
<td>10</td>
</tr>
<tr>
<td>&gt;8</td>
<td>15</td>
</tr>
<tr>
<td>5. Nocturnal stools (any episode causing wakening)</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
</tr>
<tr>
<td>6. Activity level</td>
<td></td>
</tr>
<tr>
<td>No limitation of activity</td>
<td>0</td>
</tr>
<tr>
<td>Occasional limitation of activity</td>
<td>5</td>
</tr>
<tr>
<td>Severely restricted activity</td>
<td>10</td>
</tr>
<tr>
<td>SUM OF PUCAI (0-85)</td>
<td></td>
</tr>
</tbody>
</table>
Appendix 3

Infliximab Medication in Inflammatory Bowel Disease

The aim of this leaflet is to give young people, parents and carers information about Infliximab.

Why do I need a new medicine?
Infliximab is a relatively new medicine. It is used to treat severe Crohn’s disease. It may be given to you when other medicines have not worked or have caused bad side effects and when surgery is not the right treatment for you.
Infliximab may be used for people who have fistulas that have not healed with other medical or surgical treatments.
Infliximab is also occasionally used to treat ulcerative colitis when the colitis is severe and has not improved with steroid treatment.

What does Infliximab do?
Infliximab targets a protein in the body called TNF-alpha (tumour necrosis factor-alpha). Your body produces TNF-alpha as part of its immune response, to help fight infections. In people with inflammatory bowel disease, too much TNF-alpha is made, which can cause damage to the intestine (bowel). Infliximab sticks to TNF-alpha, which stops it causing the damage.

How do I take Infliximab?
Infliximab needs to be given in hospital. This will usually be on the Day Stay ward. It takes about two hours to give the infliximab, but you will also need to stay for two hours afterwards to make sure you are OK.
Infliximab is infused (dripped) though a tiny plastic tube (luer) into a vein in your hand or arm. The infliximab is mixed with salt water and flows from a bag through some plastic tubing straight into your vein.

Will I start feeling better straight away?
Infliximab does often work quite quickly. Children usually begin to feel better after the first or second dose. You will be seen by your doctor soon after starting the Infliximab to ensure that you are feeling better.
Are there any side effects of Infliximab?
Some patients experience an allergy like reaction while or shortly after getting the infusion. This can be:

- Fever
- Chest pain or joint pain
- Breathlessness
- Sore throat
- Rash
- Swelling of the face
- Headache.

If you experience any of these symptoms please get the attention of a doctor or nurse immediately.

To reduce the chance of you getting any side effects, you will be given some steroid and anti-allergy medicine before you get the Infliximab.

Other rare side effects include:

- Heartburn,
- Diarrhoea
- Constipation
- Inflammation of the liver, gallbladder, pancreas and stomach.

Will I be at a higher risk of catching infections while taking infliximab?
Infliximab does reduce your body’s defense against infection, so you may be at increased risk for some infections. Chicken pox can be a serious infection while you are taking infliximab. We will check a blood test to see if you are protected against chicken pox before you start the infliximab. If you have had chicken pox in the past, your body will have developed antibodies that will protect you against the infection, even when you are on infliximab. If you do not have antibodies to chickenpox, we will tell you what to do if you come into contact with anyone that has chicken pox while on infliximab. There are also some vaccinations (called “live” vaccines) that you can’t have while taking infliximab. So if you are due any vaccinations you must tell the doctor or nurse that you are taking infliximab and they can advise you if the vaccination is safe.

Tuberculosis is an infection which can be dangerous if you are taking infliximab. Tuberculosis can cause a serious infection in your chest and occasionally other parts of the body. Fortunately, tuberculosis is not common in New Zealand, but it is more common in other parts of the world. It is really important to tell your doctor if you have been in contact with anybody who has Tuberculosis.
When receiving Infliximab there may be a small risk of developing tumours such as lymphomas in later life.

- It is important to remember that Infliximab is only used if it is absolutely necessary.

What other precautions are necessary?
- Regular blood tests are needed to pick up side effects early. These are done weekly for 2 weeks, then twice monthly for 2 months, then once monthly thereafter.
- Do not take any other medications without informing your doctor. This includes over the counter and herbal medicines.
- Chickenpox and shingles: If you have contact with somebody with chickenpox or shingles let your general practitioner or hospital doctor know immediately as you may need treatment to prevent you getting chickenpox.
- Although unlikely in our patient group patients should not become pregnant while on treatment with Infliximab and for six months after the last dose of Infliximab.

Vaccinations
A yearly flu vaccine should be given while on this treatment. This can be arranged at the hospital or your general practice each autumn.

Make sure you tell all your doctors and nurses that you are taking Infliximab. You should not receive any live vaccines during treatment with Infliximab and for six months afterwards. (This includes MMR, yellow fever and BCG). Close relatives and family members may have live vaccines as normal. Speak to your nurse or doctor for advice.

How long will I need to take Infliximab for?
The honest answer is that we don’t really know at the moment. If it helps you, then we will want you to stay on it for at least six months. You have some important years coming up, during which you may need to grow, develop into an adult, take exams and start a job. It is important that you are as well as possible during these years and that we try to use as little steroid medicine as possible. So, if the Infliximab works for you, it may be best that you continue taking it during this time. Your gastroenterology doctor will see you regularly while you are on the Infliximab and will talk to you regularly about whether you need to continue taking it.

Do I have to start the Infliximab medication?
The doctor has recommended Infliximab because it has a good chance of making you better. You and your parents do have a choice though and can choose not to have the new medicine if you don't want to. If you want more time to think about it, then take this leaflet home and let us know your decision in the next few days.

Who do I contact if I have any questions?
Please contact the paediatric gastroenterology team at Starship Hospital via the Secretary Dani Ta’a’ase on 09 3074949 Ext 5471.