Protocol for Infliximab Infusion (Adults)

Indications and Dosage:

Rheumatoid arthritis, used in combination with methotrexate, where a Disease Activity Score (DAS28) of >5.1 on at least 2 occasions measured a month apart and a trial of at least 2 DMARDs including methotrexate (unless contraindicated) has taken place and response has been inadequate.

- 3mg/kg IV infusion at 0, 2 and 6 weeks, then every 8 weeks thereafter depending on response/need. Clinical response is usually achieved within 12 weeks. If an inadequate response is seen within 6 months, the dose may be increased in a stepwise manner by about 1.5mg/kg, up to a maximum of 7.5mg/kg every 8 weeks, or consider giving 3mg/kg every 4 weeks. Continued therapy should be reconsidered in patients who show no evidence of therapeutic benefit within this time.

Severe, active Crohn’s disease – treatment of severe, active disease in patients who have not responded despite a full and adequate course of therapy with a corticosteroid and/or immunosuppressant; or who are intolerant or have medical contraindications for such therapies.

- 5mg/kg IV infusion at 0, 2 and 6 weeks. In patients who respond alternative strategies for continued treatment are:
- Maintenance: repeat infusions of 5mg/kg every 8 weeks depending on response/need or
- Readministration: 5mg/kg infusion if signs and symptoms recur within 16 weeks of last infusion

Fistulising, active Crohn’s disease - treatment of fistulising, active Crohn’s disease, in patients who have not responded, despite full and adequate course of conventional treatment.

- Initially 5mg/kg IV infusion, at 0, 2 and 6 weeks. If a patient does not respond after 3 doses, no additional treatment with infliximab should be given. In patients who respond alternative strategies for continued treatment are:
- Additional infusions of 5mg/kg every 8 weeks thereafter or
- Readministration if signs and symptoms of the disease recur within 16 weeks of last infusion followed by infusions of 5mg/kg every 8 weeks thereafter.

Ulcerative colitis (UC) – sub-acute manifestations of UC – not recommended

- treatment of moderately to severely active ulcerative colitis in patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine or azathioprine, or who are intolerant to or have medical contraindications for such therapies.
- acute exacerbation of UC- for severely active UC where ciclosporin is contra-indicated or inappropriate.
- 5 mg/kg IV infusion at 0, 2 and 6, then every 8 weeks thereafter.
- Clinical response is usually achieved within 14 weeks of treatment, i.e. three doses.
- Continued therapy should be carefully reconsidered in patients who show no evidence of therapeutic benefit within this time period.

Ankylosing spondylitis – no longer recommended.

Psoriatic arthritis, - treatment of severe active psoriatic arthritis with peripheral arthritis with 3 or more tender joints and 3 or more swollen joints and where the patient has not responded to trials of at least 2 DMARDs administered individually or in combination and where the patient is intolerant of or has a contraindication to etanercept, or cannot self administer etanercept.
Response assessed at 12 weeks and treatment only continued if adequate response demonstrated.

- 5mg/kg IV infusion at 0, 2 and 6 weeks, then every 8 weeks thereafter depending on response/need.

**Psoriasis** – treatment of very severe plaque psoriasis defined as total Psoriasis Area Severity Index (PASI) $\geq 20$ and Dermatology Life Quality Index (DLQI) $> 18$, where patient has failed to respond to standard systemic therapy (ciclosporin, methotrexate or PUVA) or is intolerant to or has contraindications to these treatments. Infliximab only continued beyond 10 weeks if an adequate response is seen within this time.

- 5mg/kg IV infusion at 0, 2 and 6 weeks, then every 8 weeks thereafter,

**Uveitis** – unlicensed use. Discuss with ophthalmology for dosage.

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**Pre-treatment:**

- Patients should be supplied with the package leaflet and special Alert card.

**Contraindications:**

- Patients with TB or other severe infections such as sepsis, abscesses and opportunistic infections
- Patients with moderate or severe heart failure (NYHA class III/IV)
- Hypersensitivity to infliximab, other murine proteins or any of the excipients

**Special Warnings and Precautions for Use:**

**Infusion reactions**

- Associated with acute infusion-related reactions (eg wheezing, hypotension, pallor, nausea, anaphylactic shock and delayed hypersensitivity) which may develop within seconds or within a few hours (usually 1-2 hours) following infusion. If this occurs then stop infusion immediately and refer to doctor.
- Monitor patients for 1-2 hours post-infusion – greatest risk of reaction during first or second infusion or where other immunosuppressants have been discontinued.
- For severe reactions patients may require treatment with IV hydrocortisone, nebulised salbutamol and chlorphenamine.
- For mild reactions (including: drop in systolic BP $< 40$ mmHg normal blood pressure) the infusion should be temporarily stopped until symptoms subside. Following discussion with a doctor the infusion may be restarted at a slower rate. Some patients may be rechallenged after several weeks.
- Hydrocortisone, an antihistamine and/or paracetamol 30 mins before infliximab can prevent mild and transient effects, and may be needed if recurrence of symptoms occurs.
- Delayed hypersensitivity reactions have been reported up to 12 days after infusion.

**Infections**

- Monitor closely for infections, including TB, before, during and up to 6 months after treatment.
- TB must be ruled out prior to commencing treatment which may require a chest x-ray and tuberculin test.
- Caution in patients who are carriers of hepatitis B virus (HBV) or are at risk of contracting HBV, as it may be reactivated, especially with concurrent immunosuppressant therapy.
- Screen patients for Varicella Zoster Virus if necessary.

**Cautions**

- History of malignancies, including lymphomas.
- Demyelinating CNS disorders (risk of exacerbation).
- History of prolonged immunosuppressant or PUVA treatment in patients with psoriasis.
Delays
- An interval of more than 16 weeks between doses is not recommended due to an increase in hypersensitivity reactions after this time.

When to Withhold Treatment:
- Presentation of signs and symptoms of intercurrent infection. This includes upper respiratory tract infection and skin ulcers.
- Worsening of coexisting illness such as CCF or diabetes
- Suspected malignancy
- Persistent hypotension (systolic < 100mmHg)
- Impending Surgery (4 week gap for standard procedures; 8 week gap for high sepsis-risk surgery) – restart after wound healing

Exclude Infection Prior to Each Administration:
- Take a complete history and examination
- Monitor:
  - temperature,
  - urinalysis – refer to doctor if positive for blood or protein
- Send for the following bloodtests: FBC, ESR, U&Es, LFTs, CRP
- Additional tests for RA patients: Rheumatoid factor, ANA-dsDNA

Administration and Monitoring:
- Infliximab is obtained from the Aseptic Dispensing Unit (ADU), Pharmacy. 24 hour notice is helpful.
- IV Hydrocortisone 100-200mg stat prior to infliximab - not always necessary, there is evidence to suggest that this reduces the incidence of infliximab antibodies. Check with the prescriber.
- Insert venflon and flush with normal saline. Monitor blood pressure, pulse and temperature every 30 minutes during the infusion and observation periods. Patients should be observed for at least 1-2 hours post infusion for acute infusion related reactions.
- Infliximab is given in 250ml of sodium chloride 0.9%, and should be infused over a 2 hour period.
- For carefully selected patients who have received 3 initial infusions over a 2 hour period, subsequent infusions can be infused over a shorter period of not less than 1 hour with patients observed for 1 hour afterwards for the next 5 infusions. This may then be further decreased to 30 minutes infusion with 30 minutes observation, provided there have been no adverse reactions. If an infusion reaction does occur during a shortened infusion, consideration may be given to administering subsequent doses at a slower infusion rate if therapy is to be continued.

Occasionally there are patient specific deviations from this regimen

Infliximab must be given through a normal giving set, via a 1.2-micron low-protein binding filter. Filters can be ordered from supplies:
“1.2micron filter lipid solutions priming volume 0.2cc male/female connectors” Medex code MX1483
Supplier = NHS Logistics, code FTC192

Side Effects and Toxicity:
Recognised side effects of treatment include flu-like symptoms, headache, transient fever, gastrointestinal upset and skin rashes. Please consult the infliximab data sheet available on-line at www.medicines.org.uk for a complete list. Rarely patients have become ANA positive and developed lupus-like syndromes while receiving treatment. Adverse reactions should be reported to the CSM using the “Yellow Cards” in the usual manner.
References:

- NICE guidance 2008
- Infliximab SPC (updated 17/06/2011) emc.medicines.org.uk
- BNF 58 BMJ and RPS Publishing 2009