**Infliximab Use In Paediatric Rheumatology**

Infliximab is a chimaeric monoclonal antibody that specifically binds to, and blocks the action of TNF-α. It is not licensed for the treatment of children with JIA but is widely used and accepted practice to treat those children whose arthritis is not adequately controlled by, or who are intolerant of subcutaneous Methotrexate and who cannot receive Etanercept due the presence of uveitis. It may take several weeks to become effective after commencing treatment or a dose increase. It is not a cytotoxic drug so handling and disposal do not require special precautions beyond the safe disposal of any other injected drug. Patients should also be supplied with an information sheet on Infliximab.

**PRE-TREATMENT INVESTIGATIONS** - Performed in hospital

Full Blood Count, Urea, Electrolytes, Creatinine, & Liver Function Tests

Varicella Zoster and Measles immune status

Quantiferon GOLD assay and a Chest X-ray should be performed to exclude a diagnosis of Tuberculosis before starting any TNF-blocking agent

**PRE-TREATMENT PATIENT INFORMATION**

1. Pregnancy and Breast-feeding - Both are Contra-indicated. Whilst not a known teratogen, there is little data to support its safe use in pregnancy and during breast-feeding. Adolescent patients are advised to avoid pregnancy whilst taking Infliximab and for 3 months after stopping it

2. Infections - Patients taking any TNF-blocking agent are at increased risk of infections. Adults have been reported to have an increased risk of Listeria infection and as a precaution all patients taking Infliximab are advised to adopt the dietary precautions recommended for pregnant women in the UK. Reactivation of latent Tuberculosis is also a risk but this should be minimised by the above screening

3. Alcohol - Although there is no interaction between alcohol and Infliximab many patients are also co-prescribed Methotrexate and should follow the guidance for that drug

4. Immunisations - Do not give live vaccines (MMR, BCG, Yellow Fever etc) to children taking Infliximab. Other immunisations, including the HPV vaccine may be less effective, but should be given according to the regular schedule. All children should receive an annual flu vaccine

5. Drug Interactions - There are no known drug interactions. However Infliximab should not be used in combination with other 'Biologic' agents

6. Side-Effects - Most side-effects are mild and relatively infrequent. Allergic reactions are sometimes seen and can often be prevented by pre-treatment with Hydrocortisone and Chlorphenamine. Patients have reported headaches and coryzal symptoms. There have been case reports of demyelinating diseases but the relationship to Infliximab, if any, is not clear

7. Monitoring - Patients taking Infliximab will need to have their Blood Count, ESR, U&E’s and Liver Function checked with every infusion. Transient abnormalities are common and often associated with viral infections. A neutrophil count of <1.5x10^9 usually requires the drug to be stopped for 1-2 weeks and the blood tests are then re-checked. If they have returned to normal the Infliximab can be re-started and monitoring continue as normal

8. Long-Term Side-Effects - The long-term side-effects of Infliximab are unknown. There have been case-reports of associated malignancies and the Federal Drug Administration in the United States mentions this on its website. Paediatric Rheumatologists are clear however that any possible long-term risk is outweighed, on current evidence, by the clear benefits of controlling active arthritis with Infliximab if Methotrexate therapy fails. Children taking Infliximab are recommended to be enrolled in the UK-wide registry to monitor for this, or any other long-term problems.

**FORMULATIONS**

Intravenous Infusion – Infliximab is only available in this form

**DOSAGE & ADMINISTRATION**

Usual dose is 6mg/kg given every 4-8 weeks.
INFECTIONS & IMMUNOSUPPRESSION

Infliximab in these doses is not a powerful immunosuppressant, but caution is needed as severe infections and even fatalities have been described. Some patients may notice that simple viral illnesses may be more persistent whilst taking Infliximab. Most infections should be dealt with by the patient's GP in the normal manner and it is rarely necessary to stop Infliximab during simple viral illnesses. Patients are advised to omit their Infliximab and seek medical advice if they have been febrile in the previous 48hrs before a dose is due or if they have worsening symptoms.

Varicella contacts and infection

All patients taking Infliximab should have their varicella immune status checked before starting. In those with a negative IgG result consideration is given to immunising the patient before starting Infliximab. However this is not always possible.

Any patient taking Infliximab, regardless of their immune status, who develops Chickenpox or Shingles should be admitted to their local hospital and receive at least 48hrs of IV Aciclovir and complete a total of 5 days treatment

A patient who is known to be immune to varicella does not need treatment if they come into contact with someone who has active infection. However their parents are advised to completely undress their children at least daily and check to see if spots develop.

A patient who is known to be non-immune to varicella needs treatment if they come into contact with someone who has active infection. Contact is defined as any 'kissing' contact, or being in the same room for more than 15minutes with a case, including the 48hrs before spots appear.

Treatment is either an IM injection of Varicella Immunglobulin (ZIG) if the contact occurred less than 72hrs ago or oral Acyclovir given for 2 weeks from the date of contact. Parents are advised to contact their specialist team directly to discuss the best option for their child.

Measles contacts and infection

All patients taking Infliximab should have their Measles immune status checked before starting. In those with a negative IgG result consideration is given to immunising the patient with MMR before starting Infliximab. However this is not always possible.

A patient who is known to be immune to measles does not need treatment if they come into contact with someone who has active infection.

A patient who is known to be non-immune to measles needs treatment if they come into contact with someone who has active infection. Contact is defined as any 'kissing' contact or being in the same room for more than 15minutes with a case, including the 48hrs before the rash appears.

Treatment is either an IM injection of Normal Human Immunglobulin (HNIG) if the contact occurred less than 72hrs ago or IV Immunoglobulin if the IM route is not available. Parents are advised to contact their specialist directly to discuss the best option for their child.