Etanercept Use In Paediatric Rheumatology

Etanercept is a fully humanised monoclonal antibody that specifically binds to, and blocks the action of TNF. It is licensed and approved by NICE for the treatment of children with JIA who's arthritis is not adequately controlled by, or who are intolerant of subcutaneous Methotrexate. 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 Etanercept.

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 it's safe use in pregnancy and during breast-feeding. Adolescent patients are advised to avoid pregnancy whilst taking Etanercept 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 Etanercept 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 Etanercept 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 Etanercept. 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 Etanercept should not be used in combination with other 'Biologic' agents
6. Side Effects - Most side-effects are mild and relatively infrequent. Injection-site reactions may be seen but often decrease over time. Patients have reported headaches and coryzal symptoms. There have been case reports of demyelinating diseases but the relationship to Etanercept, if any, is not clear
7. Monitoring - Patients taking Etanercept will need to have their Blood Count, ESR, U&Es and Liver Function checked every 3 months. Transient abnormalities are common and often associated with viral infections. A neutrophil count of <1.5x10⁹ 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 Etanercept can be re-started and monitoring continue as normal
8. Long Term Side-Effects - The long-term side-effects of Etanercept are unknown. There have been case-reports of associated malignancies and the Federal Drug Administration in the United States mentions this on it's 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 Etanercept if Methotrexate therapy fails. Children taking Etanercept are recommended to be enrolled in the UK-wide registry to monitor for this, or any other long-term problems.

FORMULATIONS
1. Vial and Diluent - Etanercept is most commonly prescribed as a vial and diluent for home reconstitution. A single vial contains 25mg
2. Paediatric Vial and Diluent - a 10mg vial and diluent preparation is available to reduce drug wastage in younger patients. A single vial contains 10mg
3. Pre-Filled Syringes - These are available, but the preservative within them may cause increase injection-site pain in some children so they are not widely used in paediatric practice
4. ‘MyClick’ Pen - These are available, but only in a 50mg dose for once-weekly use. In addition the preservative within them may cause increase injection-site pain in some children so they are not widely used in paediatric practice.

**DOSAGE & ADMINISTRATION**

Usual dose is 0.4mg/Kg given twice a week to a maximum of 25mg. Patients with stable disease may be switched to 0.8mg/kg given once a week, but in treatment-resistant patients doses of up to 0.8mg/kg twice a week have been used.

**INFECTIONS & IMMUNOSUPPRESSION**

Etanercept 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 Etanercept. Most infections should be dealt with by the patient's GP in the normal manner and it is rarely necessary to stop Etanercept during simple viral illnesses. Patients are advised to omit their Etanercept 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 Etanercept 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 Etanercept. However this is not always possible.

Any patient taking Etanercept, 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 15 minutes 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 Etanercept 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 Etanercept. 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 15 minutes with a case, including the 48hrs before the rash appears.

Treatment is either an IM injection of Normal Human Immunoglobulin (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 team directly to discuss the best option for their child.