Gloucestershire Hospitals
NHS Foundation Trust

Infliximab: Prescribing and Administering

1. Background:

Infliximab is an anti-tumour necrosis factor-α (Anti-TNF) antibody. It is from a group of drugs called cytokine inhibitors. Cytokines are small protein molecules, which occur in the body and are involved in inflammatory conditions. Infliximab binds to these molecules and inhibits the inflammatory response.

Infliximab is currently used at GHNHSFT within the NICE Technology Appraisals to treat a number of inflammatory conditions. This includes Ulcerative Colitis, Crohn's Disease, Rheumatoid Arthritis and Psoriasis.

For full guidance the NICE Technology Appraisals can be found at: www.nice.org.uk

Infliximab is available as a number of brands, including the originator Infliximab, Remicade® and a number of biosimilar brands such as Inflectra®, Remsima® and Flixabi®. A biosimilar medicine is a biological medicine that is highly similar to another biological medicine already licensed for use. It is a biological medicine that has not been shown to have any clinically meaningful differences from the originator biological medicine in terms of quality, safety and efficacy.

Biosimilar medicines are not considered generic equivalents to their originator biological medicines because the two products are similar but not identical. However, they will have met regulatory requirements in terms of comparative quality, safety and efficacy.

In line with MHRA guidelines, biological medicines, including biosimilars, must be prescribed by brand name to support on-going pharmacovigilance of the individual products

At the time of dispensing, a biosimilar medicine should not be automatically substituted for the originator by the pharmacist.

2. Prescribing

Prescribing for Inpatients

Infliximab must be prescribed on the ONCE ONLY section of the inpatient drug chart by **brand name e.g. Remsima®**

All details on the drug chart must be completed. This includes patients' name, DOB, address and hospital number. An addressograph is sufficient.

The allergy section of the chart must be completed and patients' weight must be documented on the chart.

Dose of infliximab usually ranges from 3mg/kg to 5mg/kg depending on indication. Refer to specialist literature for further dosing information.

Infliximab dose must be calculated by the prescriber and the dose must be prescribed in mg.

Specialties requiring IV hydrocortisone prior to infliximab must prescribe 100mg IV stat on the ONCE ONLY section of the drug chart.

Prescribe rescue medicines on the PRN side of the drug chart for use by nursing staff in the event of a reaction – refer to relevant part of policy.

Prescribing for Day Case Patients

All infliximab must be prescribed on the Infliximab Day Case Prescription chart with the specific brand required entered into the appropriate space. It is vital that the brand required is clear for the dispensing pharmacist.

All details on the chart must be completed. This includes patients' name, DOB, address and hospital number. An addressograph is sufficient.

The allergy section of the chart must be completed and patients' weight must be documented on the chart.

Declaration
All infliximab prescription charts must have the declaration for treatment completed by the prescriber. He/She must indicate if treatment is in line with the appropriate NICE Technology Appraisal by adding the technology appraisal reference number and countersigning. If treatment is outside the NICE criteria but has been agreed by a Clinical Commissioning Group, the Individual Funding Request box must be ticked and the chart countersigned.

Dose of infliximab usually ranges from 3mg/kg to 5mg/kg depending on indication. Refer to specialist literature for further dosing information.

Patients not previously treated with infliximab require initial loading, where an infusion is given at weeks 0, 2 and 6 weeks. If patient is new to infliximab complete the relevant section of the chart. Prescribe dose as mg/kg, complete indication column and sign chart.

Patients on maintenance treatment with infliximab are administered doses every 8 weeks. In some cases the frequency of administration of infliximab may be altered as per consultant review. When prescribing for maintenance patient complete the relevant section of the chart. Prescribe dose as mg/kg, complete indication column and sign chart.

Actual dose for administration is calculated by nursing staff upon patient admission based on current weight.

The reverse of the prescription chart must be signed for Paracetamol, oral and IV chlorphenamine and IV hydrocortisone in the case of an infusion reaction

Specialties requiring IV hydrocortisone 100mg IV prior to each infliximab infusion must complete and sign the preprinted section of the prescription chart.

Infliximab Day Case Prescription charts are valid for 6 months only.

Pharmacy will be unable to dispense infliximab for charts which are out of date, incorrectly completed to include brand details or where the declaration is incomplete.

3. Dose Calculation (For Day Case Patients)

Dose calculation is carried out on admission by nursing staff on the Medical Day Unit, GRH.

Patient must be weighed upon admission. Weight must be documented on the chart for each admission.

Calculate the dose required by multiplying the dose prescribed in mg/kg by patient weight e.g. for a patient weighing 70kg prescribed a dose of 5mg/kg, dose is 70 X 5 = 350mg.

Dose must be rounded to the nearest 5mg e.g. 323mg → rounded to 325mg

Dose must be documented on the prescription chart and a second calculation check must be carried out by another staff nurse or healthcare professional.

4. Patient Preparation and Pre-Treatment Investigations

Prior to administration of the first infusion, the following investigations must be performed:

- Medical History, chest X ray and T spot test to exclude tuberculosis
- Hepatitis B and C serology, HIV if appropriate
- History to confirm previous exposure to Varicella Zoster or serology test

For subsequent infusions bloods must be taken (for FBC, U&E's, LFT's and CRP) 2 weeks prior to date of infusion

On admission, carry out baseline observations Blood Pressure (BP), Heart Rate (HR), Temperature and Weight when patient arrives.

Check blood results and contact relevant clinical team if any abnormality.

Ensure no evidence of sepsis or clinically manifested infection.

Cannulate patient.

5. Preparation of Infusion

Calculate the number of infliximab vials needed. Each vial contains 100mg of infliximab e.g. a dose of 350mg will require reconstitution of 4 X 100mg infliximab vials.

Reconstitute each infliximab vial with **10 ml of water for injections**, using a syringe equipped with a blue needle.

Remove flip-top from the vial and wipe the top with a 70% alcohol swab.

Insert the syringe needle into the vial through the centre of the rubber stopper and direct the stream of water for injections to the glass wall of the vial.

Do not use the vial if the vacuum is not present.

Gently swirl the solution by rotating the vial to dissolve the lyophilised powder. Avoid prolonged or vigorous agitation. **DO NOT SHAKE**. Foaming of the solution on reconstitution is not unusual.

Allow the reconstituted solution to stand for 5 minutes. Check that the solution is colourless to light yellow and opalescent. The solution may develop a few fine translucent particles, as infliximab is a protein.

Do not use if opaque particles, discoloration, or other foreign particles are present.

See section 7 for storage instructions of reconstituted vial.

Withdraw the volume of the reconstituted infliximab (e.g. 300mgs of infliximab is reconstituted with 30mls of water) from the 250mls bag/bottle of 0.9% Sodium Chloride.

Slowly add the total volume of reconstituted Infliximab solution to the 250ml infusion bottle or bag. Gently mix.

Check the infusion with another trained member of staff and label the bag using a white sticker.

6. Administration of Infusion

Use an infusion set with an in-line, sterile, non-pyrogenic, low protein-binding filter (pore size 1.2 micrometer or less) obtained from stores.

For patients new to infliximab administer the infliximab infusion intravenously over a period of 2 hours.

Patients who have tolerated at least 4 initial 2 hour infliximab infusions, may be considered for shortened infusion times as below:

Infusions 1-4 → Administered over 2 hours and the patient must wait for 2 hours after infusion
Infusions 5-9 → Administered over 1 hour and the patient must wait for 1 hour after infusion
Infusion ≥ 10 → Administered over 30 minutes and the patient does not need to wait

It is recommended that the administration of the solution for infusion is started as soon as possible and within 3 hours of preparation.

Do not infuse Infliximab in the same intravenous line as any other agents.

7. Vial Share

Vial sharing of infliximab vials on the Medical Day Unit, GRH, has been authorised by GHNHSFT.

Any unused reconstituted solution must be stored at 2°C to 8°C in the fridge for a MAXIMUM of 24 hours.

The vial must be clearly labelled with time and date of reconstitution.

After 24 hours any unused reconstituted solution must be discarded as per local policy. Any vials unused/saved from vial sharing must be set aside in the Medical Day Unit fridge in tray labelled “Vial Sharing Returns”. Designated Pharmacist will collect stock to return to Pharmacy.

8. Monitoring of Infusion

Infliximab has been associated with acute infusion-related reaction, including anaphylactic shock and delayed hypersensitivity reactions.

Acute infusion reactions including anaphylactic reactions may develop within seconds or within a few hours following infusion.

Vital signs must be monitored every 30mins during the infusion.

If acute reactions occur, the infusion must be stopped immediately.

Patient must be made to wait post infusion for monitoring (depending on infusion number).

For patients on infusion 1 – 4 → 2 hours post infusion
For patients on infusion 5 – 9 → 1 hour post infusion
For patients on infusion ≥ 10 → does not require to be monitored post infusion

9. Treatment of Infusion Reaction

An infusion reaction is any reaction occurring during or within 1-2 hours of an infusion. This can be classified into mild, moderate and severe.

Mild reactions include: Palpitations, headache, nausea, dizziness

If patient has mild reaction:

- Stop infusion
- Give PO Paracetamol 1g and/or Chlorphenamine 4mg PO or Chlorphenamine 5-10mg IV
- Monitor vital signs every 10mins
- Restart infusion after 20mins at a slower rate (10mls/hr increasing rate every 15 mins)

Moderate reactions include: Hypo/hypertension, mild chest discomfort, shortness of breath and elevated temperature

If patient has a moderate reaction:

- Stop infusion
- Give PO Paracetamol 1g and/or Chlorphenamine 5-10mg IV
- Give IV Hydrocortisone
- Monitor vital signs every 10mins
- Restart infusion after 20mins at a slower rate (10mls/hr increasing rate every 15 mins)

Severe reactions include significant hypo/hypertension, stridor, chest discomfort or shortness of breath, bronchospasm, angiooedema of upper airway

If a patient has a severe reaction:

- STOP infusion immediately
- Obtain medical assistance
- Treat as per anaphylaxis protocol

The decision to retreat a patient with infliximab who has had a reaction to it will be made by the consultant responsible for that patient's care.

References:

1. Summary of Product Characteristics for Remicade® Last updated on the Electronic Medicines Compendium 09/06/2016. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on 10/04/2017
2. Summary of Product Characteristics for Remsima® Last updated on the Electronic Medicines Compendium 04/10/2016. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on 10/04/2017
3. Summary of Product Characteristics for Inflectra ® Last updated on the Electronic Medicines Compendium 09/2016. Accessed via the Electronic Medicines Compendium http://emc.medicines.org.uk on 10/04/2017
4. National Institute of Clinical Excellence (NICE) www.nice.org