Guideline for the use of Infliximab (Remicade ®) in patients with Inflammatory Bowel Disease (IBD)

Aim of protocol
To ensure the safe intravenous administration of Infliximab (Remincade) to patients for the treatment of IBD (Crohn's Disease and Ulcerative Colitis).

Patient Groups

1. Infliximab within the licensed indications, is recommended as treatment options for adults with severe active Crohn's disease (CD) whose disease has not responded to conventional therapy (including immunosuppressive and/or corticosteroid treatments), or who are intolerant of or have contraindications to conventional therapy. Infliximab should be given as a planned course of treatment until treatment failure (including the need for surgery) or until 12 months after the start of treatment, whichever is shorter. People should then have their disease reassessed to determine whether going treatment is still clinically appropriate.

2. Infliximab within its licensed indication, is recommended as a treatment option for people with active fistulising CD whose disease has not responded to conventional therapy (including antibiotics, drainage and immunosuppressive treatments), or who are intolerant of or have contraindications to conventional therapy. Infliximab should be given as planned course of treatment until treatment failure (including the need for surgery) or until 12 months after the start of treatment, whichever is shorter. People should have their disease reassessed to determine whether ongoing treatment is still clinically appropriate.

3. For the purposes of this guidance, severe active CD is defined as very poor general health and one or more symptoms such as weight loss, fever, severe abdominal pain and usually frequent (3-4 or more) diarrhoeal stools daily. People with severe active CD may or may not develop new fistulae or have extra-intestinal manifestations of the disease. This clinical definition normally, but not exclusively, corresponds to a Crohn's Disease Activity Index (CDAI) score of 300 or more, or a Harvey-Bradshaw score of 8 to 9 or above.

Sub-acute manifestations
This guidance relates only the use of infliximab within its marketing authorisation, for the treatment of acute exacerbations of severely active ulcerative colitis (UC). It relates to an induction course of three doses of infliximab.

*Note: Infliximab is not recommended for the treatment of **sub-acute manifestations** of moderately to severely active UC.*

Acute exacerbations
Infliximab is recommended as an option for the treatment of acute exacerbations of severely active UC only in patients in whom ciclosporin is contraindicated or clinically inappropriate based on a careful assessment of the risks and benefits of treatment in the individual patient. Its use is restricted in line with NICE TA163 and used in three doses for hospitalised patients (0, 2 and 6 week).

For patients that do not meet the criterion for acute exacerbations, Infliximab should only be used for the treatment of acute exacerbations of severely active UC in clinical trials.

Before prescribing Infliximab, it is the responsibility of the prescriber to ensure that:

1. The therapy is appropriate

2. The patient has received comprehensive counselling about the risks and benefit's of the drug and that this documented in the patients notes

3. That the patient fits the above clinical situation

4. The appropriate form has been completed for funding and submitted to Pharmacy funding team (medicine.funding@sash.nhs.uk)

Exclusion Criteria for Infliximab
- Current sepsis or infection
- Abscess (if unsure, CT Abdo, USS or CT to exclude)
- Pregnancy or Breastfeeding
- Previous sensitivity to Infliximab
- Moderate to severe heart failure
- Tuberculosis (TB) Active and latent

Note: caution must be taking when considering treatment with Infliximab in patients with known stricturing disease.

Pre- infusion screening at baseline

1. Tuberculosis (gastroenterology team at baseline)

- Full TB History (Check family history, travel history and profession)
- Please see attached proforma (Appendix 1)
- Chest x-ray prior to starting treatment
- Local patients: Please refer to TB Nurses at Crawley hospital ext 3025
- Tertiary patients: Please ask GP to refer to local TB service for TB screening (mantoux or other TB test available locally)

2. Routine blood test (gastroenterology team at baseline)

The following should all be completed prior to starting Infliximab:

- HIV serology
- Hepatitis B and C serology
- VZV serology
- Herpes simplex virus (HSV)
- Recent FBC, U&E, LFT, ESR and CRP

Blood test to be checked prior to each Infliximab infusion during nursing assessment

- FBC (Hb, neutrophils and platelets)

Note: no specific dose recommendation is required for impaired renal or hepatic function as no studies have been carried out in these patient groups. Overall monitoring will be the responsibility of the lead gastroenterology consultant.

Vaccinations

Please check the patient's vaccination history prior to starting Infliximab. However, the gastroenterology team at Surrey and Sussex Healthcare NHS Trust will not necessarily vaccinate patients. This is communicated to patients prior to initiating treatment.

Prescriber must confirm vaccination history

- No live vaccines in the last four weeks
- VZV varicella vaccine (if there is no medical history of chicken pox, shingles or VZV vaccination)
- Human papilloma virus
- Influenza (trivalent inactivated vaccine) once a year
- Pneumococcal polysaccharide vaccine (3 years)
- Hepatitis B vaccine in all HBV seronegative patients

Prescribing and Approval for Funding

Prescriber Information

Infliximab can be prescribed by a consultant Gastroenterologist, or following discussion with a Consultant Gastroenterologist. In keeping with trust policy, approval for funding for Infliximab must be obtained by submitting to Pharmacy funding team (medicine.funding@sash.nhs.uk).

Approval for funding

Please see BLUETEQ for funding requests for Infliximab for CD & UC.

Treatment and Dosage

This guide relates to the use of Infliximab for IBD within SASH. The drug is provided by Merck Sharp & Dohme (MSD) under the trade name REMICADE. The drug must be administered as defined by the manufacturer, and according to these guidelines.

Drug

Infliximab is a chimeric (human-mouse) anti-TNF Monoclonal antibody.

Dosage

Pre-printed administration charts are available for the treatment of IBD.

All patients are pre medicated with intravenous hydrocortisone 100mg and chlorphenamine 10mg.

Standard dose of infliximab for IBD is **5mg/kg at week 0, week 2 and week 6, followed by maintenance regimen if there is a positive response** (normally 5mg/kg every 8 weeks). Response to treatment is assessed (as per protocol) and reviewed in MDT meetings.

If loss of response to Infliximab other options are

- Discussion in benign Gastroenterology Multidisciplinary Meeting for consideration for Individual Funding request form (IFR). The form needs to be submitted to Pharmacy funding team (medicine.funding@sash.nhs.uk).

Administration
Infliximab is prepared as per manufacturer's guidelines and given in 250mls of sodium chloride 0.9% as detailed below. Infliximab must be given with an intravenous giving set and 1.2 micron filter via an infusion pump.

Infusion for week 0 to week 4 (number 4): Infuse over 2 hours and observe for 2 hours post infusion

Vital observations - temperature, blood pressure, oxygen saturations, pulse and respiratory rate every 15 minutes for the 1st hour and every 30 minutes for the 2nd hour. Hourly observations for 2 hour post infusion.

Infusion for number 5 to 8: Infuse over 1 hour and observe for 1hour post infusion

Observations every 30 minutes over 1 hour. Observe for 1 hour post infusion with 1 further set of observations.

Infusion number 9+: Infuse over 30 minutes and observe for 30 minutes post infusion (BUCH et al 2006, Clare et al 2009)

Observations every 15 minutes for 30 minutes. Observe for 30 minutes post infusion with 1 further set of observations.

Intravenous access must remain in-situ for each patient for the appropriate post infusion period.

Indication for reduced infusion
A reduced infusions time of 1 hour is now licensed for IBD (MSD 2013).

- Patients who have tolerated at least 4 Infliximab infusions over 2 hours without any hypersensitivity or delayed hypersensitivity reaction

Exclusion Criteria Reduced Infusion
- Patients who have less than 4 previous Infliximab infusions
- Patients who have previous infusions at a hospital other than SASH trust
- Patients who have either hypersensitivity or delayed hypersensitivity reaction including those who tolerated subsequent infusions
- Patients with known cardiac history

Infliximab can be administered in the Chemo Suite, on Comet ward at Crawley hospital and on Charlwood ward at SASH.

All areas have access a crash trolley, equipped with oxygen, suction and emergency medications. Adequate phone access is also available in these areas.

Staff administering Infliximab
The following training must be completed for staff to administer these medications (as per trust IV policy)

1. Intravenous drug administration (following trust policy)
2. Advance life support (ALS)
3. Anaphylaxis training

Administration of the therapy must be carried out by nurses trained and competent in the administration of intravenous therapy, and knowledgeable about the drug therapy.

Nursing Assessment
Written consent is obtained by the IBD nurses for all patients receiving infliximab (SASH consent form).

The accredited nurse will assess each patient prior to each infusion. This assessment includes:

1. Vital Observation (Blood pressure, pulse, oxygen saturations, respirations and temperature)
2. BMI: Weight and Height
3. Bloods: FBC (Hb, neutrophils and platelets)
4. Contraindications/side effects to treatment
5. Current infections
6. Current medication and allergies
7. Current symptoms including both HBI or SCCAI and PDAI (fistulating disease)
8. Photography of fistulating disease
9. Review of any recent investigations
10. The above assessment is completed using proforma (see Appendix 1)

Note: bloods (U&E's, LFT's, C-RP, ESR) will monitored by the gastroenterology team as part the disease evaluation and not during nursing assessment (i.e. prior to each nurse's assessment).

Infusion reaction
All infusion reactions will be dealt with according to the Infusion reaction protocol (Refer to appendix 3). Patients who have Infliximab over 1 hour and have an adverse reaction will return to 2 hourly infusions.

Documentation
All patients will have a completed proforma and observation sheet (held by the IBD Nurses). Written evidence of Infliximab administration is recorded in the patient's medical notes (MDT notes).

Ongoing monitoring
The above nursing assessment and monitoring is repeated for every admission for Infliximab by the nursing staff.

Out patients Follow- Up
All patients receiving Infliximab will be reviewed in out patients' clinic after every 3rd infusion, to document response to treatment, correspond with the patients GP, and determine ongoing management.

IBD MDT
This meeting occurs weekly and is attended by Consultant Gastroenterologists and the IBD nurse(s).

The aim of this meeting is to discuss each patient (case review) receiving biologics (Infliximab & Adalimumab).

The aim of this MDT is to;
- Review patients progress on treatment
- Monitor tolerance, side effects and use of concomitant immunosuppressant's
- Plan for re-investigation of disease & ongoing need for therapy (in keeping
- with NICE 2010, which suggests a review at 12 months)
- Confirm CCG funding status and re-apply to the relevant PCT for funding if needed

This activity for the biological MDT is recorded in the patient's medical notes. The IBD nurse may call each patient following their case review to inform them of the outcome. A letter is generated for each patient and sent to GP and CCG (if indicated) for update on patient's progress on biologics. A 12 month review will be completed as necessary. This will be sent to patients CCG.

References:

European Crohn's and Colitis Organisation (2009) Vaccination and systematic workup to consider before introducing immunomodulator therapy. Journal of Crohn's and Colitis (JCC). Vol 3 (2) p. 80-81

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National Institute for Health and Clinical Excellence (2008) Infliximab for the treatment of subacute manifestations of ulcerative colitis http://www.guidance.nice.org.uk/TA140 (accessed August 2011)

National Institute for Health and Clinical Excellence (2010) TA187 Crohn's Disease- Infliximab (review) and adalimumab (review of TA40): Guidance. http://guidance.nice.org.uk/TA187/Guidance/pdf/English (accessed August 2011)

Buch MH, Bryer D, Lindsay S, Rees-evans B, Fairclough A, Emery P (Nov 2006) Shortening infusion times for infliximab administration. Rheumatology 45:485-486

Clare DF, Alexander FC, Mike S, Dan G, Allan F, Lisa W, Peter HJ (2009) Accelerated infliximab infusions are safe and well tolerated in patients with inflammatory bowel disease. European Journal of Gastroenterology and Hepatology 21(1):71-75

MSD (2013) Summary of Product Characteristics: Remicade 100mg powder for concentrate for solution for infusion. http://www.medicines.org.uk/emc (accessed August 2013)

Appendix 1 - Infliximab Infusion – nurse's assessment

Place addressograph here		Next of kin: Contact number: Signature & Date
X-ray results satisfactory (1st visit)	Yes/No	
Bloods satisfactory - WCC >3.5 - Neut >1.5 - Platelets >150 - LFT's (not required) - Renal function (not required)	Yes/No (*if NO contact gastroenterology team*)	
Any signs of infection	Yes/No	
Coughs/colds/sore throats	Yes/No	
Raised temperature	Yes/No	
Diarrhoea / vomiting	Yes/No	
UTI	Yes/No	
Unhealed skin lesions	Yes/No	
Dental abscess	Yes/No	
Mouth infections	Yes/No	
Ear infections	Yes/No	
Any bruising	Yes/No	
Any rashes	Yes/No	
Seen by GP	Yes/No	
Allergies	Yes/No	
Pregnant	Yes/No	
Comments		

Note: bloods (U&E's, LFT's, C-RP, and ESR) will monitored by the gastroenterology team as part the disease evaluation and not during nursing assessment (i.e. each pre-infusion assessment).

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Adapted for use at Surrey and Sussex Healthcare NHS Trust (SASH) from Brighton

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