Systemic Anti-Cancer Treatment Protocol

INFLIXIMAB
For Immune-Mediated Colitis

PROTOCOL REF: MPHAINFST
(Version No: 1.0)

Indication:

Treatment of patients with severe, immune-mediated colitis who have shown resistance to conventional corticosteroid agents.

Treatment must be agreed by –

1. Consultant/ team responsible for patients care
2. A luminal gastroenterologist from RLUH experienced in immune- mediated colitis. Mr Sree Subramanian is the main authorising consultant. In his absence the on-call luminal gastroenterologist should be contacted – this will be one of the following – Mr Andrew Moore, Mr Alan Steel, Mr Martyn Dibb, Mr Ed Derbyshire, Mr Phil Smith (from October 2018)
3. A consultant from the Immuno-oncology steering group

Treatment must be prescribed by a registrar or consultant

Consent – verbal consent should be gained

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

Dosage:

Drug	Dosage	Route	Frequency
Infliximab	5mg/kg	IV	Week 0 then a second dose to be given 2 weeks later if symptoms remain (may be given 1 week after original dose if clinical symptoms indicate this). A third dose may be given a further 2 weeks later.

Supportive treatments:

Hydrocortisone 100mg IV should be administered 30 minutes before infliximab is infused.

Others as required:

Paracetamol oral 1g prn up to FOUR times a day

Chlorphenamine oral 4mgs when required up to THREE times a day

Chlorphenamine IV 10-20mg when required up to THREE times a day

Hydrocortisone IV 100mg-200mgs when required

Salbutamol nebules 2.5mgs when required

Extravasation risk:

Unlikely to cause toxic effects on normal tissues. Any adverse injection site effects should be treated symptomatically as appropriate

Administration:

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

1. The patient has received comprehensive counselling about the risks and benefits of the drug and that this documented in the patients notes
2. That the indication fits the clinical situation

Day	Drug	Dose	Route	Diluent and rate
1	Hydrocortisone	100mg	IV Infusion	**30 minutes prior**
1	Infliximab	**5mg/kg**	**IV Infusion**	**in 250mls of sodium chloride 0.9%through a 1.2 micron filter over 2 hours**
1	Sodium Chloride 0.9%	50ml	IV Infusion	**Flush**

Infusion observations every 30 minutes during infusion and for 2 hours post infusion

- temperature
- blood pressure
- oxygen saturations
- pulse
- respiratory rate

Medical/Nursing review as per patient management plan

For severe reactions, discuss with Consultant before continuing with treatment.

Main Toxicities:

Incidence	Undesirable effects
Very common (more than or equal to 1 in 10 patients)	Viral infections, abdominal pain, nausea Upper respiratory tract infections, sinusitis, infusion related reactions, pain
Common (≥1 in 100 to <1 in 10)	Bacterial infections, neutropenia, leucopenia, anaemia, lymphadenopathy, Allergic respiratory symptom, depression, insomnia, conjunctivitis, tachycardia, palpitations, flushing, hypotension, hypertension. Ecchymosis, flushing, abnormal liver function, urinary tract infections, arthralgia/ myalgia, back pain, rash
Uncommon (≥1 in 1000 to < 1 in 100)	Hypersensitivity/anaphylactic reactions, Tuberculosis, thrombocytopenia, lymphopenia, lymphocytosis, pyelonephritis
Rare (≥ 1 in 10000 to < 1 in 1000)	Meningitis, opportunistic infections, hep B reactivation, agranulocytosis

List is not exhaustive please consult current summary product characteristics for full list of known side effects

Patients must be monitored closely for infections including tuberculosis before, during and after treatment with infliximab. Because the elimination of infliximab may take up to six months, monitoring should be continued throughout this period. Further treatment with infliximab must not be given if a patient develops a serious infection or sepsis.

Investigations:

In patients receiving Anti TNFa treatment, there is an increased risk of clinical tuberculosis (TB) developing.

	Pre	Each Dose	Comments
Medical Assessment	X	X	Complete pre-treatment checklist (attached to INFLIXIMAB protocol)
Nursing Assessment	X	X	
Stool Culture negative	X		
FBC	X	X	
U&E, LFTs	X	X	
Chest X-ray	X		If patients have had a CT chest (as part of staging or investigation) within 1 month then a chest x-ray is not required
Full TB history	X		Check family history, travel history, profession, determine previous TB or recent contact
T-spot test	X		
HIV serology	X		
Hepatitis A, B and C serology	X		
VZV IgG	X		
Urinalysis	X	X	Refer to medical team if positive for protein or urinary symptoms present
Informed Consent	X		
Weight recorded	X	X	

Patients with an abnormal chest x-ray consistent with previous or latent TB may require treatment before Infliximab administration and should be referred for assessment by a respiratory consultant.

In patients with previous TB, if past treatment is considered to have been adequate by respiratory consultant they may start anti TNF treatment but will require careful monitoring with chest x-ray every 3 months and sputum cultures if respiratory symptoms develop.

Renal and Hepatic impairment

No specific dose recommendation is required for impaired renal or hepatic function as no studies have been carried out in these patient groups.

Vaccinations

Please check the patient's vaccination history prior to starting Infliximab.
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 sero-negative patients

References:

Flixabi® Summary of product characteristics, available at - https://www.medicines.org.uk/emc/product/7265/smpc accessed 29/06/2018. Date of last update 02/1018

The Royal Liverpool & Broadgreen University Hospitals Trust, Intravenous Infliximab (Remicade) Infusion guideline, BG/LMH/0602

Appendix 1

CHECKLIST TO BE COMPLETED PRIOR TO GIVING INFLIXIMAB
To be completed by SpR/Consultant
To be filed in patient notes

Patient's name: _____ CCC No: _____

Name of Clinician requesting infliximab: _____
Indication:
_____

You must ensure the following statements are true (please tick):

- ☐ Endoscopic/radiological/biochemical evidence of active disease exists (you must discuss with the consultant gastroenterologist and document this before proceeding)
- ☐ There is no evidence of active infection/sepsis (you must discuss with the consultant gastroenterologist and document this before proceeding)
- ☐ There is no evidence of abscesses (if in doubt order CT/MRI)
- ☐ No history of sensitivity to Anti TNFa or other mouse proteins
- ☐ Women of childbearing potential have been advised to take contraceptive precautions
- ☐ during and for 6 months following Anti TNFa treatment a **ward pregnancy test has been performed and is negative (FEMALES ONLY)**
- ☐ Potential risks/side effects have been fully discussed with the patient and patient information booklet given
- ☐ Chest X-ray/ CT chest (within last month) is normal, no signs of Tuberculosis(TB)
- ☐ Has the patient ever had TB or had contact with someone known to have TB? YES/NO
- ☐ Treatment has been agreed by the oncology team and a consultant gastroenterologist experienced in immune mediated colitis.

PRESCRIBE:
On Meditech, infliximab (5mg/kg) in 250ml 0.9% Sodium chloride to be given over 2 hours.
Hydrocortisone IV 100mg pre-medication
Supportive medications as required
Please ensure patient has bloods checked daily for the next 2 days, including FBC, U&E, CRP & LFTs

Signed: _____ **Name:** _____ **Date:**_____