PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

INFLIXIMAB

For Immune-Mediated Toxicities

PROTOCOL REF: MPHAINFST

(Version No.3.0)

Approved for use in:

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

Treatment must be agreed by the immunotherapy lead consultant, the immunotherapy nurse consultant or the consultant responsible for the patients care

Treatment must be prescribed by a registrar, consultant or IO nurse consultant
Consecutive cycles can be prescribed by the IO Advanced Nurse Practitioner team.

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
- Those with an Ejection Fraction <20%
- 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. Subsequent doses are rare but can be given up to monthly if clinically required
Infliximab	10mg/kg only to be considered in refractory colitis	IV	Week 0 then repeated in week 1-2. The return to 5mg/kg if further doses required

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 to 20mg when required up to THREE times a day (max 40mg daily)

Hydrocortisone IV 100mg to 200mgs when required

Salbutamol nebules 2.5mgs when required

To include pre-medication and supportive treatment post SACT including anti-emetics.

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 IO Consultant/IO Nurse 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
Clinical Assessment	X	X	Complete pre-treatment checklist for 1st dose only (attached to INFLIXIMAB protocol)
Nursing Assessment	X	X	
Stool Culture negative	X		Only for colitis patients
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
Quantiferon-TB Gold 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. Date of last update 02/1018

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

Cooksley et al. Multinational Association of Supportive Care in Cancer (MASCC) 2020 Clinical Practice Recommendations for the management of immune-mediated adverse events from checkpoint inhibitors. 2020. Supportive Care in Cancer. 6107-6181. https://link.springer.com/collections/daahcggbef

Hindryckx P et al. Dose optimisation of infliximab for acute severe ulcerative colitis. 2017. Aliment Pharmacol Ther . 45(5):617-630 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6658182/

Appendix 1

CHECKLIST TO BE COMPLETED PRIOR TO GIVING INFLIXIMAB
To be completed by Immunotherapy Team/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):

- ☐ Biochemical/ Endoscopic/radiological/ evidence of active disease exists
- ☐ There is no evidence of active infection/sepsis
- ☐ 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 had an Interferon-TB Gold test? Has the result been documented on Meditech? YES/NO
- ☐ Treatment has been agreed by the oncology team.

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
Signed: _____ Name: _____

Circulation/Dissemination

Date added into Q-Pulse	9th November 2023
Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
August 2023	3.0	**Trudy Guinan**	Review and update