

## Who can administer

May be administered by registered competent doctor or nurse/midwife

## Important information

- **All new gastro/rheumatology patients will be commenced on Inflectra (biosimilar).**
- The **brand name** to be used **must be specified** by the prescriber, i.e. Remicade or Inflectra
- Monitoring requirements - see below
- In order to improve the traceability of biological medicinal products, **the name and the batch number of the administered product should be clearly recorded.**
- **Anaphylaxis** can be a concern with this drug - ensure adrenaline, corticosteroids, antihistamine and paracetamol are available during administration
- Before the administration of each dose, the patient should be examined for the presence of infection, and consideration given to delaying treatment should infection be present - see 'Further information' below also.
- Confirm patient does **not have a history of current or recent infection**, or recent exposure to chicken pox or TB
- Infliximab should be used with caution in patients with mild heart failure, and should not be used in patients with moderate to severe **heart failure**

## Available preparations

Remicade 100mg vial

Inflectra 100mg vial

Baxter manufactured Inflectra Bags

## Reconstitution

### Water for Injections

- 10ml per 100mg vial
- Use a syringe with a 21-gauge (0.8mm) or smaller needle
- Direct the stream of Water for Injection to the glass wall of the vial, rather than directly at the powder.
- Gently rotate the vial to dissolve the lyophilised powder
- **Do not shake** - Foaming may occur
- Allow the reconstituted solution to stand for five minutes
- Check that the solution is colourless to light yellow and opalescent

## Infusion fluids

Sodium chloride 0.9%

## Methods of intravenous administration

**Intermittent intravenous infusion (using an electronically controlled infusion device)**

- Dilute required dose to 250ml infusion fluid as follows:
- Withdraw a volume of the sodium chloride 0.9% from the infusion bag, equal to the volume of reconstituted Infliximab to be added.
- Example: if a 300mg dose is being used, this is 30ml of the drug solution, so withdraw 30ml of the infusion fluid before the 30ml drug solution is added.
- Slowly add the reconstituted drug to 250ml infusion fluid and **gently mix** (note, maximum concentration of 4mg/1mL cannot be exceeded)
- **Administer required dose over 2 hours**
- In **carefully selected adult patients** who have tolerated **at least three initial 2-hour infusions** of Infliximab (induction phase) and are receiving maintenance therapy, consideration may be given to administering subsequent infusions over **a period of not less than 1 hour**. If an infusion reaction occurs in association with a shortened infusion, a slower infusion rate may be considered for future infusions if treatment is to be continued. **Shortened infusions at doses greater than 6mg/kg have not been studied**
- Use an infusion set with an in-line sterile, non-pyrogenic, low protein-binding filter (pore size 1.2microns or less)(Sterifix reference number 409 9303)
  - MPUH- available from Stores
  - UCH: available from pharmacy

## Dose in adults

- Use actual body weight for **obese patients** (ref 1)
- Given the 100mg vial presentation, dosing on a mg/kg basis and the need to promote cost-effective use dose-rounding is permitted by physicians to the tune of 5% ( for rheumatology) and 10% (for gastroenterology) (ref 2).
- See Further information section for guidance on administration when interval between doses is greater than 8 weeks

### Moderate to severely active Crohn's disease

- **Initial dose 5mg/kg, repeated two weeks later**
- If **no response** after two doses - no additional doses should be given
- In patients who respond, there are two options:
  - a: Repeat 5mg/kg dose six weeks after initial dose, followed by further doses every eight weeks
  - b: Re-administration of 5mg/kg if signs and symptoms of the disease recur
- Higher doses than 5mg/kg- see 'Further information'

### Fistulating active Crohn's disease

- **Initial dose 5mg/kg** single dose, repeated at two and six weeks after the first infusion
- If the patient does not respond after these 3 doses, no additional treatment with infliximab should be given
- In patients who respond: two options
  - a: Repeat 5mg/kg dose every eight weeks, or
  - b: Readministration of 5mg/kg if signs and symptoms of the disease recur, followed by infusions of 5mg/kg every eight weeks
- Higher doses than 5mg/kg- see 'Further information'

### Ulcerative colitis

- Initial dose 5mg/kg, repeated at two and six weeks after the first dose, then every eight weeks thereafter
- If there is no response after 14 weeks (ie. three doses), continued therapy should be carefully

reconsidered

### Higher doses for Gastrointestinal disease (unlicensed)

- Local, specialist recommendation <sup>(ref 5)</sup>:
  - Dosing may change dependent on trough drug levels and clinical requirements
  - With Consultant authorisation, a 10mg/kg dose may be used for sicker patients, and the interval between doses may be shortened

### Ankylosing spondylitis

- **Initial dose:** 5mg/kg single dose, repeated at two and six weeks after the first infusion
- If a patient **does not respond** by six weeks (ie after 2 doses), no additional doses should be given
- If a patient **does respond**, the dose may be administered every six to eight weeks thereafter

### Rheumatoid arthritis

- **Unlicensed regimens** in use in Rheumatology Day Ward: 5mg/kg on week 0, then 5mg/kg on week 4, and 3mg/kg every **eight weeks** thereafter (ref 3)
- **Licensed dose: Initial dose** 3mg/kg, repeating at two and six weeks, then every eight weeks thereafter (licensed only in conjunction with methotrexate, check with consultant if patient is not on methotrexate)
- If a patient loses response or has an inadequate response after twelve weeks, the dose may be increased in increments of 1.5mg/kg up to a maximum of 7.5mg/kg every eight weeks. Alternatively, 3mg/kg may be given every four weeks
- Continued therapy should be carefully reconsidered in patients who show no evidence of therapeutic benefit within the first 12 weeks of treatment or after dose adjustment

**For other indications (including psoriatic arthritis, psoriasis), please contact pharmacy department.**

### Renal and/or hepatic impairment

- Infliximab has not been studied in these patient populations. No dose recommendations can be made

## Monitoring

- Monitor the patient for infusion-related reactions **every 30 minutes** during the infusion
- The manufacturers advise that patients continue to be monitored for at least one to two hours post infusion for infusion-related reactions
- Local policy (GI indications) suggests that the patient be monitored for 60 minutes post infusion (1st three infusions), and for 30 minutes after the fourth and subsequent infusions <sup>(ref 4)</sup>
- If adverse reactions occur, slow or stop the infusion. Refer to Medication protocol: Management of Infusion Related Patient Reactions in nurse-led infusion settings at Galway University Hospital QPulse [CLN-NM-0118](#)
- Patients may be pre-treated with antihistamines, hydrocortisone, and/or paracetamol to decrease the risk of infusion related reactions
- Trough levels may be measured - see [below](#) for letter re TDM in GUH

## Further information

### Pre-screening (ref 2)

- Chest x ray

- Mantoux test
- Hepatitis screen (HepBcAb, or if prior vaccination to HepB check HepBsAb)
- VZV IgG
- HIV Ab

### Infection risk and vaccinations

- Patients must be monitored closely for infections including tuberculosis before, during and for six months after treatment with infliximab
- Further treatment with infliximab should not be given if a patient develops a serious infection or sepsis
- **Vaccine recommendations (ref 2)**
- Seasonal influenza annually
- Pneumococcal (every 3 to 5 years)
- Varicella vaccine (if VZV IgG negative)- this needs to be given **prior** to starting infliximab therapy
- Human Papilloma Virus (HPV) for female patients aged 14 to 26 years. Females over 26 years are encouraged to have annual cervical smear test
- Tetanus booster every 10 years

### Readministration after a break in therapy (Crohn's disease and rheumatoid arthritis)

- If signs and symptoms of disease recur, infliximab may be re-administered within 16 weeks of the last infusion. In clinical trials, DELAYED HYPERSENSITIVITY REACTIONS have occurred after **infliximab-free intervals of less than 1 year**

See also '**Policy for the use of Biosimilar Medicines in GUH**' available on Q pulse [CLN-PHAR/UCH-091](#)

## Storage

- Store between 2 and 8°C
- **For reconstituted vials only:** since no preservative is present, it is recommended that the infusion be used as soon as possible (within 3 hours) of reconstitution and dilution
- **For Baxter manufactured bags** - See bag label for expiry date

## References

Inflectra SPC 03/2021

Remicade SPC 16/09/2021

1: Email communication with MSD March 8th, 2016

2. Infliximab prescribing, vial optimisation and administration in Merlin Park Hospital outpatients units. Q-Pulse document [CLN-GAST-002](#)

3: Signed prescription sheet from Rheumatology Day Ward MPUH (Dr C.O'Sullivan)

4: Email communication with ANP and Gastroenterologists 01/12/2021

5: Email communication with Prof Eoin Slattery, February 2022

## Therapeutic classification

Tumour necrosis factor alpha inhibitor