



## **Infliximab (Remicade) in IBD** **Patient Information Leaflet**

### **General Information**

#### Crohn's disease

Infliximab (also known as Remicade) has been licensed by The National Institute for Clinical Excellence for the treatment of Crohn's disease that is either severe or fistulating (when a tunnel forms from the bowel to another organ or the skin) and has not improved on conventional medication (eg. immunosuppressive agents like Azathioprine). Local PCTs will fund it for 1 year (unless there are extenuating circumstances) or until a fistula has healed.

#### Ulcerative Colitis

Infliximab has been licensed as rescue therapy for use in severe Ulcerative Colitis, but normally only for 3 doses. There is strong evidence to support its use as maintenance therapy but funding for this has not yet been guaranteed.

### **What is it?**

Infliximab is a monoclonal antibody produced by a special technique which involves combining human and mouse DNA.

### **How does it work?**

Infliximab is an antibody that targets a protein in the body called Tumour Necrosis Factor Alpha (TNF $\alpha$ ). You make TNF $\alpha$  automatically as part of the immune system to help fight against infection. Part of the problem with IBD is that the inflammatory cascade seems to continue long after the trigger has been cleared and seems to escape regulation. In these cases Infliximab helps bind to the TNF $\alpha$ , "mopping it up" and therefore breaking the perpetual inflammatory cascade. This in turn allows the bowel lining to heal, relieving symptoms and preventing secondary complications.

### **How is Infliximab given?**

It is given in our St Mary's Day Unit, by the nurses. You need to arrive in the unit by lunchtime. You will sit in a reclining arm chair. The nurse will insert a

cannula (small hollow plastic tube) into your vein and then attach this to the drug infusion. It will go through a pump that will alarm if there are any problems with the administration of Infliximab. You do not need to undress. You will receive an injection of hydrocortisone and antihistamine before the Infliximab infusion to reduce your chance of reacting (developing your own antibodies) to the Infliximab. Infusion reactions are rare, but we monitor patients closely when they are in the unit. The nurses will check your temperature, pulse and blood pressure before starting the infusion, 1/2hourly during the infusion and 1/2hourly after the infusion. Usually you will be able to go home in a few hours.

Infliximab cannot be swallowed as your digestive system would destroy the antibodies.

### **How long does it take to work?**

Most people start to feel better after 2-6 weeks.

### **How much does it cost?**

**For you it should cost nothing (except for the parking, and time off from work). In general, however, it costs the PCT (Primary Care Trust) approximately £1,000 per infusion. It is because it is so costly that the PCT (unfortunately) like to restrict its use and demand (rightly so) the close monitoring of its use.**

### **How long will I need to take it?**

Most people have the first infusion (counted as week 0) then the 2<sup>nd</sup> is 2 weeks later and the 3<sup>rd</sup> is 4 weeks later. This is known as induction. For Ulcerative Colitis patients this may be the full course.

For Crohn's patients, if it is successful, then the PCT allow us funding for maintenance therapy every 8 weeks for up to a year (provided we can prove its working). If it is not working then there would be no benefit in continuing the infusions.

### **How effective is Infliximab?**

Research studies (Leuven, ACT 1+2, ACCENT1) into the clinical effectiveness of Infliximab show that:-

- 60-90% of patients have some improvement in their symptoms
- 40-60% achieve longterm maintenance and mucosal healing
- 45% of patients with fistulas noticed healing of the fistula within 12 weeks.
- It is very good at inducing remission of acute IBD when other standard therapies fail (eg. steroids)
- It reduces the need for surgery in some patients (decreases colectomy rate by 50% - Swedish UC Study - from 67% to 29% at day 90).

These benefits appear to be increased when using Infliximab in combination with Azathioprine (SONIC Trial).

### **How safe is Infliximab?**

So far more than half a million people around the world have been treated with Infliximab. Evidence from the largest single IBD group using Infliximab in Leuven (Belgium), shows it is as safe as the other conventional medicines used.

### **What are the risks of potential side effects?**

13% can develop side effects (Leuven - Safety Data).

Of these;-

- 20% suffer acute infusion reactions (actual risk 2.3%)
- 50% have delayed reactions (actual risk 6%)
- 30% have a serious side effects (actual risk 3.5%)
  - Infections (actual risk 6%)
  - Skin rashes (reversible psoriatic reaction) (actual risk 20%)
  - Autoimmune / vasculitis (actual risk 0.6%)

### **What about in pregnancy and breast feeding?**

It appears to be safe in pregnancy, and medical experts agree that Infliximab does not pass the placenta barrier until the third trimester (about week 26 of a pregnancy). We would therefore suggest trying to stop it in the 6<sup>th</sup> month of pregnancy (3<sup>rd</sup> trimester), to prevent there being any possible carry over effect on the development of the babies immune system. However, research would suggest that it is better for the baby to keep the mother healthy during her pregnancy, whilst avoiding IBD flare ups. There are generally more problems with a pregnancy if the mother has unstable IBD during gestation.

The baby should NOT have live vaccines until it is 6 months old.

### **Is breastfeeding safe?**

Infliximab is considered safe to take whilst breastfeeding. It is a large protein so unlikely to pass into the breast milk, and even if it was ingested by your baby it would most likely be broken down and digested instantly. However the long term effects of Infliximab on a baby's immune system, if transmitted through the placental blood stream, are not yet known.

### **Is there a Cancer risks?**

The Leuven review found no increased risk of cancer. Caution is required if you have suffered a cancer before.

There does however appear to be a small increased risk of lymphoma, observed among patients receiving this drug compared with control patients. During clinical studies of Infliximab the incidence of lymphoma was higher than expected compared to the general population, but the occurrence of lymphoma was rare.

The risks of Lymphoma (an abnormal over production of white blood cells);-

2 in 10,000 - within the general population

4 in 10,000 - if you have Crohn's disease

6 in 10,000 - if you have Crohn's disease and are taking Infliximab

As you can see the use of Infliximab increases the risk of Lymphoma by 50%, but the real increase in risk is marginal. To try and understand the real risks in a pictorial form please see the graphical image at the end of this information sheet provided by Abbott.

### **Is there an increased risk of picking up infections?**

There does indeed appear to be an increased risk of picking up infections. There have been reports of serious infections on Infliximab, including Tuberculosis (TB). It is important that your immune status is checked before commence a biological therapy (as suggested by the European Crohn's and Colitis Organisation). We are now expected to test all IBD patients at diagnosis for a range of infections including;-

- TB (T spot test and CXR)
- Hepatitis
- HIV
- Chicken Pox virus
- Epstein Barr virus
- Human papilloma virus (in young women)

If you develop an infection, have a temperature or are taking antibiotics on the run up to your Infliximab infusion please let your IBD nurse and the St Mary's Day Unit nurses know. The infliximab infusion may need to be delayed until you are better.

If it is found that you have TB you will need to be checked by the respiratory team before starting infliximab. If they prescribe treatment for TB then the infliximab will be delayed for 3 months.

If you have a fistula you may need an MRI screen first to check that there is no associated abscess collection. If there is an abscess this will need to be treated (+/- drained) before starting infliximab.

Pre-screening also includes checking for a history of heart disease as Infliximab could aggravate the situation. You would need very close cardiac monitoring if this was the case.

If you have a history of neurological problems – such as multiple sclerosis or Guillain-Barre syndrome then the risks and benefits need to be carefully considered.

### **Vaccinations when on Infliximab**

You should avoid **LIVE** vaccines such as polio, rubella (German Measles), yellow fever, MMR (Measles, Mumps and Rubella) and the BCG (TB). The **INACTIVE** polio can be given. Flu vaccines such as swine flu and pneumovax are safe to have as they are not live vaccines.

### **Alcohol and Infliximab**

Alcohol does not appear to have any effect on Infliximab. However it is better to avoid drinking excessive amounts of alcohol. The current recommendation for the Department of Health is 2-3 units a day for a woman and 3-4 units a day for a man.

### **Possible reactions to the infusion**

1. Swelling of the hands, feet, ankles, face, lips, mouth or throat
2. tenderness or pain in the chest, muscles, joint or jaw
3. difficulty in breathing or swallowing
4. rise in temperature
5. rash/itching
6. change in blood pressure

If you experience these then infusion will be slowed down or stopped for a while. If symptoms settle then it may be possible to restart the infusion at a slower rate.

Other potential side effects include:

1. headache
2. sore throat
3. rash/hives
4. joint or jaw pain
5. nausea
6. diarrhoea
7. abdominal pain
8. feeling cold.

After the infusion has finished you may need to stay for a while for the nurses to monitor you. This time may be reduced after a while if you do not suffer from any adverse events / reactions.

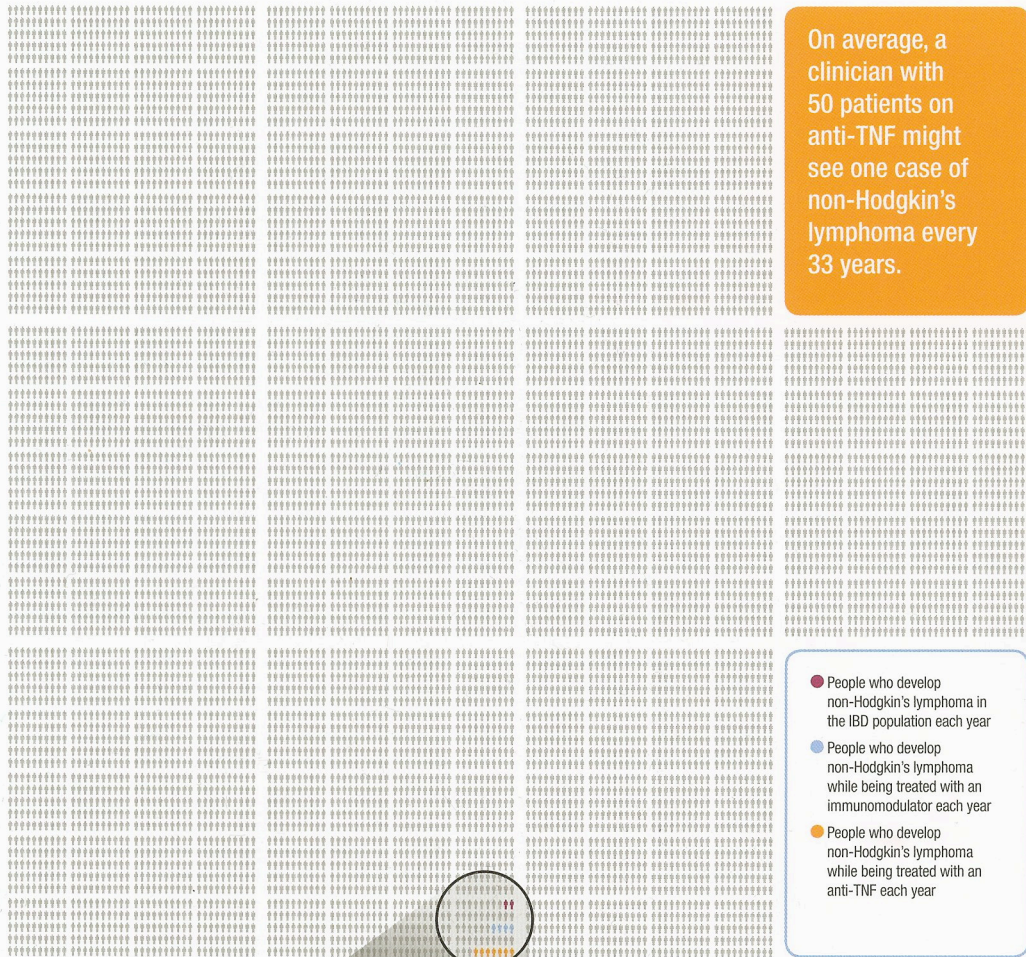
The nurses in St Marys day unit will make sure you have a further blood request form to check things 2 weeks before your next infusion. They will also make sure you have fixed the date for your next infusion.

If you have any concerns about your Infliximab treatment please discuss this with your IBD nurse specialist or your IBD Consultant.

# Annual risk of lymphoma

For full safety information, please read your Patient Information Leaflet.

Ten thousand people



**Crohn'sCare**  
From Abbott

**HUMIRA**  
adalimumab

 **Abbott**