



INFORMATION SHEET

BIOLOGICAL DRUGS

INTRODUCTION

Biological drugs (also known as biotherapeutics or biopharmaceuticals) are a form of treatment for Crohn's Disease and Ulcerative Colitis (the two main forms of Inflammatory Bowel Disease - IBD). In general they are prescribed for people with moderate to severe IBD when other treatments have not worked. This information sheet gives a brief overview of the different biological drugs used in IBD, and looks in more detail at 'biosimilars' – a new type of biological drug that has become available recently.

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My main concern with starting infliximab was the safety of the drug, both in the short and long term. Knowing that it had undergone rigorous clinical trials helped give me the confidence to go ahead with it. Five years on it's still allowing me to enjoy a normal quality of life.

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Rebecca, 32

Diagnosed with Crohn's Disease in 2007

WHAT IS A BIOLOGICAL DRUG?

Biological drugs are made from proteins and other substances which occur in nature. They are produced by a biological rather than chemical process – for example they can be created inside living cells. Biological drugs are a lot larger in size and more complicated than normal chemical drugs used in IBD, such as steroids, 5ASAs and azathioprine.

WHAT BIOLOGICAL DRUGS ARE USED IN IBD?

There are several different biological drugs used in IBD. These are:

- Infliximab (brand names Remicade and the biosimilars Inflectra and Remsima)
- Adalimumab (brand name Humira)
- Vedolizumab (brand name Entyvio)
- Golimumab (brand name Simponi)
- Ustekinumab (brand name Stelara)

The two most common biological drugs currently used in IBD are infliximab and adalimumab. These are referred to as 'anti-TNF drugs' because they work by targeting a protein in the body called TNF alpha. This protein is found in everyone's blood as part of the body's response to infection. However, in people with IBD, too much TNF alpha is produced, and this causes excessive inflammation. Biological drugs such as infliximab and adalimumab block the action of TNF alpha, and reduce inflammation. There is also another newer anti-TNF drug called golimumab, which is currently less widely used.

BIOLOGICAL DRUGS

Vedolizumab works in a different way to the anti-TNF drugs, because it is a 'gut-selective integrin blocker'. White blood cells are made by the immune system to fight against infection. However, in Crohn's Disease and Ulcerative Colitis, overproduction of white blood cells leads to inflammation – vedolizumab works by stopping the white blood cells from entering the lining of the gut. This means that the drug only targets the gut, rather than the whole of the body like the anti-TNF drugs do, and may cause fewer side effects.

Ustekinumab is known as an "anti-Interleukin" because it targets the proteins interleukin-12 (IL-12) and interleukin-23 (IL-23). These are increased in IBD and contribute to ongoing inflammation in the digestive system. Ustekinumab binds to both IL-12 and IL-23 which prevents them from working, helping to relieve inflammation and symptoms. Ustekinumab is an 'immunosuppressant' because it dampens down the activity of the immune system.

WHAT ARE THESE DRUGS USED FOR?

Infliximab, adalimumab, vedolizumab, golimumab and ustekinumab are all used to treat people with IBD.

- **Infliximab** and **adalimumab** are licensed for use in adults and children with moderate to severe active Crohn's Disease where other drugs such as immunosuppressants and steroids have not worked or are unsuitable. They are also a possible treatment for moderate to severe Ulcerative Colitis if conventional therapy hasn't worked or isn't suitable.
- **Golimumab** is licensed for use in adults with moderate to severe Ulcerative Colitis who have failed to respond to, or have not tolerated, other treatments.
- **Vedolizumab** has been recommended by NICE (National Institute for Health and Care Excellence) as a treatment option for adults with moderate to severe Ulcerative Colitis. It has also been recommended for people with moderate to severe Crohn's Disease after other treatments including either infliximab or adalimumab have not worked well enough or are unsuitable.
- **Ustekinumab** is a possible treatment for adults with moderate to severe active Crohn's Disease. It may be given if non-biological therapies or tumour necrosis factor (TNF) alpha inhibitors haven't worked or aren't suitable.

HOW ARE BIOLOGICAL DRUGS GIVEN?

Current biological drugs cannot be given as tablets by mouth because the digestive system would break down and destroy the drug. Both infliximab and vedolizumab are given by an infusion through a drip in the arm. Adalimumab and golimumab are given via a subcutaneous injection (injection under the skin), either into the thigh or stomach. Ustekinumab is given as an infusion through a drip in the arm for the first dose, followed by regular injections under the skin.

HOW ARE BIOLOGICAL DRUGS MADE?

Biological drugs are made using living organisms, such as modified plant and animal cells. The cells receive a gene (a piece of DNA) which instructs them to make a specific protein – in the case of infliximab the protein is the antibody which targets TNF alpha. The cell with the gene in it then multiplies, and produces the biological protein which can be ‘harvested’.

The cells that are the best at producing the protein are identified and grown on an industrial scale - these special cells are called a ‘cell line’ and are unique to each manufacturer. The cell line is then grown in huge tanks, and the final product harvested. This is an extremely complex process, and very small changes to it can lead to very large changes in the final product.

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My experience of having been on Humira, Remicade and Remsima are only positive, all can be life changing, and when they work it is like you no longer have IBD. Ensure you keep in contact with your IBD team and let them know how you are doing – remember they have lots of experience of IBD and are the best people to talk to.

”

Barry, 41

Diagnosed with Crohn’s Colitis in 2006

WHAT IS A BIOSIMILAR DRUG?

If you have been prescribed infliximab, you may come across the term ‘biosimilar’. All drugs when they are first discovered are subject to a patent. A patent is an exclusive set of rights given to the inventor of a new product or drug, which allows them to be the only person or company making and selling that particular drug. This allows them to offset the huge costs involved in the research and development of a new drug. Patents can last for twenty years before they expire – after which other pharmaceutical companies can manufacture the drug.

Infliximab (Remicade) was the first biological drug to be used in IBD, and the patent expired in February 2015, meaning that other companies can now produce their own versions of the same drug. However, biologic drugs are not like other ‘chemical’ drugs, and are made by living cells, which means that the process by which they are manufactured is much more complicated. Each manufacturer has its own unique cell line and manufacturing process – so the final products can never be exactly identical because they are made using different cells. Hence we have biosimilars, which are similar to, but not identical to the original biological drug.

However, in order for a biosimilar to gain approval to be used, it has to meet strict standards to show it is as safe and effective as the original biologic drug, and to have the same quality, although it may have small structural differences.

WHAT ARE THE BIOSIMILARS USED IN INFLAMMATORY BOWEL DISEASE?

So far, there are two biosimilar drugs widely used in the UK for IBD. These are Inflectra and Remsima, the biosimilar versions of Infliximab. They came onto the market in February 2015 when the patent for Remicade expired. Inflectra and Remsima are both given as an infusion, and at the same dose and frequency as Remicade. They are currently less expensive than Remicade, meaning that more IBD patients may eventually have access to these drugs.

The patent for adalimumab is due to run out in Europe in 2018, so biosimilar versions of the drug may be available.

HAVE INFLECTRA OR REMSIMA BEEN TRIALLED ON PATIENTS WITH IBD?

As yet, there have been no formal clinical trials on the use of biosimilars in IBD patients. However, there has been research into the use of infliximab biosimilars in two other autoimmune diseases: Rheumatoid Arthritis and Ankylosing Spondylitis (a form of arthritis which affects the spine). These trials did not show any differences in safety or effectiveness between the original biological drug and the biosimilar, so the European Medicines Agency (EMA) has allowed them to be licensed for IBD. This is called 'extrapolation', and has to be viewed with some caution because people with IBD may react differently from people with Ankylosing Spondylitis and Rheumatoid Arthritis.

There are currently several ongoing clinical trials studying the effect of biosimilars on IBD, that should provide more answers. Meanwhile, it is worth noting that infliximab biosimilars are already being used for IBD patients in countries such as Norway and Hungary, and the current results from these countries suggest that they are as effective and safe as Remicade. In summary, while the evidence suggests that biosimilars may be a good option for people with IBD, they should still be used cautiously until the results of the clinical trials for IBD have become available.

People on Inflectra and Remsima will be monitored carefully to make sure that all side effects are quickly identified and recorded correctly. New medicines and vaccines that are under additional monitoring have an inverted black triangle symbol (▼) displayed in their package leaflet. You can help with this monitoring by reporting any side effects you may have – this could either be telling your doctor or IBD nurse, or directly using the Yellow Card Scheme (www.mhra.gov.uk/yellowcard)

Biosimilars of infliximab must always be prescribed by brand name - so Inflectra, Remsima, or Remicade, instead of infliximab. This is so there is no uncertainty about which type of infliximab is being used, and so that any side effects can be assigned to the correct drug.

SWITCHING FROM REMICADE TO INFLECTRA OR REMSIMA

The view of Crohn's and Colitis UK is that people with IBD who are stable on Remicade should not be switched to Remsima or Inflectra as a matter of course without full discussion with the patient.

This means that people with IBD should be fully informed about the drugs they are being prescribed, and have their views taken into account in any discussions about switching. However, if your doctor does recommend switching you from Remicade to Inflectra or Remsima, the evidence so far suggests there should be no difference in the effectiveness and safety of the drug.

It is also important that pharmacists do not substitute Inflectra or Remsima for Remicade – so prescriptions should always be written by the brand name to prevent any such substitutions occurring.

If you are concerned about anything to do with your treatment, you should discuss this with your IBD team. We also produce a range of information sheets about the drugs used in IBD, that provide specific information about each drug, including side effects and dosage. These can be found on our website.

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I was moved from Remicade to a biosimilar in February 2015, when the patent expired. I have found the biosimilar to be no more different in effect from infliximab: I have had no side effects and it is just as an effective a treatment for me.

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Claire, 64

Diagnosed with Ulcerative Colitis in 2009

HELP FROM CROHN'S AND COLITIS

We offer more than 50 publications on many aspects of Crohn's Disease, Ulcerative Colitis and other forms of Inflammatory Bowel Disease. You may be interested in our comprehensive booklets on each disease, and other topics such as **Food and IBD**. We also publish information sheets on a wide range of topics, from individual medicines to coping with symptoms and concerns about relationships, school and employment.

All publications are available to download from www.crohnsandcolitis.org.uk/quick-list

Health professionals can order booklets in bulk by using our online ordering system, available from the webpage above.

If you would like a printed copy of a booklet or information sheet, please contact our Helpline.

Our Helpline is a confidential service providing information and support to anyone affected by Inflammatory Bowel Disease.

Our team can:

- help you to understand more about IBD
- provide information to help you to live well with your condition
- help you to understand and access disability benefits
- be there to listen if you need someone to talk to
- put you in touch with a trained support volunteer who has a personal experience of IBD

Call us on **0300 222 5700** or email info@crohnsandcolitis.org.uk
See our website for Live Chat: www.crohnsandcolitis.org.uk/livechat

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ABOUT CROHN'S & COLITIS UK

We are a national charity established in 1979. Our aim is to improve life for anyone affected by Inflammatory Bowel Diseases. We have over 35,000 members and 50 Local Networks throughout the UK. Membership starts from £15 per year with concessionary rates for anyone experiencing financial hardship or on a low income.

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