Roche in association with Plain English Campaign

Crystal Mark 21287
Clarity approved by Plain English Campaign

Speaking Plainly

Biologic treatment options for rheumatoid arthritis

A guide to help healthcare professionals talking to patients with rheumatoid arthritis

RXUKCOMM01108b Date of prep: July 2014

Foreword

By Chrissie Maher, founder of Plain English Campaign

For more than 30 years, it has been our mission to make sure that people receive crystal-clear information in all parts of their lives. Whether information is from the legal, financial or medical sectors, it is vital that the intended audience can understand the complicated terminology used. Everyone should be able to understand public information, and act on it, after reading it once.

Nowhere is this more important than healthcare. In an increasingly technical world, with new medicines which work in complex ways, it is vital that patients understand their disease and are well informed about the best treatment for them.

> Ill-health can be terrifying, and for scared, distressed or despondent patients it is especially important for information to be in language that anyone can understand.

This guide is intended to be used to help rheumatologists, GPs and other healthcare professionals who need to speak to patients with rheumatoid arthritis. It includes suggestions of ways they can provide the key facts, figures and treatment options in a simple, straightforward way. The suggested answers to questions that patients might ask are written in a conversational style with language suitable for discussions with patients.

We believe that guides such as this, for healthcare professionals in busy working environments, are invaluable in making sure that patients receive the best, clearest information.

Where appropriate in this guide we specify where certain information comes from. That information is indicated by a number in the text (for example , ...used together[6]) and the source of the information is given on page 18.

RXUKCOMM01108b Date of prep: July 2014

Contents

RXUKCOMM01108b Date of prep: July 2014

Communication in RA

The following booklet can be used as a guide to talk to patients with rheumatoid arthritis. It also gives facts and figures to help explain difficult concepts.

Rheumatoid arthritis affects people from all walks of life and backgrounds. Many will have very little medical knowledge, and until their diagnosis, little interest in their health. Some will be the opposite, with many questions and potential misconceptions which need correcting. For some patients, their English may be limited, perhaps because it is not their first language. Others may simply find understanding difficult.

Healthcare professionals have to constantly adapt their communication about rheumatoid arthritis to different types of patients. Treatments for rheumatoid arthritis have changed dramatically in recent years, and even well-educated patients can need explanations of all the treatment options.

As rheumatoid arthritis is a chronic condition, patients will be in contact with specialist doctors and nurses, probably for the rest of their lives. So building a relationship with and understanding the person who is treating them is very important for patients. Suitable language can help with this.

The language you need to use may change as patients move through stages of the disease – from diagnosis, to experiencing controlled disease, to relapse. Their emotions at each step on this journey are likely to alter and could include shock and disbelief, acceptance, resignation, anger or grief.

We have produced this guide to encourage best practice on communicating clearly. Rheumatoid arthritis is a complex disease, but all patients should be given understandable health knowledge to help them cope with the illness. Language is key to this.

It is important to introduce patients to patient advisory groups such as the National Rheumatoid Arthritis Society and Arthritis Care. The opportunity for patients to talk to people facing the same emotions and experiences is invaluable.

RXUKCOMM01108b Date of prep: July 2014

Rheumatoid arthritis, the immune system, and treatments

The disease

Patients want to understand their condition, how many people it affects, when it tends to strike and the effect it will have on their life. This is helpful for their own understanding and enables them to explain it to family and friends.

What is rheumatoid arthritis?

Rheumatoid arthritis is a disease of the joints and surrounding tissue. It is permanent and gets worse with time. It causes intense pain, destroys the joints and causes other problems such as fatigue and anaemia.

It is a systemic disease, which means it can affect the whole body and other organs such as the lungs, heart and eyes, although not everyone experiences this.[1]

Who does it affect?

Rheumatoid arthritis affects approximately 690,000 people in the UK, and three times as many women as men. It often begins in a person's 40s. A third of adults with rheumatoid arthritis will have to stop working within two years of onset, and around 50% will not be able to work within 10 years.[2]

RXUKCOMM01108b Date of prep: July 2014

Rheumatoid arthritis, the immune system, and treatments

The immune system

Many people know what the immune system is, but you may have to explain it to some.

What is the immune system?

The immune system is made up of many cells, chemicals and organs working together. It defends the body from disease and infection.[1]

What does rheumatoid arthritis have to do with the immune system?

Rheumatoid arthritis is called an 'auto-immune disease'. This is where a person's immune system attacks part of their body – in this case the joints.

Normally, white blood cells recognise foreign bodies such as bacteria and viruses. With rheumatoid arthritis, the white blood cells fail to recognise the body's own tissue and cells within the joint and so attack them. These continuous attacks leave the joint painful and inflamed.[1]

RXUKCOMM01108b Date of prep: July 2014

Rheumatoid arthritis, the immune system, and treatments

Treatment pathways

What are disease modifying anti-rheumatic drugs?

The standard drugs for rheumatoid arthritis are known as 'disease modifying anti-rheumatic drugs', or DMARDs. These calm down the inflammation and slow the course of the disease.[3]

Patients may take one or more DMARD. Common DMARDs include methotrexate, sulfasalazine, leflunomide and hydroxychloroquine. These drugs can be difficult for some people to take and are not suitable for others. Patients can fail to respond to them, or stop responding to them, after time.

What are biologics?

New 'biologic drugs' work in a different way. They slow or even stop the progression of the disease. They work by targeting particular chemicals and cells that are known to be important in inflammation. There are now four different types of biologic drugs available in the UK – anti-TNFs, IL-6 blockers, B-cell therapy and T-cell therapy.

Why do some need to change to a biologic?

Not all DMARDs can stop joint damage, and they do not always significantly improve quality of life.[4] Up to 40% of people given methotrexate do not respond to it well enough, or they experience side effects and need other drugs to help control their inflammation.[5] So other types of treatment are needed.

What is combination therapy and what is monotherapy?

Combination therapy is where a number of different DMARDs, or DMARDs and a biologic treatment, are used together.[6]

Monotherapy is treatment with a single drug. It is a term used if a patient takes a DMARD without any other DMARD or biologic, or takes a biologic drug without any other biologic or DMARD. Monotherapy is another option for patients who cannot have, or no longer want to continue, combination therapy.

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

Anti-TNFs

What are anti-TNFs?

In the UK there are five anti-TNFs available for people with moderate to severe disease.[1]
Those are:

- Humira® (adalimumab);
- Cimzia® (certolizumab pegol);
- Enbrel® (etanercept);
- Simponi® (golimumab); and
- Remicade® (infliximab).

Anti-TNFs are usually taken in combination with DMARDs, but they can be taken as a single treatment by some patients.

Humira® (adalimumab), Cimzia® (certolizumab pegol), Enbrel® (etanercept), and Simponi® (golimumab) are injected under the skin (subcutaneously), which can be done at home.

Remicade® (infliximab) is given through a drip or infusion into a vein (intravenously), which is done in hospital. These methods of giving the drugs mean that they do not go into the stomach. This prevents them from being broken down or digested, which could prevent them from working properly.

How do anti-TNFs work?

In inflamed joints, different kinds of chemicals (cytokines) are present. Cytokines send messages from one cell to another. Some are very good at causing inflammation. One particular cytokine is called tumour necrosis factor (TNF).

Anti-TNFs work by blocking this cytokine, reducing or stopping some of the inflammation by reducing the flow of white blood cells, which wrongly think the tissue is a foreign body, into the joint.

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

Anti-TNFs

What results can be seen?

In clinical trials for these drugs, most patients treated with anti-TNFs had at least a 20% improvement after three months. The improvements included less pain and stiffness, and fewer inflamed joints. Many patients were more able to perform daily activities such as dressing, walking, getting out of bed and carrying out daily chores.[1]

Anti-TNFs are usually taken with methotrexate. However, studies have shown that when patients did not also take methotrexate, taking one of three anti-TNFs on their own (Humira, Cimzia and Enbrel), which are injected, was effective in reducing the symptoms of rheumatoid arthritis.[7,8,9,10]

In the UK there are several biologic treatments available for people with moderate to severe RA. Some can be taken on their own, while others have to be taken with other treatments.

What are the side effects?

Many patients take anti-TNFs without suffering serious or unmanageable side effects. The most common side effects with these drugs relate to how they are given (for example, minor reactions at the site of the injection) and the increased risk of infection, which can include reactivating TB.[1]

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

IL-6 blockers

What are IL-6 blockers?

IL-6 stands for interleukin 6, a small chemical that causes inflammation and destroys the joint, as well as causing fatigue (feeling tired), anaemia and osteoporosis.[11] These symptoms are known as whole-body symptoms.

IL-6 blockers, also known as IL-6 receptor inhibitors, are another type of biologic drug. One medicine which has been developed using these blockers is called RoActemra® (tocilizumab). It is given in hospital through an hour-long drip once every four weeks. Or it can be taken at home, as an injection under the skin, once a week.

How do IL-6 blockers work?

The drug blocks the interleukin 6 from working, reducing the inflammation in the joint and improving the whole-body symptoms.[12] The treatment benefits 33 to 75% of rheumatoid arthritis patients.[1]

IL-6 blockers can be used on their own or with DMARDs.[12]

What results can be seen?

Clinical trials have shown the benefit of RoActemra when used on its own and with methotrexate. In one study, 40% of patients taking both RoActemra and methotrexate, and 35% taking only RoActemra, had a significant reduction in symptoms (known as remission).[13]

RoActemra has also been shown to be more effective against rheumatoid arthritis than when a patient is receiving methotrexate alone.[14] Another study showed that, after one year of treatment with RoActemra and methotrexate, the joint damage of over 80% of patients had not progressed, compared to 67% of those who took methotrexate alone.[15]

As a biologic treatment taken without methotrexate, RoActemra has been shown to be more effective in reducing signs and symptoms of rheumatoid arthritis than one of the leading anti-TNF treatments.[16]

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

IL-6 blockers

What are the side effects?

Studies have shown that side effects of RoActemra when taken with methotrexate were very similar to the side effects experienced by patients taking methotrexate alone.[17]

The most common reactions, seen in more than 5% of patients, are:[12]

- infection of the throat or airways;
- colds;
- headache;
- high blood pressure; and
- minor liver complaints.

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

B-cell therapy

What is B-cell therapy?

In the UK there is one B-cell therapy, MabThera® (rituximab), licensed in combination with methotrexate for treating rheumatoid arthritis where there has been an inadequate response or intolerance to other disease-modifying anti-rheumatic drugs (DMARD) including one or more tumour necrosis factor (TNF) inhibitor therapies.

MabThera is suitable for adults who have severe active rheumatoid arthritis and who:[18]

- have not seen enough improvement in their condition when taking traditional DMARDs; or cannot take DMARDs due to side effects; and
- have been treated with an anti-TNF but it has failed to improve symptoms.

MabThera is given in two drips, two weeks apart.[1] Following this initial dose, treatment is usually given by two drips every six to 12 months.

How does B-cell therapy work?

B-cells are white blood cells that are produced in the bone marrow and move throughout the bloodstream and lymphatic system as part of the body's immune system. When B-cells are more active in the body, patients with rheumatoid arthritis show more symptoms of the disease.[19]

A substance called CD20 is found on the surface of B-cells. MabThera attaches to this and destroys the B-cells, reducing the production of antibodies (proteins which act as the body's natural defences). This action also reduces the activity of T-cells (other cells involved in the immune system). These actions can interrupt the development of rheumatoid arthritis.[20]

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

B-cell therapy

What results can be seen?

MabThera is a suitable treatment option for patients who stop treatment with anti-TNFs because they:[21]

- do not see a good enough improvement; or
- suffer side effects they cannot manage.

Approximately two thirds of patients treated with MabThera experience a significant improvement in their joint pain, joint swelling and sense of fatigue.[1] Also, 32% of patients treated with MabThera and methotrexate for five years found that their joint damage had not progressed (compared with 21% of those receiving methotrexate alone).[22]

What are the side effects?

The majority of patients do not suffer serious or unmanageable side effects.[1]

The most common side effects are:

- infections of the throat and airways (upper respiratory-tract infection);
- infections of the bladder (urinary-tract infections); and
- reactions to the intravenous drip, such as high blood pressure, nausea (feeling sick), rash, fatigue (feeling tired) and headaches.[23]

In rare cases an infection called progressive multi focal leukoencephalopathy (PML) has been associated with using MabThera.[23] PML is an infection of the brain where a virus causes inflammation and damage to cells referred to as 'white matter': this can be fatal.[24] All patients receiving treatment with MabThera will be monitored closely for PML if symptoms appear.

RXUKCOMM01108b Date of prep: July 2014

Biologic treatments – key facts

T-cell therapy

What is T-cell therapy?

This therapy is available as a treatment called Orencia® (abatacept). It is given as an intravenous drip, in hospital. This procedure takes 30 to 60 minutes. After the first dose, another is given two weeks later, then two weeks after that, then once a month.

In the UK, Orencia is approved for being used with methotrexate by patients whose disease has not improved with two other DMARDs, including methotrexate.[25]

How does T-cell therapy work?

T-cells are a type of white blood cell. They co-ordinate the attack on foreign bodies in cells and tissues. They can cause inflammation when a patient has rheumatoid arthritis because the T-cells wrongly assume cells within the joints are foreign bodies. Orencia blocks the activity of these T-cells and so reduces inflammation.

What results can be seen?

A number of studies have shown the benefit of Orencia for people with rheumatoid arthritis. It has improved joint pain and swelling, improved patients' quality of life, reduced fatigue, and reduced bone and joint damage.[1]

One study followed patients who were not doing well on methotrexate. After a year, nearly three quarters of patients who received this treatment gained some benefit.[26]

Another study found that around 50% of patients had a significant benefit with Orencia following inadequate improvement with anti-TNF treatments.[1]

What are the side effects?

Orencia causes few side effects. For people it does affect, it can cause headaches, throat and airway infections and nausea.[1] The most common side effects are dizziness and headaches, but these are not usually serious.[27]

RXUKCOMM01108b Date of prep: July 2014

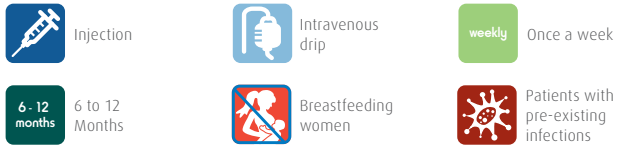
Biologic treatments work in several different ways including blocking the activity of various substances that have a role in the development of RA.

The language you need to use may change as patients move through stages of the disease – from diagnosis, to experiencing controlled disease to relapse.

RXUKCOMM01108b Date of prep: July 2014

Treatment	How it is given	Frequency of dose	Combination therapy – treatment with another drug as well	Monotherapy – treatment with just this drug	Contraindications – (factors that would make the treatment unsuitable)	Possible side effects
Anti-TNF			Anti-TNFs are usually given as combination therapy. In clinical trials for all of the anti-TNFs, most patients receiving anti-TNF therapy had at least a 20% improvement after treatment for three months. Improvements included a reduction in pain and stiffness, and fewer inflamed joints.[1]	Three of the four injectable anti-TNFs (Humira, Cimzia, and Enbrel) can reduce the signs of symptoms of rheumatoid arthritis when taken without methotrexate.[7,8,9,10] Remicade is not recommended for use without methotrexate.		Minor reactions at the site of the injection or drip, and the increased risk of infection, which includes reactivating TB.[1]
IL-6 blockers			40% of patients on combination therapy experienced a significant reduction in symptoms (clinical remission).[13] The benefits of receiving this treatment can include improvements in the number of swollen joints, the degree of swelling, the pain associated with the joints and fatigue (feeling tired).[1]	35% of patients on monotherapy had a marked reduction in symptoms.[13]		The most common side effects in more than 5% of patients are upper respiratory-tract infection, colds, headache, high blood pressure and minor liver complaints.[12]
T-cell therapy			The benefits of T-cell treatment include less joint pain and swelling, improved quality of life, reduced fatigue, and reduced bone and joint damage.[1]	T-cell therapy is not recommended for monotherapy without methotrexate.[28]		The most common side effects are dizziness and headaches while being given the drip, but these are not usually serious.
B-cell therapy			B-cell therapy is only given as combination therapy with methotrexate. Approximately two-thirds of patients with rheumatoid arthritis experience significantly less joint pain, swelling and fatigue.	B-cell therapy is not recommended for monotherapy (use without methotrexate).[23]		The most common side effects are upper respiratory-tract or urinary-tract infections, and reactions related to being given the drip, such as high blood pressure, nausea, rash, fatigue and headaches.[23]

Key to the table



RXUKCOMM01108b Date of prep: July 2014

RXUKCOMM01108b Date of prep: July 2014

References

1 NRAS Biologics The Story So Far January 2013 p5. Available from http://www.nras.org.uk/includes/documents/cm_docs//2013/b/biologics_lo_res_jan_2013_with_copyright_and_ammended_text.pdf [last accessed December 2013]

2 National Audit Office.Services for people with rheumatoid arthritis. July 2011. Available from http://www.nao.org.uk/report/services-for-people-with-rheumatoid-arthritis/ [last accessed December 2013]

3 NHS. Rheumatoid arthritis – Treatment: http://www.nhs.uk/Conditions/Rheumatoid-arthritis/Pages/Treatment.aspx [last accessed December 2013]

4 Kremer JM et al. The Safety and Efficacy of a JAK Inhibitor in Patients With Active Rheumatoid Arthritis; Results of a Double-Blind, Placebo-Controlled Phase IIa Trial of Three Dosage Levels of CP-690,550 Versus Placebo. Arthritis & Rheumatism 2009;60(7):1895–1905

5 Pincus T, et al. Underestimation of the efficacy, effectiveness, tolerability, and safety of weekly low-dose methotrexate in information presented to physicians and patients. ClinExpRheumatol 2010;28(Suppl.61):S68–S79

6 Goekoop YP, et al. Combination therapy in rheumatoid arthritis. CurrOpinRheumatol. 2001;13(3):177-83

7 van de Putte LBA, et al. Efficacy and safety of adalimumab as monotherapy inpatients with rheumatoid arthritis for whom previous diseasemodifyinganti-rheumatic drug treatment has failedAnn Rheum Dis 2004;63:508–516.

8 Lethaby A, et al. Etanercept for the treatment of rheumatoid arthritis. Cochrane Database Syst Rev. 2013 May 31;5

9 Takeuchi T, et al. Golimumab monotherapy in Japanese patients with active rheumatoid arthritis despite prior treatment with diseasemodifying anti-rheumatic drugs: results of the phase 2/3, multicentre, randomised, double-blind, placebo-controlled GO-MONO study through 24 weeks. Ann Rheum Dis. 2013;72(9):1488-95.

10 Fleischmann R, et al. Efficacy and safety of certolizumab pegol monotherapy every 4 weeks in patients with rheumatoid arthritis failing previous disease-modifying anti-rheumatic therapy: the FAST4WARD study. Ann Rheum Dis. 2009 Jun;68(6):805-11.

11 Choy E. Inhibiting interleukin-6 in rheumatoid arthritis. CurrRheumatol Rep. 2008;10:413-417.

12 RoActemra® (tocilizumab) Summary of Product Characteristics. Roche Products Ltd. October 2013

13 Dougados M et al. Tocilizumab (TCZ) plus methotrexate (MTX) does not have superior clinical efficacy to TCZ alone in RA patients with inadequate response to MTX: 24-week results of the ACT-RAY study. Arthritis Rheum 2011;63(10 Suppl): S1032-10

14 Jones G, et al. Comparison of tocilizumab monotherapy versus methotrexate monotherapy in patients with moderate to severe rheumatoid arthritis: The AMBITION study. Ann Rheum Dis 2010; 69:88–96.

15 Kremer JM et al. Tocilizumab Inhibits Structural Joint Damage in Rheumatoid Arthritis Patients With Inadequate Responses to Methotrexate; Results From the Double-Blind Treatment Phase of a Randomized Placebo-Controlled Trial of tocilizumab Safety and Prevention of Structural Joint Damage at One Year. Arthritis & Rheumatism. 2011; 63(3):609–621

16 Gabay C, et al. Tocilizumab monotherapy versus adalimumab monotherapy for treatment of rheumatoid arthritis (ADACTA): a randomised, double-blind, controlled phase 4 trial. The Lancet 2013;381(9877): 1541-1550

17 Emery P et al. IL-6 receptor inhibition with tocilizumab improves treatment outcomes in patients with rheumatoid arthritis refractory to anti-tumour necrosis factor biologicals: results from a 24-week multicentre randomised placebo-controlled trial Ann Rheum Dis. 2008;67:1516-1523

18 NICE technology appraisal guidance TA195. 'Adalimumab, etanercept, infliximab, rituximab and abatacept for the treatment of rheumatoid arthritis after the failure of a TNF inhibitor'. August 2010. Available at: http://publications.nice.org.uk/adalimumabetanercept-infliximab-rituximab-and-abatacept-for-the-treatment-of-rheumatoid-ta195 [last accessed December 2013]

19 Gottenberg GE, et al. Markers of B-lymphocyte activation are elevated in patients with early rheumatoid arthritis and correlated with disease activity in the ESPOIR cohort. Arthritis Res Ther. 2009;11(4):R114

20 Shaw T, et al. B-cell therapy for rheumatoid arthritis: the rituximab (anti-CD20) experience. Ann Rheum Dis 2003;62(Suppl.2):ii55–59

21 Hyrich KL, et al. Outcomes After Switching From One Anti–Tumor Necrosis Factor - Agent to a Second Anti–Tumor Necrosis Factor -Agent in Patients With Rheumatoid Arthritis. Arthritis Rheum. 2007;56(1):13–20

22 Keystone EC, et al. Sustained inhibition of structural damage in patients with rheumatoid arthritis and an inadequate response totumour necrosis factor inhibitors prior to rituximab treatment: 5-year data from the REFLEX study. Ann Rheum 2012;71(Suppl.3):374 and poster number 0183

23 MabThera® (rituximab) Summary of Product Characteristics. Roche Products Ltd. August 2013

24 MHRA. Adverse drug reactions in focus: progressive multifocal leukoencephalopathy. March 2009. Available at:http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON088120 [last accessed December 2013]

25 NICE technology appraisal guidance TA280. 'Rheumatoid arthritis - abatacept (2nd line) (rapid review of TA234)'. April 2013. Available at: http://guidance.nice.org.uk/TA280 [last accessed December 2013]

26 Kremer JM et al. Effects of abatacept in patients with methotrexate-resistant active rheumatoid arthritis: a randomized trial. Ann Intern Med. 2006 Jun 20;144(12):865-76

27 Arthritis Research UK. Abatacept: What are the possible side-effects? Available at:http://www.arthritisresearchuk.org/arthritisinformation/drugs/abatacept/possible-side-effects.aspx#sthash.nfK5wRVx.dpuf [last accessed December 2013]

28 Orencia®(abatacept) Summary of Product Characteristics. Bristol-Myers Squibb. June 2013.

Do you want to know more?

There are lots of sources of help and support for patients who want to discuss biologic therapy options further.

The National Rheumatoid Arthritis Society (NRAS)

NRAS provides support, information and education for people with rheumatoid arthritis.

Freephone: 0800 298 7650 (9.30am to 4pm Monday to Friday)

Email: helpline@nras.org.uk

Arthritis Care

Arthritis Care provides support and information for people with all forms of arthritis.

Helpline: 0808 800 4050 (10am to 4pm Monday to Friday)

Email: helplines@arthritiscare.org.uk

RXUKCOMM01108b Date of prep: July 2014