NRAS is the only patient-led charity in the UK specifically for people with rheumatoid arthritis, their families and carers, providing information, support, advocacy and campaigning.

- The NRAS freephone helpline 0800 298 7650 is open from 9.30am to 4.30pm Monday to Friday. Our trained helpline staff are there to answer your questions on all aspects of living with RA, with support from our team of medical and allied health professional advisers.

- Our website www.nras.org.uk has a wealth of information about living with RA, treatments, the latest research and developments, and an online members’ forum. It also has a full list of useful charities and organisations. If you don’t have access to the internet, and think you need to contact other organisations, call us and we’ll provide the information you need.

- If you’d like to talk on the phone to another person who has RA, we can put you in touch with one of our trained volunteers. NRAS has a national network of support volunteers – people with RA who understand what you’re going through. They’re available at the end of the phone to chat and listen. If you’d like to arrange for someone to contact you, call us on the helpline number or 0845 458 3969.

- Local NRAS groups meet regularly around the country. To find out details of your local group, call 0845 458 3969 or visit www.nras.org.uk/helpforyou

Contact us

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NRAS would like to thank all the expert contributors for their help in producing this booklet, and all our members who helped to review it.
The last 10 years have seen fantastic changes in the way that rheumatoid arthritis is treated and in the increase in research that the anti-TNF drugs have spawned. But with greater choice of biologic and other new drugs in the pipeline comes more difficulty in patients being able to make informed decisions about their care and treatment.

Whenever there is a media story about a new biologic therapy, calls to the NRAS helpline increase. Understandably, people want to know how they can get this new treatment. People with RA who are not already on biologic therapy are often not aware of the eligibility criteria they have to meet before they can receive a biologic drug.

In this booklet we aim to give you the essential information: what biologic treatments are, why they are different from standard disease modifying drugs such as methotrexate, and how they work. We’ve covered the different biologic drugs and how you take them, and also what the eligibility criteria are and what the NHS will fund.

The National Institute for Health and Clinical Excellence (NICE) and the Scottish Medicines Consortium make the decisions about whether a drug is clinically effective and cost effective for use in the NHS. NRAS does a great deal of work with these organisations when they are appraising new RA drugs, to ensure that patients’ views are taken into consideration. This booklet explains a little more about these processes. It can be devastating when clinically effective therapies are not approved for funding, and many people therefore cannot get a treatment that may help them.

We’ve also peeked into the future, looking at the long-term monitoring of biologics, and at current research. There’s much more to find out about why some people respond to one biologic drug but not to another. Like many others, I am concerned to know what my choices are, if my current (biologic) therapy should become less effective.

Biologics have already changed thousands of lives for the better. Do dip into this booklet to find what’s useful for you. We’ve tried to be comprehensive, so that everyone can find what they need. It’s a complicated subject, but we hope it’s not a daunting read!

I’d like to thank all the health professionals who gave their time and expertise to help write this booklet, and all the NRAS members and volunteers who reviewed it. We plan to update it as new drugs are licensed and approved – and of course the NRAS helpline will always have the latest information.

We hope you find this booklet helpful. Good luck with your treatment and with your biologic therapy.

Ailsa Bosworth
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1. Rheumatoid arthritis: key facts

- Rheumatoid arthritis (RA) is a chronic, progressive and disabling auto-immune disease affecting 580,000 people in England – which suggests that over 690,000 adults in the UK live with the condition. It is a disease in which the immune system attacks the tissue within the joint, leaving it painful and inflamed. If the disease is left untreated, the joint can lose its shape and alignment, and can eventually become unstable and ultimately, destroyed.

- It is a painful condition, and can lead to disability, although every person’s disease is different. It is a progressive disease, but this varies significantly between individuals. It can progress very rapidly, or more slowly, but ultimately causing damage to cartilage and bone around the joints. Any joint may be affected but it is commonly the hands, feet and wrists. Some people have very little damage to their joints, and about one person in 20 has severe damage in several joints.

- RA is a systemic disease which means that it can affect the whole body and other organs such as the lungs, heart and eyes, although this is not the case for everyone with RA.

- RA affects approximately three times more women than men and its onset is generally between 40 and 60 years of age, although it can occur at any age. There are around 12,000 children under 16 with the juvenile form of the disease. RA is more common than leukaemia and multiple sclerosis. However, because the condition and its effects are not well understood, it is often only those who are directly affected and their relatives who are aware of its severity.

- RA has major economic implications, with an estimated cost to the UK economy in terms of productivity – of £8 billion per year.

- We now know that uncontrolled RA increases mortality through an increased risk of cardiovascular disease such as heart attacks and strokes. The need for early treatment therefore is imperative.

- We do not know exactly what causes RA. There is a genetic element which, when combined with an environmental ‘trigger’ such as virus, infection, stress or trauma, can cause the immune system to malfunction. Cigarette smoking is an important precipitating factor (and it also makes the outlook for the RA worse). So far, we cannot cure RA, but we now understand much more about the inflammatory process and how to manage it.

- The good news is that the prognosis today, if RA is diagnosed and treated early, is significantly better than it was 20 to 30 years ago. Many people have a much better quality of life in spite of having RA.
By John D Isaacs, Professor of Clinical Rheumatology and Director, Wilson Horne Immunotherapy Centre, Institute for Cellular Medicine (Musculoskeletal Research Group), Newcastle University.

Rheumatoid arthritis is an auto-immune disease. In these conditions, the cells in your immune system don’t behave as they should. This section looks at what happens in the body’s immune system response, where it goes wrong in RA, and how treatments tackle the problem.

THE IMMUNE SYSTEM IS LIKE AN ‘ARMY’

An immune response resembles a battle between the body’s immune ‘army’ and a foreign ‘invader’, which can be a virus, a bacterium or perhaps a tumour. The immune system is a highly sophisticated army, with different parts playing distinct roles: scouts, generals, troops and even bomb disposal units.

Its weapons include antibodies and a wide range of chemicals, and it is capable of making highly focused and well co-ordinated attacks. It minimises any collateral damage by making each attack very specific and by precise timing, stopping an attack as soon as the invader has been destroyed. A frequent immune ‘experience’ is the common cold: it leads to unpleasant symptoms for a few days followed by rapid resolution – that is, the disappearance of the infection – once the immune system has been called into action, with minimal after effects.

Our immune system has the difficult task of distinguishing between our body’s own cells and tissues (‘self’) and the outside world (‘non-self’). To do this it uses a complex set of receptors on the surface of white blood cells, which recognise ‘non-self’. A second set of receptors on the white blood cells also helps the immune system to sense danger signals in the presence of bacteria and viruses.

When the immune system is fighting an infection (non-self), it mobilises a response:

- First, danger signals cause white blood cells to pour into the site of danger and the blood vessels to become leaky. This leads to the signs of acute inflammation: redness, swelling, warmth and pain.

- The ‘scouts’ of the immune system (called dendritic cells) become activated and they carry signals back to ‘immune headquarters’ in the lymph nodes. This is where the subsequent attack develops.

- Specialised white blood cells (called T-cells) are the generals that become activated by the scouts to co-ordinate a specific attack against the invaders.

Some T-cells can kill virus-infected cells themselves. Others release chemicals that help other cells to join the fight. An important group of these chemicals is called cytokines.
Certain cytokines released from T-cells help cells called B-cells to make antibodies. Antibodies are highly specialised proteins that stick to the invader (the virus or bacteria) and either kill it or neutralise it. Both T-cells and B-cells have receptors that very precisely recognise the invaders, ensuring that their attack is well co-ordinated and directed only against non-self.

- The chemicals released during an immune attack result in further acute inflammation, which leads to a chain reaction: more cells (troops) arrive and join the battle, until the invader is overcome.

Once the invader is destroyed and the stimulus to the immune system ‘resolves’ (ceases), the immune response dies down. This is an important aspect of the immune response: it switches itself off at the appropriate time without causing damage.

The immune system and RA: what happens?

In rheumatoid arthritis, something goes wrong. We’re not sure why, but the joints are mistakenly seen as ‘non-self’, so the concentrated immune attack is focused on the body’s own tissues.

In these circumstances the supposed ‘invader’ (in this case it’s the joint tissue) never goes away and so there is no stop signal: the immune attack continuously reinforces itself by producing more inflammation. So now the acute inflammation becomes chronic. People with RA recognise these signs very well, as they experience swelling and pain in their joints.

TREATING RA

RA is usually treated with one or more of the many disease modifying anti-rheumatic drugs (DMARDs) that are available. In various ways, these calm down the activity of the immune system so that it stops attacking and damaging the joints.

Conventional DMARDS for RA (such as methotrexate, sulfasalazine) and drugs such as steroids are effective, but they tend to suppress many aspects of the body’s immune response at once. As we have learnt more about the abnormal immune response that happens in RA, it has become possible to develop treatments that target very specific aspects of it: these are biologic therapies.
Biologic therapies for RA

By Peter C. Taylor MA, PhD, Norman Collisson Professor of Musculoskeletal Sciences, Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK.

In this section: an overview of how biologic drugs have been developed, and how they target aspects of the body’s immune response.

HOW DID BIOLOGIC THERAPIES DEVELOP?

Biologic drugs for the treatment of rheumatoid arthritis (RA) are made from proteins. They work by blocking the activity of a key chemical or cell involved in inflammation that gives rise to joint swelling and other symptoms. They are powerful and specific therapies.

In the 1980s it was discovered that the actively inflamed joints of people with rheumatoid arthritis contain many different chemicals that cause inflammation or contribute to it, produced by cells in the joint. Among these chemicals, it was discovered, many were small proteins called cytokines, whose job is to send chemical messages from one cell to another. There are many different cytokines: some switch off inflammation while others are particularly potent at causing it.

Laboratory experiments followed, using tissue from rheumatoid joints – taken, with patients’ consent, when they had joint replacement surgery. The experiments found that cells in this tissue spontaneously produced inflammatory cytokines. One important observation was about a particular cytokine, called tumour necrosis factor (TNF): TNF was responsible for regulating a number of other important inflammatory cytokines.

TNF, the reasoning went, acted like a chemical ‘ringleader’, encouraging other inflammatory cytokines to cause the clinical features associated with rheumatoid arthritis such as pain, swelling and stiffness. Clinical trials were designed that made use of biologic therapies that inhibit the activity of TNF and these showed very clearly that the majority of patients, although not all, got much better with treatment.

HOW ARE BIOLOGICS DIFFERENT FROM STANDARD DISEASE MODIFYING DRUGS?

The standard disease modifying drugs we use now (such as methotrexate) came into use as a result of the careful observations of doctors. Over the years, they noted that different drugs worked for some patients in particular circumstances. This type of approach to discovery of drugs is termed ‘empirical’.

For example, many decades ago, tuberculosis (TB) was common and often fatal. Patients were treated with gold injections, which were known to have some effect on killing the bacteria responsible for tuberculosis. Doctors found that when some of their TB patients, who also had RA, were treated with gold injections, their arthritis also improved in a proportion of cases.
Similarly, methotrexate, originally used in high doses as a cancer drug, was found to be very effective in much lower doses once weekly in rheumatoid arthritis.

Biologic therapies are different: they are protein drugs that specifically target one chemical known to be important in the inflammation associated with rheumatoid arthritis. There are several potential chemical ‘targets’ that biologic therapies could work on – some might be found floating in the fluids in between cells and others are found on the surface of cells. Current biologic therapies specifically inhibit different types of cells and cytokines, each working in different ways.

Standard DMARDs are non-specifically acting drugs that have a variety of effects on different inflammation processes, and biologics are ‘designer drugs’ that specifically act on important inflammation pathways.

HOW DO BIOLOGICS WORK?

Biologics work by targeting particular chemicals or cells involved in the body’s immune system response.

Anti-TNF drugs, for example, were the first biologics to be developed. These therapies work by blocking the activity of TNF, a chemical messenger. TNF itself has many different actions, so anti-TNF drugs result in many biological effects, which tend to reduce or stop different aspects of inflammation.

They reduce the flow of white blood cells (inflammatory cells) into the rheumatoid joint from blood vessels around the joint. (As explained above on page 6, when white blood cells pour into an area, you get redness, swelling and pain.) By preventing this movement of inflammatory cells, anti-TNFs help to reduce the swelling in joints and also reduce the damage to the joints that can be caused by those cells.

Anti-TNFs may also ‘switch off’ the production of other inflammatory molecules, including cytokines (chemical messengers) that are regulated by TNF. Stopping the ‘chemical ringleader’, TNF, also brings other molecules involved into line. (Think of it as capturing the ‘godfather’; if successful – the lesser hoodlums then lose direction and go away…)

Other, newer biologics target other areas of the immune system that are involved in the processes of inflammation. These include various other cytokines such as IL-6 and cells such as B and T lymphocytes. There’s more detail about these, for example, on page 15 about tocilizumab, on page 18 about rituximab and on page 21 about abatacept.

DO THEY WORK FOR EVERYONE?

Biologics have significant benefit for most people, but unfortunately they do not work for everyone. Some people have to stop taking them because of side effects, others because they experience no benefit. At present, doctors do not have a reliable way to work out in advance who will benefit; it’s a question of trying it out and waiting to see if it works. Most people experience a significant benefit within three to four months although a few have to wait as long as six months. After six months of treatment, about two thirds of people have usually improved.
4. Biologic drugs available in the UK

This section has details of the biologic drugs that are currently licensed for the treatment of RA in the UK, and explains which are approved for use by the NHS.

Drugs are approved for use by the NHS by the National Institute for Health and Clinical Excellence (NICE) and the Scottish Medicines Consortium (SMC). See page 30 for more information about the process of approving drugs and the role of NICE and the SMC.

This booklet gives the correct and complete position as of December 2012, but the situation is evolving. The NRAS helpline 0800 298 7650 can tell you what the latest news is.

This section covers:

- the anti-TNF drugs (adalimumab, certolizumab pegol, etanercept, infliximab and golimumab)
- tocilizumab
- rituximab
- abatacept

Please note: This booklet does not cover anakinra (brand name Kineret). This biologic was licensed in the UK but not approved by NICE as it was found not to be sufficiently clinically effective (it did not work well enough) for the treatment of rheumatoid arthritis (RA). It is a type of biologic called an ‘interleukin-1 inhibitor’. Very few people with RA are taking this therapy, however, it can be very effective in some periodic fevers, gout and is sometimes, though rarely, effective in RA.

**Anti-TNF drugs**

There are currently five anti-TNF drugs licensed for RA in the UK. All have been approved by NICE for use by the NHS in England, Wales and Northern Ireland and by the SMC for use in Scotland.

In alphabetical order, these drugs are:

<table>
<thead>
<tr>
<th>Generic drug name</th>
<th>Brand name</th>
<th>Manufacturer</th>
<th>Approved by NICE and SMC</th>
</tr>
</thead>
<tbody>
<tr>
<td>adalimumab</td>
<td>Humira</td>
<td>Abbott Laboratories</td>
<td>yes</td>
</tr>
<tr>
<td>certolizumab pegol</td>
<td>Cimzia</td>
<td>UCB</td>
<td>yes</td>
</tr>
<tr>
<td>etanercept</td>
<td>Enbrel</td>
<td>Pfizer (formerly Wyeth)</td>
<td>yes</td>
</tr>
<tr>
<td>golimumab</td>
<td>Simponi</td>
<td>Schering Plough (MSD)</td>
<td>yes</td>
</tr>
<tr>
<td>infliximab</td>
<td>Remicade</td>
<td>Schering Plough (MSD)</td>
<td>yes</td>
</tr>
</tbody>
</table>
These drugs are all within the class of biologic known as anti-TNFs. They all block TNF, but they each do that job in a slightly different way, and we don’t know which one an individual is going to respond best to – it’s a case of trying and seeing. Many people have tried two and some have even tried three (though this isn’t within current NICE guidance – there are more details about this on page 27).

WHAT IS THE BENEFIT OF TAKING AN ANTI-TNF DRUG AND HOW WILL IT AFFECT MY SYMPTOMS?

Anti-TNF therapies are used to reduce the signs and symptoms of rheumatoid arthritis and to reduce joint damage in people with moderate to severe disease.

In clinical trials for all of the drugs, the majority of patients receiving anti-TNF therapy had at least a 20% improvement after treatment for three months, which included reductions in pain, stiffness and the number of inflamed joints. Many patients were better able to perform daily activities such as dressing, walking, getting out of bed and daily chores.

Anti-TNFs often work quite rapidly and many patients begin to feel better as soon as two weeks after the first treatment. In general, you should feel the benefits of treatment within 12 weeks as inflammation in your joints reduces and the damage to your joints slows down. This makes everyday activities easier. Many people often find that they have more energy and less fatigue.

HOW DO YOU TAKE ANTI-TNF DRUGS?

Anti-TNF is a protein. As proteins are rapidly broken down and digested in the stomach, you have to take these drugs in a way that bypasses the stomach (‘parenterally’). In this case, it is either a subcutaneous (under the skin) injection or an intravenous (into a vein) infusion.

Adalimumab, certolizumab pegol, etanercept and golimumab are given by subcutaneous injection with a special pre-filled syringe.

The manufacturers of adalimumab, etanercept and golimumab provide an auto-injector – this is like a pen, and conceals the needle which is released when you press a button. Syringes are delivered to your home by a home healthcare delivery company, together with the ‘sharps bin’ for used syringes, and alcohol swabs for cleaning your skin. Most people can learn how to do subcutaneous injections themselves, though they are sometimes done by a health professional, or a family member can learn.
When you start a biologic therapy, you get a complete pack of information from the drug's manufacturer, which covers how to inject. This usually includes both written information and a DVD. Your Nurse Specialist – find out about their role on page 26 – can answer your questions about injecting.

**Infliximab** is given by intravenous infusion often called a drip: you attend hospital for part of a day to receive the drip treatment, usually given by a nurse. Some of drugs have a 'loading dose', that is, a larger first dose, followed by a smaller dosage thereafter.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>adalimumab</td>
<td>40mg by subcutaneous (under the skin) injection every other week</td>
</tr>
<tr>
<td>certolizumab pegol</td>
<td>400mg by subcutaneous injection at weeks 0, 2 and 4 (given as two injections of 200mg), and then 200mg every other week thereafter</td>
</tr>
<tr>
<td>etanercept</td>
<td>25mg twice a week, or 50mg weekly by subcutaneous injection</td>
</tr>
<tr>
<td>golimumab</td>
<td>50mg monthly by subcutaneous injection</td>
</tr>
<tr>
<td>infliximab</td>
<td>3mg per kg of body weight, repeated 2 weeks and 6 weeks after the first infusion, then every 8 weeks</td>
</tr>
</tbody>
</table>

You usually take methotrexate in combination with anti-TNFs and almost always with infliximab (NICE only approve infliximab if combined with methotrexate) because these two drugs work well together and give a better outcome than either alone.

The manufacturers of infliximab and adalimumab suggest that the dose can be increased beyond the starting dose (if you do not respond sufficiently), this is not endorsed by NICE for RA patients.

**HOW DO I STORE ANTI-TNF DRUGS?**

All the anti-TNF drugs should be stored between 2° C and 8° C (in the fridge) in the original containers until used. They should be protected from light and should not be frozen. (If you do accidentally freeze them you may need to throw them away – ask your team or the home healthcare company that provides your injections for advice if this happens.)

If you need to take your drug with you, for example when you’re travelling, store it in a cool carrier with an ice pack and protect it from light. Contact your home healthcare company for advice on travelling with injections and cool carriers.
HOW DO I GET THESE DRUGS?

There are strict eligibility criteria, and there is more information about these on page 27. In summary, you may be eligible if:

- you have failed to respond to treatment with at least two standard disease modifying drugs, one of which must be methotrexate (unless you cannot take methotrexate because there is some medical reason to avoid it).

- your rheumatoid arthritis disease activity score (DAS 28) is measured as 5.1 or over, on two occasions, one month apart.

There is more information about DAS 28 on page 27. You can also ask NRAS for a booklet, Know your Disease Activity Score (DAS) and watch a DVD clip about DAS at www.nras.org.uk

CAN I TAKE ANTI-TNF DRUGS IF I AM TAKING OTHER MEDICINES FOR MY RA OR OTHER CONDITIONS?

Yes, you can take other medicines prescribed by your doctor while on anti-TNF therapy (for example, steroids, non-steroidal anti-inflammatory drugs such as naproxen or prescription pain relievers, methotrexate or other disease-modifying anti-rheumatic drugs). Make sure you tell your doctor about any other medicines you are taking for other conditions (for example, high blood pressure medicine) before you start taking anti-TNF therapy. You should also tell your doctor about any over-the-counter drugs, herbal medicines and vitamin and mineral supplements you are taking.

ARE THERE ANY MEDICAL REASONS WHY I CAN’T TAKE THESE DRUGS?

You are screened before starting treatment to exclude an increased risk of side effects, in particular for a past history of tuberculosis (TB), multiple sclerosis, recurrent infection, leg ulcers and a past history of cancer. You will be asked to have a chest x-ray if a recent one is not available, to exclude signs of previous TB (sometimes unknown to anyone, including you), and to exclude signs of heart failure. You also have blood tests to check blood count, liver function tests and in some cases to exclude hepatitis B and C. All of these tests are routine for your protection and safety.

If you’re pregnant or planning to become pregnant you would not be given this therapy.

WHAT ARE THE RISKS OR SIDE EFFECTS?

The most common side effects of these drugs are related to how they are given – for example, minor reactions at the site of injection – and the increased risk of infection, which includes reactivation of TB. The side effects of these drugs may be similar, but because they work in different ways, there may be subtle differences. Your rheumatology team will go through these with you when you’re considering treatment with a particular anti-TNF drug.
4. Biologic drugs available in the UK (cont.)

WHAT MONITORING WILL I HAVE?
People usually continue to take methotrexate when on biologic therapy because it has been shown to make anti-TNF therapy more effective. If you are intolerant to methotrexate, you can take adalimumab, certolizumab pegol, etanercept and golimumab on their own, but infliximab must be given with methotrexate. Your usual methotrexate monitoring blood tests and follow-up will continue as normal.

IN WHAT CIRCUMSTANCES WOULD I HAVE TO STOP TREATMENT?
These drugs can increase the possibility of getting an infection, such as a cold or respiratory infection. If you get any kind of infection, contact your rheumatology nurse specialist or GP to seek advice. There is a possibility that you will have to stop taking the drug until the infection has cleared up, though with most minor infections you can continue.

It is generally deemed advisable and good practice to come off anti-TNF treatment two weeks before elective surgery or invasive dental procedures, and remain off until at least two weeks after surgery. Your team can give you further advice on this.

If you do not respond to treatment within six months, you will be taken off the treatment and will need to consider other options.

CAN I TAKE ANOTHER TYPE OF BIOLOGIC THERAPY WHILE I’M ON ANTI-TNF THERAPY?
Much more research is needed to know whether it would be beneficial or safe to take more than one biologic at a time. If you are on anti-TNF therapy and doing well, you will not be considered for additional biologic therapy. If you did not respond, you could be considered for another biologic but you would not start the next one until you had completely come off the current therapy.

HOW LONG CAN I STAY ON THIS TREATMENT?
There is now data on people who have been on anti-TNF therapy for as long as 10 years. You can stay on the drug for as long as you continue to respond well to it.

The UK Biologics Register is collecting data about how people are doing on biologics and their safety in the long term. There’s more information about this on page 33.

CAN I GET PREGNANT OR BREASTFEED WHILE I’M TAKING ANTI-TNF THERAPY?
If you are on any biologic therapy and decide to plan a family, you should discuss it with your rheumatologist. If you’re planning to become pregnant you will not be given anti-TNF as not enough is known about the safety of the foetus associated with the anti-TNF therapy. However, there are some mothers who have given birth while on anti-TNF treatment with no apparent adverse effects on the child. Some standard treatments are safe to take when planning to become pregnant and your team can advise you.
There is no known problem regarding the use of currently available biologic therapy and fathering children. It is not necessary to discontinue biologic therapy in those male patients who wish to start or to enlarge a family. However, if you are taking methotrexate together with your biologic drug, which is recommended with several, but not all biologics, it does need to be stopped for 12 weeks prior to an attempted conception and appropriate contraception applied prior to being off methotrexate for that time. Sulfasalazine can cause a reversible reduction in sperm counts and motility.

There is very little information available about breastfeeding while on anti-TNF. If you have had a baby and your arthritis is flaring up, see your rheumatologist or nurse specialist to discuss the best way of controlling your arthritis so that it will have no harmful effect on your baby.

**CAN I HAVE IMMUNISATIONS?**

You should not have live vaccines such as yellow fever or live polio. But you may be able to have other vaccinations and should discuss each case with your GP and rheumatology specialist.

**CAN I DRINK ALCOHOL?**

If your liver tests are satisfactory, you can drink alcohol in moderation. However, anti-TNF drugs and other drugs often taken with it, such as methotrexate, can cause abnormalities in liver tests. If you do have abnormal liver function tests your specialist may recommend that you do not drink alcohol, either temporarily, or in rare cases, permanently.

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**Tocilizumab**

*By Peter C. Taylor MA, PhD, Norman Collisson Professor of Musculoskeletal Sciences, Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK.*

Tocilizumab (brand name RoActemra, manufactured by Roche Products Ltd) is a new biologic therapy that has been shown to be very successful for treating RA in a number of circumstances. It is a type of biologic called an ‘IL-6 (interleukin 6) receptor inhibitor’.

**WHAT IS INTERLEUKIN 6?**

Interleukin 6 (IL-6) is the name of a small protein in the body that causes inflammation. It is a member of the family of proteins called cytokines, which deliver chemical messages between cells in the body. There are many different cytokines present in the joints of patients with rheumatoid arthritis. Some, including IL-6, are involved in switching on inflammation; others attempt to switch it off. In RA, the inflammatory effects of cytokines outweigh their anti-inflammatory effects. IL-6 is the most abundantly present cytokine in the rheumatoid joint.

IL-6 also has effects on the liver, making it produce chemicals associated with inflammation; on bones, including thinning of bones; and on the blood, including production of platelets in the blood which increase the tendency of the blood to clot. IL-6 also seems to have other effects away from the joint, which include increasing the risk of heart disease and hardening the arteries.
WHAT IS THE BENEFIT OF TAKING TOCILIZUMAB AND HOW WILL IT AFFECT MY SYMPTOMS?
At present, tocilizumab is the only available biologic that works by interfering with the effects of IL-6 in inflammation. It has benefits for between two-thirds and three-quarters of patients. The benefits include rapid improvements in the numbers of swollen joints, the degree of swelling, the pain associated with the joints and tiredness. One of the reasons tocilizumab improves fatigue is that it improves the anaemia associated with active rheumatoid arthritis.

HOW DO YOU TAKE TOCILIZUMAB?
Tocilizumab is given by intravenous drip once every four weeks, in hospital. You don’t keep the drug at home. The dose is usually 8mg for every kilogram of body weight but in some circumstances the dose can be reduced. It takes about an hour to give the drip treatment.

HOW DO I GET TOCILIZUMAB?
Following a rapid review of Technology Appraisal 198 (TA 198) in February 2012 NICE recommended tocilizumab as an option for treating rheumatoid arthritis at the same point in the treatment pathway as the anti-TNF therapies. The eligibility criteria used are as shown at the top of page 13. In brief this is where the disease has responded inadequately to DMARDs and that tocilizumab is used as described for the anti-TNF treatments (in NICE guidance TA 130). The guidance also includes using tocilizumab, as originally recommended in TA 198, for people whose disease responded inadequately after both rituximab and anti-TNF therapies were tried and, a recommendation on tocilizumab when rituximab cannot be used after anti-TNF treatment has failed. In all cases this is on the basis that the manufacturer provides tocilizumab with the discount agreed as part of the patient access scheme.

Following final guidance from NICE, children and young people with systemic juvenile idiopathic arthritis (JIA) can now be prescribed the drug tocilizumab (RoActemra) subject to certain conditions i.e. available to children and young people aged 2 years and older who have not had an adequate response to previous treatments.

There is more about NICE on page 30
CAN I TAKE TOCILIZUMAB IF I AM TAKING OTHER MEDICINES FOR MY RA OR ANY OTHER CONDITION?

Yes. You can take tocilizumab if you’re also taking anti-inflammatory drugs, non-biologic DMARD drugs such as methotrexate, sulfasalazine, leflunomide or hydroxychloroquine, whether singly or in combination. Tocilizumab also works very well on its own without the need to take another non-biologic DMARD, such as methotrexate with it. It can also be taken if you are taking drugs for other non-rheumatic conditions but you need to discuss the details of all your medication with your rheumatologist. You cannot have tocilizumab if you are receiving other biologic drugs.

ARE THERE ANY CONTRAINDICATIONS?

There are few absolute contraindications. Women should not become pregnant on tocilizumab. If you have recurrent infections or a serious infection then tocilizumab may not be appropriate as it might reduce your body’s ability to fight infection. Always discuss your individual circumstances with your specialist.

WHAT ARE THE RISKS OR SIDE EFFECTS?

Overall, tocilizumab is well tolerated.

Infusion reactions can occur, but they are uncommon. Tocilizumab’s overall safety profile is consistent in all studies. The most common adverse reactions (in about 5% of patients, taking tocilizumab alone or in combination with DMARDs) are: upper respiratory tract infection, nasopharyngitis (common cold), headache, hypertension (high blood pressure) and increased alanine transaminase (ALT) (minor liver abnormalities). A minority of patients are also found to have significant changes in blood cholesterol and other lipids. Your doctor will arrange for intermittent blood tests to check on this. However, as with all RA therapies, a small proportion of more serious side effects have been seen. Your rheumatologist will discuss the details with you.

WHAT MONITORING WILL I HAVE?

Regular blood tests are recommended to monitor liver function, blood cholesterol as well as blood counts, usually every four to eight weeks. The frequency may be reduced after six months but this depends on other drugs you are taking, as other DMARD drugs such as methotrexate, sulfasalazine or leflunomide also need blood monitoring. Blood pressure must be checked regularly.

IN WHAT CIRCUMSTANCES WOULD I HAVE TO STOP TREATMENT?

You’d need to stop taking it if there were a serious side effect considered to be due to the biologic (such as an allergic reaction), if it was not effective, or if you were intolerant to the drug.

Biologics should not be administered around the time of surgery. You should let your rheumatologist know if you are having surgery or invasive dental procedures, so that your treatment can be adjusted accordingly.
4. Biologic drugs available in the UK (cont.)

**CAN I TAKE ANOTHER TYPE OF BIOLOGIC THERAPY WHILE I’M ON TOCILIZUMAB?**

Much more research is needed to know whether it would be beneficial or safe to take more than one biologic at a time. It’s not currently recommended.

**HOW LONG CAN I STAY ON THIS TREATMENT?**

This is a new treatment and the longest time that patients have taken tocilizumab is a few years, if they have been involved in clinical trials. If the treatment is working well, there are no side effects, and there is funding available, you can expect to stay on the treatment for several years.

**CAN I GET PREGNANT OR BREASTFEED WHILE I’M TAKING TOCILIZUMAB?**

If you are on any biologic therapy and decide to plan a family, you should discuss it with your rheumatologist. It is not advised to become pregnant on tocilizumab. It is made from a type of antibody that may pass from the blood into breast milk. It is not known whether tocilizumab is excreted in human breast milk as there is very little information about this. If you have had a baby and your arthritis is flaring up, the best thing to do is to see your rheumatologist or nurse specialist to discuss the best way of controlling your arthritis so that it will have no harmful effect on your baby. There is no known problem regarding the use of currently available biologic therapy and fathering children. It is not necessary to discontinue biologic therapy in those male patients who wish to start or to enlarge a family. However, concomitant methotrexate, which is recommended with several, but not all biologics, does need to be stopped for 12 weeks prior to an attempted conception and appropriate contraception applied prior to being off methotrexate for that time. Sulfasalazine can cause a reversible reduction in sperm counts and motility.

**CAN I HAVE IMMUNISATIONS?**

You should not have live vaccines such as yellow fever or live polio. But you may be able to have other vaccinations. Discuss each case with your GP and rheumatology specialist.

**CAN I DRINK ALCOHOL?**

If your liver tests are satisfactory, you can drink alcohol in moderation. However, tocilizumab and other drugs often taken with it such as methotrexate can cause abnormalities in liver tests. If you have abnormal liver function tests your specialist may recommend that you do not drink alcohol, either temporarily, or in rare cases, permanently.

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**Rituximab**

*By David Isenberg, MD, FRCP, FAMS, Professor of Rheumatology, University College London.*

The biologic therapy rituximab (brand name Mabthera, manufactured by Roche Products Ltd) targets a molecule called CD20, found on a set of white blood cells known as lymphocytes. Lymphocytes develop into antibody-producing cells. It’s often known as a ‘B-cell depletion therapy’.
WHAT IS CD20?
CD20 is a molecule present on many, but not all, lymphocytes (a type of white blood cell) known as B lymphocytes or simply B-cells. It is not however present on the plasma cells which produce antibodies.

WHAT IS THE BENEFIT OF TAKING RITUXIMAB AND HOW WILL IT AFFECT MY SYMPTOMS?
Approximately two thirds of patients with RA experience significant improvement in their joint pain, joint swelling and sense of fatigue. The benefits often become apparent within a few weeks of taking the drug, though sometimes this takes longer. Curiously some people who do not respond to the drug first time, do then get a benefit on the second occasion. But it is far less likely to work if the person with RA does not have rheumatoid factor or anti-CCP antibodies in their blood (that is, if they are ‘sero-negative’).

HOW DO YOU TAKE RITUXIMAB?
It is usually given as an intravenous infusion (one gram) on two occasions two weeks apart although some centres give smaller weekly injections for four weeks. It is infused in hospital under medical or nursing supervision.

It is prescribed with methotrexate, and this combination produces a depletion (absence) of the B-cells that have CD20 present (called ‘CD20+ B-cells’), for approximately six months. Symptoms may be absent for longer than that. Further doses of rituximab are usually given every six to 12 months, if clinically necessary.

HOW DO I GET RITUXIMAB?
Rituximab has to be prescribed by a rheumatology unit. It can only be prescribed for you if your RA has not responded to a first anti-TNF drug.

CAN I TAKE RITUXIMAB IF I’M TAKING OTHER MEDICATIONS FOR MY RA OR OTHER CONDITIONS?
Yes. Most patients, though not all, are prescribed methotrexate (not if you’re intolerant to it) together with rituximab as the two drugs together appear to work better when used in this way. You can also take other drugs for your RA, for example, steroids, non-steroidal anti-inflammatory drugs such as aspirin or prescription pain relievers, and other disease-modifying anti-rheumatic drugs.

Make sure you tell your doctor about any other medicines you are taking for other conditions (for example, high blood pressure medicine) before you start taking rituximab. You should also tell your doctor about any over-the-counter drugs, herbal medicines and vitamin and mineral supplements you are taking.

ARE THERE ANY CONTRAINDICATIONS?
Rituximab is an antibody that contains a small amount of synthetically produced mouse protein (it does not come from an actual mouse!). A small number of people with RA (probably less than 5%) may develop a reaction to the mouse component that is left in the antibody structure. Occasionally, allergic reactions occur, and as a result, occasionally the removal of the ‘CD20+ B-cells’ may be inadequate. This drug is not recommended for pregnant women.
WHAT ARE THE RISKS OR SIDE EFFECTS?
Most people experience no side effects.

A small number of patients have a marked reduction in their immunoglobulin levels, and there is then a concern about infection, as there is for conventional DMARDs (Disease Modifying Anti-Rheumatic Drugs). Rituximab has a consistent safety profile over several courses of treatment. The most frequent side effects are infusion reactions (up to one third) such as hypertension (high blood pressure), nausea and upper respiratory tract infections. Giving some intra-venous steroids at the same time as the rituximab will reduce the frequency and severity of any side effects. Fewer reactions are observed with the second infusion. However, as with all RA therapies, a small proportion of more serious side effects have been seen for example a skin rash and swelling of the lips. Your rheumatologist will discuss the details with you.

WHAT MONITORING WILL I HAVE?
You will have follow-up blood monitoring every one to two months. Most people treated with rituximab also take traditional DMARDs (usually methotrexate) and therefore have regular monitoring of their blood count, kidney and liver function and inflammatory markers.

If you are not taking methotrexate with your rituximab and therefore not having methotrexate monitoring, you should expect to be routinely monitored in clinic every three months or so, though the exact timing may vary.

IN WHAT CIRCUMSTANCES WOULD I HAVE TO STOP TREATMENT?
If you develop an obvious allergic reaction to the drug or if previous doses have led to very low immunoglobulin levels, you are advised not to continue taking it.

Biologics should not be administered around the time of surgery. You would probably need to wait around 12 weeks after an infusion before having surgery. Let your rheumatologist know if you are going to have surgery or invasive dental procedures, so that your treatment can be adjusted accordingly.

CAN I TAKE ANOTHER TYPE OF BIOLOGIC THERAPY WHILE I’M ON RITUXIMAB?
Much more research is needed to know whether it would be beneficial or safe to take more than one biologic at a time. It is not currently recommended.

HOW LONG CAN I STAY ON THIS TREATMENT?
There is no clear cut answer to this question, but the Centre for Rheumatology at University College Hospital London has treated patients annually for up to seven years as of January 2012.

CAN I GET PREGNANT OR BREASTFEED WHILE I’M TAKING RITUXIMAB?
If you’re pregnant or planning to become pregnant you would not be given this therapy. If you have had a baby and your arthritis is flaring up, the best thing to do is to see your rheumatologist or nurse specialist to discuss the best way of controlling your rheumatoid arthritis so that it will have no harmful effect on your baby.
If you’re a woman of childbearing age, you should use contraception during treatment and for 12 months following rituximab therapy. You should not breastfeed while you’re being treated and for 12 months following rituximab treatment. There is no known problem regarding the use of currently available biologic therapy and fathering children. It is not necessary to discontinue biologic therapy in those male patients who wish to start or to enlarge a family. However, concomitant methotrexate, which is recommended with several, but not all biologics, does need to be stopped for 12 weeks prior to an attempted conception and appropriate contraception applied prior to being off methotrexate for that time. Sulfasalazine can cause a reversible reduction in sperm counts and motility.

**CAN I HAVE IMMUNISATIONS?**

Before you start rituximab, your vaccination status should be assessed and you should complete any required vaccinations first. The use of live vaccines has not been studied and is not recommended if you’re receiving rituximab.

**CAN I DRINK ALCOHOL?**

Yes, but obviously in moderation.

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**Abatacept**

*By Dr Andrew J K Östör, Consultant Rheumatologist and Associate Lecturer, School of Clinical Medicine, University of Cambridge, and Director, Rheumatology Clinical Research Unit.*

Abatacept (brand name Orencia, manufactured by Bristol-Myers Squibb) is effective and safe for a significant proportion of people with RA, and is an option for those who have responded insufficiently to methotrexate and/or anti-TNF treatment. Abatacept is an antibody that blocks the activation of T-cells, which are involved in the inflammation occurring in RA.

Two events prompt T-cells to work. First a receptor on a T-cell recognises ‘self’ (see page 6 for an explanation of self and non-self), presented to it by specialized ‘antigen presenting cells’. But nothing happens until the T-cell receives a second message (co-stimulation) from the antigen presenting cell. After this, the activated T-cell promotes inflammation, leading to the damage which occurs in RA. Abatacept blocks this second message and so halts the development of inflammation at a very early stage.

**WHAT IS THE BENEFIT OF TAKING ABATACEPT AND HOW WILL IT AFFECT MY SYMPTOMS?**

Multiple studies have shown the benefit of abatacept for people with RA. It has improved joint pain and swelling, improved quality of life, reduced fatigue, and reduced bone and joint damage seen by X-rays.

One study followed patients who were not doing well on methotrexate for one year, and nearly three quarters of patients who received abatacept gained some benefit (40% in the placebo group also obtained benefit). Another study found that around 50% of patients had a significant benefit with abatacept following unsuccessful treatment with anti-TNF agents.
These and other studies have also shown longer-term improvements, with some people staying on the treatment for more than nine years. For many patients, the benefit increased the longer they were on abatacept.

**HOW DO YOU TAKE ABATACEPT?**

Abatacept is given as an intravenous infusion, in hospital, of 500mg, 750mg or 1000mg (depending on your weight) over 30 to 60 minutes. After the first dose it is given two weeks later, then two weeks after that, then monthly thereafter.

**HOW DO I GET ABATACEPT?**

NICE has now approved the use of abatacept for RA by the NHS. They have determined that abatacept may be used in those patients who have failed anti-TNF therapy and are unable to receive rituximab or have failed rituximab due to a side-effect/poor tolerability (TA195). In addition patients must be continuing to take methotrexate in order to receive abatacept by NICE criteria.

(Jan 2013 - Abatacept is currently subject to a NICE rapid review and guidance is expected in April 2013 to determine its use as a first line biologic treatment).

There is more about NICE and its approval process on page 30.

**CAN I TAKE ABATACEPT IF I AM TAKING OTHER MEDICINES FOR MY RA OR ANY OTHER CONDITION?**

Abatacept may be given on its own but normally it is added to other medications for RA including methotrexate, sulfasalazine, hydroxychloroquine and/or leflunomide. You cannot take it with another biologic agent as this increases the risk of infection. It may be given with medications for other conditions, and your specialist can advise you regarding this.

**ARE THERE ANY CONTRAINDICATIONS?**

You cannot have abatacept if you have an active infection, if you have cancer, if you may be pregnant or are breast feeding. It should not be given to anyone who has had a serious adverse event whilst taking abatacept before, such as a severe infection or allergic reaction. It must not be given to anyone taking another biologic agent. It should be used with caution for patients who have significant respiratory disease, such as bronchiectasis or Chronic Obstructive Pulmonary Disease – as always, your rheumatologist will advise you regarding your particular circumstances.

**WHAT ARE THE RISKS OR SIDE EFFECTS?**

Overall abatacept is safe and well-tolerated. Most people experience no side effects. Common side effects (for up to 13% of people taking abatacept) include headache, upper respiratory tract infections and nausea. In all studies, serious infections such as pneumonia, bronchitis and urinary tract infections occurred in 3% of patients on abatacept, compared with 1.9% of those on placebo (those in the comparison group who were not receiving active treatment).

We have not seen an increase in infections or cancers following prolonged abatacept treatment.

**WHAT MONITORING WILL I HAVE?**

You are screened before starting treatment to make sure you do not have TB.
No specific monitoring tests are required. Most people treated with abatacept however will also be receiving traditional DMARDs (usually methotrexate) and therefore will have regular monitoring of their blood count, kidney and liver function and inflammatory markers.

IN WHAT CIRCUMSTANCES WOULD I HAVE TO STOP TREATMENT?
You’d have to stop taking it if you developed a serious infection such as pneumonia, any of the serious problems mentioned above, or if you had a significant allergic reaction.

Biologics should not be administered around the time of surgery. You should let your rheumatologist know if you are having surgery or invasive dental procedures, so that your treatment can be adjusted accordingly.

CAN I TAKE ANOTHER TYPE OF BIOLOGIC THERAPY WHILE I’M ON ABATACEPT?
Combining biologic drugs is not recommended, as studies have shown that it increases the risk of infection without giving an additional improvement in symptoms. This has been seen when abatacept was combined with anti-TNF treatment.

HOW LONG CAN I STAY ON THIS TREATMENT?
If you respond well and have no significant side effects, you can stay on the treatment indefinitely. Some patients have been on abatacept for over nine years and are still doing well.

CAN I GET PREGNANT OR BREASTFEED WHILE I’M TAKING ABATACEPT?
Abatacept is not recommended for women who want to conceive or who are breastfeeding.

There are no adequate and well-controlled studies of abatacept’s use in pregnant women. As many drugs are excreted in human milk, you should not breastfeed while taking abatacept. Talk to your doctor if you are pregnant or planning a pregnancy. There is no known problem regarding the use of currently available biologic therapy and fathering children. It is not necessary to discontinue biologic therapy in those male patients who wish to start or to enlarge a family. However, concomitant methotrexate, which is recommended with several, but not all biologics, does need to be stopped for 12 weeks prior to an attempted conception and appropriate contraception applied prior to being off methotrexate for that time. Sulfasalazine can cause a reversible reduction in sperm counts and motility.

CAN I HAVE IMMUNISATIONS?
You can have normal vaccinations including flu vaccine, pneumovax and swine flu, but not live vaccines such as yellow fever and oral polio.

CAN I DRINK ALCOHOL?
There’s no specific contraindication, but if you’re also taking a DMARD such as methotrexate or leflunomide you should only drink alcohol in moderation. If a change in liver function tests develops then you may need to reduce the amount you drink or even stop completely – discuss this with your doctor.
5. The sequence of therapy

By Peter C. Taylor MA, PhD, Norman Collisson Professor of Musculoskeletal Sciences, Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, UK.

There are many therapies available, so which is recommended first? Current guidelines set out a recommended order in which biologics should be prescribed for particular patients, based on our knowledge about effectiveness and about cost.

NICE and rheumatology organisations in the UK and Europe recommend that people with rheumatoid arthritis should first be treated with conventional DMARDs, one of which is usually methotrexate, and that the dose should be carefully adjusted to achieve as much improvement as possible as quickly as possible. If this is not successful after six months, and you have high disease activity you may be eligible for a first-line biologic drug (this includes all of the anti-TNF drugs and tocilizumab) on the NHS. There are more details about the eligibility criteria on page 27.

CAN I START BIOLOGIC TREATMENT WITH ANY OF THE DRUGS AVAILABLE?

When doctors prescribe drugs they try to get the maximum benefit for you and also minimize any possibility of side effects. Anti-TNFs were the first type of biologic drug to be launched, and after over a decade of use, their overall safety record is very good. So if a biologic therapy is appropriate, it is usual to start treatment with an anti-TNF or, following more recent NICE guidance, tocilizumab. (See pages 15 -17 for more information on tocilizumab)

HOW DO I MAKE AN INFORMED DECISION ABOUT WHICH DRUG TO HAVE?

The choice of a first-line biologic needs to be made carefully, with your specialist. It will be influenced by whether an intravenous or subcutaneous drug is most appropriate, which of these you prefer, and whether certain differences in side effects and benefits might best suit your particular situation.

If you could be at a high risk of a particular side effect, one drug may be recommended over another. For example, if you have had TB in the past, a rare but potentially serious side effect is the reactivation of TB. In this case, you may need to have anti-TB treatment before you start a first-line biologic, though etanercept has a lower risk of reactivation of TB than the other agents.

If there is an equal chance that any one of the available drugs will suit you, you may be able to make the final choice. Your decision may depend on what you feel about the different drug delivery devices such as auto-injectors, traditional syringes or specially adapted syringes. Make sure you discuss the choice and get advice from your doctor and nurse specialist.

WHAT HAPPENS IF MY FIRST BIOLOGIC DRUG DOESN’T HELP? CAN I HAVE ANOTHER?

If you have a side effect or do not respond to your first biologic drug (normally one of the anti-TNFs or tocilizumab at present), there are several possible alternative options for licensed therapies although there are guidelines set by NICE that in effect restrict which drugs might be made available. The guidelines themselves have been changed several times in recent years as new information about biologic treatments and their cost has emerged. The options available under these guidelines depend on the individual patient’s circumstance. If an alternative biologic choice recommended in a particular circumstance meets the most recent guidelines from NICE, the Primary Care Trust concerned will normally provide funding for this once the rheumatologist provides documentary evidence.
that the conditions of the guidelines are fulfilled. However, where those conditions are not fulfilled, funding is unlikely to be made available unless it can be successfully argued that there are some exceptional circumstances.

If the first anti-TNF was infliximab, which is given intravenously, the total dose given per year can be increased, either by increasing the frequency of the drip to every six weeks (instead of every eight weeks) or by increasing the amount of the drug in each drip.

The following are options permitted by NICE guidelines after “failure” of a first-line biologic:

1. To switch to an alternative first-line biologic. European guidelines currently recommend trying a second anti-TNF or a biologic treatment with an alternative mechanism of action if the first-line biologic is unsuccessful.

   However, NICE only approve use of first-line biologic switching on the NHS in the event of the following circumstances:

   a) intolerance to the first-line biologic within the first 6 months

   b) if there has been very little or no benefit from the first-line biologic and the patient is intolerant of methotrexate. In such a case etanercept, adalimumab or tocilizumab could be used on their own without the need for concomitant methotrexate.

   c) if there has been very little or no benefit from the first-line biologic but the patient is able to take methotrexate but should not for any reason receive a biologic drug that works in a different way, called rituximab.

2. To use a biologic drug that works in a different way, called rituximab. See page 18. This option is approved by NICE for use on the NHS.

3. If rituximab is not tolerated, NICE guidelines allow switching to an alternative intravenous biologic treatment called abatacept or alternatively, to try a different first-line biologic not previously failed for any reason such as lack of benefit or side effects. In the case of both tocilizumab and abatacept, new subcutaneous (injectable under the skin) formulations of each drug are being tested. A self-injected version of abatacept will become available early in 2013. Abatacept works in a very different way but clinical trials have shown that very similar proportions of patients having failed on a previous first-line biologic benefit after six months of treatment.

NB: If a drug has not yet been passed by NICE or the SMC for use in the NHS, until NICE/SMC makes its guidance final, you should be able to get it. But in practice, the financial constraints in the NHS make it very difficult to get a treatment funded by Primary Care Trusts and Health Boards, until it has been approved.

WILL THERE BE ANY OTHER OPTIONS?

As more information becomes available about the newer drugs, as pricing structures change and as research advances, the situation described above will continue to evolve. We continue to gain knowledge about drugs, first from carefully conducted clinical trials and then from experience in everyday clinical use once the drugs become available. Information from clinical trials, from clinical experience and registry data (see page 33 for info about the UK Biologics Register) is reviewed by clinicians and organisations within the medical profession, and the findings help to inform current thinking about the best sequence of treatment. Remember that you can ask your rheumatologist and nurse any questions, and work with them to try and get the most suitable medication for you.
Questions? Concerns? Ask your Specialist Nurse – this section explains their role.

In most UK rheumatology units, Rheumatology Specialist Nurses (or Practitioners) are involved in the care of people who are receiving biologic treatments. Their jobs vary: some are ‘Biologics Nurses’ and this is their sole responsibility, while for others this work is just one part of their specialist role. The Specialist Nurse is there to support you through what can seem a long and complex process: from the time biologic treatment is first mentioned, through screening, to starting on the treatment and continuing with it. He or she can provide information about the treatment options that have been suggested to you, and discuss any questions or anxieties you may have, so that you can make an informed choice.

The Specialist Nurse is likely to be involved in the initial assessment process, working in partnership with the medical team to complete your assessment or screening, in line with the eligibility requirements such as measuring your Disease Activity Score (DAS 28). In some units the nurse also coordinates the application for treatment funding.

If your treatment involves injections, the Specialist Nurse can teach you how to administer them so that you are confident doing them yourself at home. Or you may be taught at home by a nurse from the company that supplies you with your injections. Intravenous treatments are usually organised by the Rheumatology Specialist Nurse, and you’re given these in a day care unit or hospital ward, either by the Specialist Nurse or a nurse from the day care team.

Specialist Nurses are also involved in your ongoing care and monitoring, including measuring your DAS at regular intervals so as to assess your response to the treatment.

In most departments the Specialist Nurse runs a telephone advice line. This is important, so that you have a first point of contact in the department for any problems or questions that come up. He or she will also give you a Biologic Alert Card which you should carry at all times and show to any other person you consult about your health.

There is more information about the DAS 28 on page 27. You can also ask NRAS for a booklet, Know your DAS and watch a DVD clip about DAS at www.nras.org.uk
Are you eligible?  Read this section to find out more.  It covers what the criteria are, how long you may need to wait – and why many rheumatologists and NRAS think this needs to change.

In February 2009 NICE published Rheumatoid arthritis: the management of rheumatoid arthritis in adults, Clinical Guideline CG79. The Guideline, and a summary for patients, are both available at www.nice.org.uk. In February 2012 NICE carried out a rapid review (TA 247) of its guidance on the use of tocilizumab. The guidance and summary for patients on tocilizumab are also available at www.nice.org.uk.

The NICE RA Guideline states that to be eligible for biologic drugs, patients with RA should have:

- **High levels of persistent disease activity**

  This is measured by a scale known as the Disease Activity Score in 28 joints (DAS 28 for short) on two separate occasions, a month apart. This is a clinical score that combines: the number of swollen joints and tender joints; the patient’s own rating of their health on a scale from best imaginable state to worst; and a blood test measure of inflammation, usually the erythrocyte sedimentation rate (ESR) but it may also be the C-Reactive Protein (CRP). These measures are amalgamated in a complex calculation to produce a score of disease activity. NICE states that for a patient to be eligible for a first-line biologic (an anti-TNF or tocilizumab) their score should be over 5.1 at both assessments. This represents high levels of disease activity.

  There is more information about DAS 28 on page 27. You can also ask NRAS for a booklet, Know your Disease Activity Score (DAS) and watch a DVD clip about DAS at www.nras.org.uk

A recent study has suggested that the month between assessments before starting a first-line biologic is an unnecessary delay, because patients who fulfilled the criteria one month before commencing treatment had a 97.2% chance of doing the same at the first assessment. The overwhelming majority of patients therefore have an unnecessary wait with very active disease.

- **Failed on two disease modifying anti-rheumatic drugs (DMARDs), one of which must be methotrexate, unless it is contraindicated for some reason.**

Conventional disease modifying drugs like methotrexate can work well for many people, particularly if they are used early and intensively in the course of the disease. Although there is evidence to support the benefits of first-line biologics in early RA before other drugs have been tried, a recent study suggested patients can do just as well on conventional combination therapies.
Some patients may have disease that does not respond to drugs like methotrexate, and they may benefit from early access to biologic drugs, but at present it just isn’t feasible to identify them in advance.

Much more work is needed on how to identify patients who are likely to have poor outcomes without early use of biologics. At present the cost of these drugs makes the widespread early introduction of biologics unfeasible, especially as other, much cheaper drugs can work well for many patients.

**HOW QUICKLY CAN I GET BIOLOGICS IF I FAIL ON STANDARD TREATMENT?**

The NICE RA Guideline specifies that conventional drugs like methotrexate should be tried for six months, unless toxicity limits the treatment. If single drugs are used in sequence and you tolerate them, this would mean a minimum wait of one year before you can have a first-line biologic drug.

However, the NICE RA Guideline states that in early active RA, combinations of conventional disease modifying drugs should be used – that is, more than one drug at the same time – along with steroids in some form. NICE anti-TNF Technology Appraisal TA130, does not say whether patients should try DMARDs as single drugs or combinations, but it is consistent with the NICE RA Guidelines to use them simultaneously, called ‘combination’ therapy. Many rheumatologists therefore interpret this to mean that if a patient has failed on two conventional DMARDS given at the same time, this shortens the wait to six months. This will be even shorter if patients are unable to tolerate the drugs.

The NICE RA Guideline places great emphasis on monitoring patients closely for disease activity, with monthly follow-up in the early stages, and on action to suppress disease activity whenever it is not adequately controlled. This is based on the well-established principle that uncontrolled inflammation leads to damage in the joints, and this translates into disability. The severity and duration of inflammation are the main drivers of damage and disability. Therefore this suggests that patients who do not respond to appropriate use of conventional DMARDs should have access to biological therapies as soon as possible. The Guideline also states that if patients are having difficulties in decreasing or stopping steroids, then biological therapies should be considered. Long-term steroids should be a treatment of last resort in patients who do not respond to other therapies, as the advantages of steroids can be outweighed by the disadvantages.

**CAN I STAY ON BIOLOGIC THERAPY IN THE LONG TERM?**

To stay on biologic drugs, patients need to have a drop in their disease activity score (DAS 28) of 1.2, and maintain this lower score in assessments every six months thereafter.

It has been argued that this is an inappropriately large drop, and is not based on how the DAS 28 was originally designed to be used. If you start at a lower baseline score, you may get a smaller drop in DAS 28 than 1.2, but still feel a lot better on a first-line biologic. For many patients, a drop of 0.6 can constitute a
significant improvement, and the British Society for Rheumatology (BSR) argues that the response criteria should be changed and NRAS supports this view.

If you get side effects on a first-line biologic in the first six months, the Guideline allows you to transfer to an alternative first-line biologic. It is not usual for people to get side effects after their first six months, but it can happen in clinical practice.

People who fail to show a response to a first-line biologic at six months are not currently allowed access to a second one, under current NICE and SMC guidance. This is in spite of a great deal of evidence showing that a second first-line biologic can work well after the first has failed. This is particularly the case if someone has an initial response to the first anti-TNF that then seems to diminish. A second first-line biologic may be less likely to work if a patient shows no response at all to the first one.

If a first first-line biologic fails, the only other biological drug available for NHS patients, according to NICE guidelines, is rituximab (and in Scotland, additionally,tocilizumab). Rituximab can work well, and patients who respond may not need further intravenous infusions for many months. However, there are also concerns. First, patients who are sero-negative for rheumatoid factor and anti-CCP may be less likely to respond – that is, those who have RA but do not have certain ‘autoantibodies’ in their blood.

**SHOULD THE GUIDANCE BE CHANGED?**

We need much more data on the best and most cost-effective approaches for patients who do not do well on their first first-line biologic. Many patients and rheumatology professionals find the current guidelines frustratingly restrictive, particularly for patients with the most aggressive and therapy-resistant disease.

The BSR has produced evidence that the current eligibility criteria for a first-line biologic are set too high. It argues that the criteria deny access to a first-line biologic for patients with less active disease, who would do just as well on a first-line biologic treatment as those with more active disease.

The health economic models that NICE and the SMC use are complicated, and access to treatment is decided by disease activity levels. The cost-effectiveness (value for money) of treatment is determined by the functional benefits that patients experience when they are on the drug. The BSR has summarised evidence from a number of studies. It shows that patients with moderate disease activity (DAS 28 of more than 3.2 and less than 5.1) have just as good a functional improvement as patients with more active disease (DAS 28 of more than 5.1). The BSR also analysed data from the Biologics Register, with a similar result. In other words, patients with less active disease can get just as good and cost-effective a benefit from a first-line biologic as patients with severely active disease. The BSR and others, including NRAS, will continue to make the case to NICE for reducing the required DAS 28 score from 5.1.

See also page 24 which discusses the sequence of therapies.
Many new and often expensive treatments are now being licensed for use in the UK, and the government long ago accepted that the NHS cannot afford to make all new treatments available to everyone. In 1999 it created the independent National Institute for Clinical Excellence (NICE), and passed legislation that required the clinical effectiveness and cost effectiveness of all new medicines be evaluated by NICE. NICE expanded its remit in 2005 to include public health guidance and became the National Institute for Health and Clinical Excellence (still known as NICE). When responsibility for healthcare was devolved to the Scottish Parliament, a similar process was set up for Scotland and the Scottish Medicines Consortium (SMC) was formed in 2001.

8. NHS funding for biologics: the approval process

NICE is responsible for providing national guidance on promoting good health and on preventing and treating ill health. It produces guidance in three areas:

- **public health** - guidance on the promotion of good health and the prevention of ill health for those working in the NHS, local authorities and the wider public, private and voluntary sector.

- **health technologies** - guidance on the use of new and existing medicines, treatments and procedures within the NHS. In this area it publishes Technology Appraisals (recommendations on the use of medicines and treatments) and Interventional Procedures (procedures used for diagnosis or treatment, for example surgical procedures).

- **clinical practice** - guidance on the appropriate treatment and care of people with specific diseases and conditions within the NHS. In this area it publishes Clinical Guidelines and Quality Standards (recommendations on appropriate treatment and care).

NICE guidance is developed using the expertise of the NHS and the wider healthcare community including NHS staff, healthcare professionals, patients and carers, industry and the academic world. This guidance determines what the NHS will fund, and it sets out the standards of care that patients can expect.

Assessment of new biologic drugs by NICE comes under the heading of Technology Appraisals.
The table below sets out where the different types of NICE guidance apply in the UK.

<table>
<thead>
<tr>
<th>guidance applies in:</th>
<th>England</th>
<th>Wales</th>
<th>Scotland</th>
<th>Northern Ireland</th>
</tr>
</thead>
<tbody>
<tr>
<td>clinical guidelines</td>
<td>y</td>
<td>y</td>
<td></td>
<td>y* (after general review)</td>
</tr>
<tr>
<td>technology appraisals</td>
<td>y</td>
<td>y</td>
<td></td>
<td>y** (after local review)</td>
</tr>
<tr>
<td>interventional procedures</td>
<td>y</td>
<td>y</td>
<td>y</td>
<td>y</td>
</tr>
<tr>
<td>public health guidance</td>
<td>y</td>
<td>no formal status but a useful source of reviewed evidence</td>
<td>disseminated after local review by NHS Healthcare Improvement Scotland</td>
<td>y* (after local review)</td>
</tr>
</tbody>
</table>

* with advice on implementing in the context of the health service in Northern Ireland from the Department of Health, Social Services and Public Safety
** only multiple technology appraisals, with advice on implementing in the context of the health service in Scotland from NHS Healthcare Improvement Scotland

THE SCOTTISH MEDICINES CONSORTIUM (SMC)

The Scottish Medicines Consortium (SMC) performs a similar role to NICE in Scotland for drug appraisals. It provides advice to NHS Boards and their Area Drug and Therapeutic Committees (ADTCs) across Scotland about the status of all newly licensed medicines, all new formulations of existing medicines and new indications for established products (licensed from January 2002). It makes advice available as soon as practical after the launch of the product involved. It also carries out ‘horizon scanning’: it aims to improve financial and service planning within NHS Boards by providing them with early intelligence about new medicines in development. Unlike the NICE process SMC does not publicly consult on its draft advice. However it does provide opportunities to involve relevant patient interest groups and clinical experts in the decision making process. In relation to implementation, NHS Scotland boards and directors are expected to take account of SMC advice when deciding which medicines should be prescribed, but it is not mandatory.

NB: NICE Multiple Technology Appraisals –where more than one drug is being considered - are reviewed by NHS Healthcare Improvement Scotland and, if deemed appropriate, are applied to Scotland where they replace the published SMC advice. However, where only one drug is being evaluated – Single Technology Appraisals – these go through the SMC who conduct their own evaluations.

APPROVALS AND FUNDING

When NICE passes a drug for use, NHS organisations in England and Wales are expected to fund and resource them, usually within 3 months of the guidance being issued. In Northern Ireland (NI), the Department of Health, Social Services and Public Safety (DHSSPS) will conduct a local review to assess the applicability of NICE Technology Appraisals and NICE Clinical Guidelines, in terms of the NI legal and policy context. The local review of NICE Technology Appraisals is normally completed within four weeks of the final NICE decision, whereas the majority of NICE Clinical Guidelines are expected to be reviewed within 8 weeks of publication by NICE.
If endorsed or partially endorsed with caveats, the DHSSPS will issue the guidance to the local commissioners, the Health and Social Care (HSC) Board, requesting that they prepare a Commissioning Plan in respect of Technology Appraisals or a Board Response in respect of Clinical Guidelines. In both of these cases, the HSC Board is expected to return a Commissioning Plan to the DHSSPS within 15 weeks of notification of endorsement of the guidance. The DHSSPS will either approve the Commissioning Plans and Board Responses or refer them back to the HSC Board for further consideration. However, the DHSSPS does provide opportunities to involve relevant patient interest groups and clinical experts in the decision making process and forwards comments to NICE.

WHAT HAPPENS IF NICE OR THE SMC DO NOT APPROVE A DRUG?

NICE or SMC may decline to approve a drug for use on the NHS, on the grounds either that it is not clinically effective (it doesn’t work well enough) or not cost effective (it’s not good value for money).

All the biologic drugs licensed for use in the UK in rheumatoid arthritis have been shown to be clinically effective, through clinical trials. However NICE or SMC has rejected some biologic drugs on the grounds that they are not cost effective; in other words, the drug is not considered to be good value for money for the NHS.

When a drug is not approved for use in the NHS, either by NICE or the SMC, the PCTs* and Health Boards (Wales, Scotland and Northern Ireland) are not obliged to fund it. Consultants cannot therefore routinely prescribe it. However, consultants can apply for an individual prescription to be funded on what is called a ‘named patient basis’. These individual funding requests are considered by the Priorities Committee of the local PCT* or Health Board. If they refuse funding, which they have the right to do, your consultant then has a limited time within which to appeal – talk to your consultant for more information.

WHAT CAN I DO IF MY HEALTH AUTHORITY WON’T FUND THE TREATMENT?

Your local PCT* or Health Board is legally required to fund your treatment if the drug has been approved for use in the NHS by NICE or the SMC, if you have been correctly assessed in accordance with the guidance and you meet the required eligibility criteria. If it will not fund treatment in these circumstances, you and your healthcare team can involve NRAS and your local politician, write to the PCT* or Health Board and challenge the decision very robustly.

If it still refuses to fund, then there is the option to take your PCT* or Health Board to a Judicial Review: that is, take them to court to try and overturn their decision. NRAS does not know of anyone who has done this, so you would need further investigation and legal advice. However, in a climate of funding cuts, as more people are likely to have funding requests turned down, we may see people taking up this option.

It may be that the drug your rheumatologist is recommending has not been through a NICE or SMC approval process. While this is not itself a reason for health authorities not to fund it, in practice they often do refuse funding under these circumstances. Your only option is to ask your healthcare team to apply for an individual prescription to be funded on a ‘named patient basis’.

*at the time of writing the UK Government is proposing to abolish PCTs and replace them with local Clinical Commissioning Groups, who will take over responsibility for funding biologics from April 2013.
9. Monitoring the safety of biologic drugs

By Professor David G.I. Scott, MD, FRCP, Norfolk & Norwich University Hospital NHS Trust, and NRAS Chief Medical Advisor.

A national database is keeping track of how people are responding to different biologic drugs. This section explains how it’s providing vital information about their safety in the long term – and the results so far are encouraging.

The British Society for Rheumatology (BSR) represents people in the UK (and some abroad) who have a professional interest in musculoskeletal diseases. They include consultants, trainees, allied health professionals and scientists. In the 1990s the BSR proposed guidelines for the use of biologic drugs, and also proposed the development of a national register of all patients in the UK on these drugs, to study their long term safety. This register was established in 2001: the BSR Biologics Register. The National Institute for Health and Clinical Excellence (NICE) endorsed it and recommended that all patients who started taking an anti-TNF agent should be asked to participate in the register.

The BSR Biologics Register is based at the Arthritis Research UK Epidemiology Unit, University of Manchester, and funded, via the BSR, by the pharmaceutical companies whose drugs are being used because they have been passed by NICE, i.e. Abbott, Pfizer (Wyeth), Roche, Schering Plough (MSD), UCB. The BSR manages the relationship with the University of Manchester and the contracts with the companies.

The Biologics Register and patient care

By Professor Deborah Symmons, Professor of Rheumatology & Musculoskeletal Epidemiology, and Dr Kimme Hyrich, Senior Lecturer in Rheumatic Disease Epidemiology, both at the Arthritis Research UK Epidemiology Unit, University of Manchester.

Between 2001 and 2011, over 12,000 people with rheumatoid arthritis who started anti-TNF therapy were included on the BSR Biologics Register: about 4,000 for each of three drugs, adalimumab, etanercept and infliximab and almost 1500 patients who started rituximab. It also now collects data on certolizumab pegol (a new anti-TNF therapy) and tocilizumab.

The study collects regular information from the people and their rheumatology teams, including how well their arthritis is controlled and whether they have experienced any adverse events (new health problems). It also includes almost 4,000 people with rheumatoid arthritis who are not receiving biologic therapy. It is important to have this second group, to help us understand differences between people who are being treated with biologics therapies and people who are not. This information will help us provide feedback to doctors and patients so that they can make informed decisions about their treatment.
9. Monitoring the safety of biologic drugs (cont.)

We continue to collect data on all the people who are registered, some of whom have been on the Register for over ten years. After the first three years, the information comes either from rheumatology teams or from central sources such as the national cancer and death registers. All patients who are on the Register receive a regular newsletter, and you can visit the Biologics Register website at: www.arc.man.ac.uk/webbiologiesreg.htm.

WHAT HAVE WE LEARNT FROM THE REGISTER?
As well as the BSR Biologics Register, there are similar biologics registers in Sweden and Germany, and smaller studies in many other European countries. These studies have provided information about the benefits and the risks of biologic drugs.

- Overall the results from the study so far have been reassuring. There is no reason why patients who have responded to anti-TNF therapy and are feeling well should not continue on this therapy.

- People do have a moderately increased risk of infection, especially in the first three months after starting treatment. Most of these infections are common in the general population, such as chest infections and skin infections (e.g. cellulitis). Anti-TNF therapy is also associated with an increased risk of shingles, and may increase the risk of some unusual infections, in particular tuberculosis (TB), salmonella and listeria. Because we know this, we can take steps to minimise those risks. For example, people are screened for TB before starting treatment, and advised to avoid possible sources of salmonella and listeria such as undercooked meats and eggs or unpasteurised foods.

- All treatments that suppress the immune system are associated with an increased risk of skin cancer. The BSR Biologics Register has found a modest increase in the occurrence of skin cancer in patients receiving biologic therapy and in patients receiving standard DMARD therapies including methotrexate, and people with a previous history of skin cancer are particularly at risk. Skin cancers generally occur on sun-exposed skin and are readily treatable if they are diagnosed early.

- More recently, the register has found that overall anti-TNF therapy does not appear to increase the risk of other kinds of cancer. However, it has always been recommended that people who have had cancer in the last 10 years should avoid anti-TNF therapy. This advice has been followed in the great majority of cases, so we don’t have any evidence about what would happen if people who’d had cancer were to have anti-TNF therapy. This advice therefore remains.
HOW WILL THE REGISTER DEVELOP?

While the results so far about the use of anti-TNF therapies are reassuring, we want to continue following patients in case there are any unexpected effects from long term use. The average follow-up for each person in the register is still less than 5 years.

There are other registers that collect similar data from people who are receiving these drugs for other conditions (for example, lupus) and a register of children and adolescents receiving them for juvenile idiopathic arthritis. Findings from all these registers are shared with consultants and nurse specialists, both through regular newsletters and through presentations at medical conferences.

The BSR Register is recruiting people who are starting on certolizumab or tocilizumab. We hope that as other new biologic agents become available in the UK that people starting these drugs will join the register as well. Many of the new agents act at different stages of the inflammation pathway so their pattern of side effects may be different.
Biologic therapies have had a major impact on RA but there’s still a lot to learn. This section looks at current research, and how it’s exploring new ways of getting the best from these powerful treatments.

LOOKING AHEAD

The cost of biologic drugs is a major concern. Not every person responds to every therapy, so a lot of money could be saved if we could identify the best drug for each individual. This is the concept of ‘personalised (or stratified) medicine’. A further important advantage of this would be that RA would be brought under control much more rapidly, because it would avoid the prescribing of ineffective therapies. A great deal of effort is being directed towards identifying ‘biomarkers’ in a person’s blood or in their genes, that can identify the most appropriate therapy for that individual. (A biomarker is a bit like a cell fingerprint.)

Personalised medicine applies to conventional drugs just as much as it does to biological therapies. In trials of early arthritis, for example, about a third of patients achieve low disease activity or remission on methotrexate alone. So as with biological therapies, there is a lot of effort aimed at identifying those people who are most likely to respond to methotrexate, and those who are likely not to: those who are not, could be offered an alternative from the start, such as triple DMARD therapy (methotrexate plus sulfasalazine plus hydroxychloroquine) or perhaps a biological therapy.

Research is also focused on ‘treatment-to-target’ (T2T) strategies. Traditionally, RA patients were reviewed every three to six months and treatment was altered at that time as necessary. But this often left people with active RA without review for several months or even longer, resulting in joint damage. Current research and guidelines suggest that instead people should be assessed frequently, perhaps monthly, and treatment should be escalated until a pre-agreed level of disease activity is reached, which could be low disease activity or remission.

Trials are exploring different ‘T2T’ strategies and, whichever strategy is chosen, the outcome is always better than with ‘standard’ treatment. Once a person is in remission, it may be possible to ‘step down’ their treatment so that they remain in remission but on minimal drug therapy.

Other research is focused on finding the best order of biologic therapy for an individual patient. At present, either anti-TNF or tocilizumab can be prescribed as first biologic therapy, followed by rituximab (as mandated by NICE and SMC guidelines). But there are no tests that we can perform to tell us which is the best drug for each patient – if there were then this would dictate the order of therapy. Personalised medicine ‘biomarkers’ would go some way to answering this question, and trials are also starting that compare different biologics ‘head to head’ in people with different patterns of disease. They will help to understand what are the best options when
people do not respond to an anti-TNF drug, for example. For some, it might be to ‘cycle’ to (move directly onto) a second anti-TNF, and for others it might be to switch to a drug with a different mechanism of action, such as rituximab, abatacept or tocilizumab.

Research is also looking at the very early stages of inflammatory arthritis. Some people, when rheumatologists first see them, do not fit the diagnostic criteria for RA and are considered to have ‘undifferentiated arthritis’ (UDA). But about 40% of these patients do go on to develop RA (the rest either develop a different joint disease or their symptoms clear up of their own accord). Traditionally we have not treated UDA but research is looking at treatment strategies for this early stage, and also searching for biomarkers to identify the people with UDA who are most likely to develop RA.

Public health research also is looking for ways to identify inflammatory arthritis earlier. There is pressure for GPs to refer patients with potential inflammatory arthritis at an earlier stage, and we also need to ensure that the general public can recognise the symptoms and seek a consultation when they suspect they may be developing RA.

HOW WILL RA BE TREATED IN 10 YEARS TIME?

How might things be different? People may seek medical care earlier, and treatment may start earlier, at the UDA stage of disease. Joint imaging, particularly ultrasound, may help in the earlier diagnosis of joint inflammation. People will probably continue to receive methotrexate as their first-line therapy, usually combined with other traditional DMARDs if they have more aggressive disease. ‘Treatment to target’ strategies will ensure that treatment is escalated rapidly until people are in remission, and that when traditional therapies fail, patients receive biologic therapies earlier in the course of their disease than they do now. We may be able to ‘personalise’ biologic therapy according to clinical features or biomarkers but, if not, there will be a recommended sequence of drugs as there is today.

The most valuable development in treating RA will be ‘biomarkers’ to help diagnose it early, identify those with more severe disease (requiring more aggressive treatment), and indicate the most appropriate therapy for each person. Biomarkers may even help to decide the best time to step down therapy when a patient is in remission.

There is a huge amount of research taking place, which reflects the excellent relationships between rheumatology health care professionals and people with RA. Patients are actively participating in research, to help scientists reach answers more quickly. We hope that this will, in time, change RA from a chronic, disabling disease to an acute condition that is potentially curable.
11. More information

NRAS PUBLICATIONS
The following publications are all available to download or to order, free of charge, from NRAS.
To order visit www.nras.org.uk/help_for_you/publications/default.aspx

- Newly diagnosed with rheumatoid arthritis?
  A guide to your next steps

- Managing Well:
  Living with rheumatoid arthritis

- Raise it with your doctor
  A guide to talking with your doctor of nurse about rheumatoid arthritis

- Fatigue:
  Beyond tiredness

- Know about your Disease Activity Score (DAS)

- How to claim Disability Living Allowance

- Benefits and Rheumatoid Arthritis

- I want to work...
  A self help guide for people with RA

- When an employee has rheumatoid arthritis:
  An employer’s guide
NICE : Rheumatoid arthritis: the management of rheumatoid arthritis in adults (CG79)

BSR and BHPR rheumatoid arthritis guidelines on eligibility criteria for the first biological therapy

The Kings Fund Report (2009) Perceptions of patients and professionals on rheumatoid arthritis care

National Audit office (2009) Services for people with rheumatoid arthritis

NRAS report (2010) The economic burden of RA

Technology Appraisal information for all biologic drugs mentioned in this booklet available from the NICE website and individual drug information sheets available from NRAS and Arthritis Research UK

References available on request.