Resource

Anti-TNFs

The anti-TNF drugs were the first of the biologic drugs to be introduced for RA, the first of which came in 1999. They work by targeting the ‘TNF?’ cells.

Print

Background

The anti-TNFs were the first of the biologic medicines to be introduced for RA, starting with infliximab, in 1999. They are expensive to develop and produce, so were expensive for the NHS to buy. They had to go through appraisal by the National Institute for Health and Care Excellence (NICE), who determine whether or not new medicines are cost and clinically effective for use in the NHS. NICE also set the eligibility criteria to allow people access to high cost medicines and the appropriate clinical pathway of medicine use. Not everyone has access to them if they don’t meet the criteria due to their disease severity and response to standard disease modifying medications.

How do they work?

RA is an auto-immune disease, meaning that the body’s own immune system is attacking the body (in the case of RA, by attacking the lining of the joints). Biologic medicines work by targeting proteins called cytokines, which are responsible for the inflammation caused by the immune system. In the case of ‘anti-TNF’ medicines, the cytokines being targeted are called ‘TNF’ (tumour necrosis factor). Here is a list of the current anti-TNF medications available:

Biologic drug	Method of administration
Adalimumab	subcutaneous (under the skin) injection every other week
Certolizumab pegol	subcutaneous injection at weeks 0, 2 and 4 (given as two injections), and then one injection every other week thereafter
Etanercept	subcutaneous injection, once or twice a week
Golimumab	monthly by subcutaneous injection
Infliximab	intravenous infusion, repeated 2 weeks and 6 weeks after the first infusion, then every 8 weeks

Most commonly reported side effects

As with any medication, anti-TNF medicines do have possible side effects. It is important to remember that these are only possible side effects. They may not occur at all.

Common side effects may include:

- High blood pressure (hypertension)
- Skin problems, including rash and dry skin
- Dizziness
- Indigestion (dyspepsia)
- Infections
- Headache
- Nausea, vomiting or stomach pain
- Muscular pain
- Allergic reactions
- Nerve problems
- Blood disorders

Skin cancer

Skin cancer is reported as a potential side effect of anti-TNF medications. These medicines target the TNF cells, which play a role in fighting off cancerous cells within the body. The possibility of increased risk of cancer has therefore always been a concern with these medicines. However, information gathered by The British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (published 2016) has shown that:

“To date, analyses of data from the BSRBR-RA have not identified an increased risk of non melanoma skin cancer or solid organ cancer.”

The risk of any type of cancer will continue to be monitored closely, and current guidelines suggest that these medicines should only be used with caution in people who have had cancer in the last 10 years.

> More information on side effects can be found in the patient information leaflet for your individual anti-TNF medicine.
>
> Remember to report any concerns about possible side effects to the doctors and nurses.

Anti-TNFs with other medicines

Some biologic medicines are known to interact poorly with other biologics. You may therefore be asked to leave a gap between stopping one biologic medicine and starting another, so that the first biologic has time to work its way out of your system.

Certolizumab pegol and infliximab have been reported to interact with the anti-psychotic medicine ‘clozapine’.

Your healthcare team can advise you of any known interactions with your medication, so it is important to let them know about all the medicines you are taking, whether they are prescribed or

over-the-counter. You should also let them know if you are taking any supplements or herbal medicines as these can also interact with medicines.

If you start taking any new medicines, check with a doctor, nurse or pharmacist that they are safe to take with any medicines you are currently taking.

Anti-TNFs during pregnancy and breastfeeding

Studies have demonstrated that there is no increase in adverse pregnancy outcomes (such as abnormalities or miscarriages) in babies whose mothers fell pregnant while on anti-TNF medication. However, it is important to remember that all the anti-TNF medicines are slightly different so do not necessarily behave in the same way. Anti-TNF therapies can be prescribed in women whilst trying to conceive and generally up until the end of the second trimester (at 26 weeks), although guidance does vary as to when different anti- TNFs should be stopped.

Certolizumab pegol does not cross the placenta and can be taken throughout pregnancy if clinically needed. Ideally, it should be stopped shortly prior to delivery to reduce the risk of infection in the mother while giving birth.

Both etanercept and adalimumab can be used throughout pregnancy if clinically needed. However, both of these medicines cross the placenta in varying amounts and therefore might affect a baby's immune system if taken by their mother in the third trimester.

Anti-TNF medicines can be taken whilst breast-feeding (although there is limited data available for some of these medicines).

If you do receive anti-TNF medicines in pregnancy or whilst breastfeeding, ensure that your baby's GP, paediatrician and health visitor are aware of this as it could affect some of the live vaccines your child is offered (i.e. rotavirus, MMR and tuberculosis vaccination).

Ideally these discussions are best had before trying for a baby or early in pregnancy and your rheumatology team are best placed to understand your condition and how it affects you. Your rheumatologist will be able to discuss with you the options of when to stop treatment, advise about vaccinations and liaise directly with your obstetrician.

Pregnancy information in this booklet is based on British Society for Rheumatology (BSR) guidelines on prescribing medicines in pregnancy and breastfeeding.

Before starting a family it is recommended that you get advice from the consultant or clinical nurse specialist about when to start a pregnancy.

Anti-TNFs and alcohol

You can drink alcohol on these medications. However, it is not uncommon when taking a biologic medicine to be on other medications, where different guidance applies. For example, methotrexate can affect the liver, so for those taking methotrexate alongside their biologic, moderate intake of alcohol is recommended in line with government guidelines.

Common side effects may include:

- High blood pressure (known as hypertension)
- Skin problems, including rash and dry skin
- Dizziness
- Indigestion (known as dyspepsia)
- Infections
- Headache
- Nausea, vomiting or stomach pain
- Muscular pain
- Allergic reactions
- Nerve problems
- Blood disorders

Skin cancer

Skin cancer is reported as a potential side effect of anti-TNF medications. These drugs target the TNF cells, which play a role in fighting off cancerous cells within the body. The possibility of increased risk of cancer has therefore always been a concern with these drugs. However, information gathered by The British Society of Rheumatology Biologics Register for Rheumatoid Arthritis (published 2016) has shown that: “To date, analyses of data from the BSRBR-RA have not identified an increased risk of non-melanoma skin cancer or solid organ cancer.” The risk of any type of cancer will continue to be monitored closely, and current guidelines suggest that these drugs should not be used, unless clinically necessary, in patients with a history (within the last 10 years) of cancer.

More information on side effects can be found in the patient information leaflet for your individual anti-TNF drug.

Remember to report any concerns about possible side effects to the doctors and nurses.

Anti-TNFs with other medicines

Some biologic drugs are known to interact poorly with other biologics. You may therefore be asked to leave a gap between stopping one biologic drug and starting another, so that the first drug has time to work its way out of your system.

The anti-TNF drugs certolizumab pegol and infliximab are known to interact poorly with the anti-psychotic drug ‘clozapine’.

Anti-TNFs during pregnancy and breastfeeding

Studies have demonstrated that there is no increase in adverse pregnancy outcomes (such as foetal abnormalities) in babies whose mothers fell pregnant while on anti-TNF medication. However, it is important to remember that all the anti-TNF drugs have slightly different structures so do not necessarily behave in the same way.

Anti-TNF therapies can be prescribed in women whilst trying to conceive and generally up until the end of the second trimester, although guidance does vary between drugs as to when they should be stopped.

Studies have shown that certolizumab pegol does not cross the placenta and can therefore be prescribed throughout pregnancy if clinically needed. Certolizumab pegol (Cimzia) has a European Medicines Agency (EMA) licence wording change to reflect this. However, like all anti-TNF drugs, it should be stopped shortly prior to delivery to reduce the risk of infection in the mother during the delivery period.

Both etanercept (Enbrel) and adalimumab (Humira) have also recently had an EMA licence wording change stating that they can be used throughout pregnancy if clinically needed. However both of these drugs cross the placenta in varying amounts and therefore have the potential to affect a baby's immune system if taken by their mother in the third trimester. To make things more complicated, it should also be noted that these licence changes are not yet reflected in biosimilars of etanercept or adalimumab.

Anti-TNF drugs can be taken whilst breast-feeding (although there is limited data available for some of these drugs).

If you do receive anti-TNF drugs in pregnancy or whilst breastfeeding, ensure that your baby's GP, paediatrician and health visitor are aware of this as it could affect some of the live vaccines your child is offered (i.e. rotavirus, MMR and tuberculosis vaccination).

Ideally these discussions are best had before trying for a baby or early in pregnancy and your rheumatology team are best placed to understand your condition and how it affects you. Your rheumatologist will be able to discuss with you the options of when to stop treatment, advise about vaccinations and liaise directly with your obstetrician.

Pregnancy information in this booklet is based on British Society for Rheumatology (BSR) guidelines on prescribing drugs in pregnancy and breastfeeding.

Before starting a family it is recommended that you get advice from the consultant or clinical nurse specialist about when to start a pregnancy.

Anti-TNFs and alcohol

You can drink alcohol on these medications. However, it is not uncommon when taking a biologic drug to be on other medications, where different guidance applies. Methotrexate, for example, can affect the liver, so for those taking methotrexate alongside their biologic, moderate intake of alcohol is recommended in line with government guidelines.

Anti-TNFs and immunisations/ vaccinations

Live vaccines cannot be given to anyone who is already taking anti-TNF medicines. The live vaccines used in the UK include: measles, mumps and rubella (MMR), chickenpox, BCG (for tuberculosis), yellow fever, oral typhoid or oral polio (injectable polio and thyroid vaccines can be used). If anti-TNF medicines have not yet been started, it is important to seek advice on how long a gap to leave after having a live vaccine.

Annual flu vaccine is strongly recommended. It is available in two forms: an injection for adults and a nasal spray for children. The injectable vaccine is not a live vaccine so is suitable for adults taking

anti-TNF medicines. The nasal spray is a live vaccine and not suitable for adults taking anti-TNFs. You can have a flu vaccination at your GP surgery or local pharmacy.

Annual ‘Pneumovax’ vaccination (which protects against pneumococcal pneumonia) is not live and is strongly recommended. Vaccination with Pneumovax should ideally be given before starting anti- TNF medicines.

Shingles (Herpes zoster) vaccine is recommended for all adults turning 65, those aged 70 to 79 and those aged 50 and over with a severely weakened immune system. The vaccination is given as two doses, two months apart. at your GP surgery. It is available as a live or non-live vaccine, so it is important to make sure you are given the non-live version.

Covid-19 vaccines and boosters are not live and are generally recommended for people with RA. Your GP can advise if you are eligible for free flu, Pneumovax, shingles and Covid vaccinations, depending on the medications you are taking and their doses.

> Vaccination of close family members can help to protect someone with a lowered immune system from infection.

Medicines in rheumatoid arthritis

We believe it is essential that people living with RA understand why certain medicines are used, when they are used and how they work to manage the condition.

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