Psoriatic Arthritis- Second Line Treatments

Second line treatments for Psoriatic Arthritis (PsA) are usually prescribed by a Rheumatologist, Dermatologist, or in a combined clinic where both the Dermatologist and Rheumatologist are present. They cannot be prescribed by a GP. The second line treatments that you may be offered all come under the heading of Disease Modifying Anti Rheumatic Drugs (DMARDs), meaning they actually treat the disease, rather than just the symptoms. The DMARD category for PsA includes:

- Methotrexate
- Sulfasalazine
- Leflunomide
- Otezla (apremilast)
- Biologic therapies – Cimzia (certolizumab pegol), Cosentyx (secukinumab), Enbrel (etanercept), Humira (adalimumab), Remicade (infliximab), Simponi (golimumab), Stelara (ustekinumab)

DMARDs work by attacking the causes of inflammation in the joints. They lessen the activity of arthritis by reducing swelling and stiffness, reducing the pain as well. These treatments act quite differently from anti-inflammatory medications and can help to stop the arthritis from getting any worse. Psoriatic arthritis can cause irreversible damage to joints if effective DMARD treatment is not given when appropriate.

It can take a number of months for a DMARD to reach its full effect. However, they can often be taken in conjunction with other first line medications, such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and painkillers, to help ease symptoms whilst the DMARD begins to work. Most DMARDs work on the immune system in some way and are designed to be taken long-term, and therefore there is a possibility of more significant side effects than with painkillers and NSAIDs alone.

When should DMARDs be prescribed?

The British Society for Rheumatology (BSR) has published guidance on the appropriate treatment ‘pathway’ for people with psoriatic arthritis. The National Institute for Health and Care Excellence (NICE) and Scottish Medicines Consortium (SMC) have published criteria for the prescription of various available biologic treatments for psoriatic arthritis.
DMARDs should be considered if: -
There is active disease (i.e. inflammation is present in several joints despite using NSAIDs). The individual is unable to go about daily living, work or recreation easily. Many joints are affected.

Biologic Treatments should be considered if: -
The person has arthritis with three or more joints that are tender to touch and three or more joints that look or feel swollen, and at least two other DMARDs haven’t worked or cannot be tolerated (i.e. caused side effects that meant treatment had to be stopped).

As with psoriasis, it is often a process of trial and error to find a treatment or combination of treatments that work well for each person with psoriatic arthritis. Because of this, the BSR guidelines recommend that a second biologic treatment is tried if no acceptable improvement is seen after 12 weeks on an initial biologic.

The following is a brief summary of some of the commonly-prescribed DMARDs for psoriatic arthritis. Further information on each of these treatments is available from the Psoriasis Association.

Methotrexate (also referred to by its commercial names Matrex or Ebetrex)
Methotrexate is an immunosuppressive medication (meaning it affects the way that the immune system works) that is widely prescribed to treat both psoriasis and psoriatic arthritis. Methotrexate works to suppress the overactive immune system which causes inflammation, swelling and stiffness in joints. Because of this suppression, a person taking methotrexate is likely to be more prone to infections.

Methotrexate is usually taken in tablet form once a week, but in some cases it is given as an injection. It can take up to 12 weeks to become fully effective. People taking methotrexate will need regular blood tests to monitor liver and bone marrow function, and check for infections. They should also have an annual flu jab.

It may be possible to take ibuprofen or similar NSAIDs whilst taking methotrexate, but this must be discussed with the prescribing doctor (usually a Dermatologist or Rheumatologist) first. Do check with your doctor before taking other over-the-counter or prescribed medication, or herbal remedies. Also check with your doctor or on the treatment patient information leaflet (PIL) for information relating to alcohol and pregnancy whilst taking methotrexate.
Sulfasalazine (also referred to by its commercial name Salazopyrin)
Sulfasalazine reduces inflammation in the joints, and decreases pain, swelling and stiffness. Some people will start to notice results within a few weeks of starting the treatment, however, it may take around 12 weeks for sulfasalazine to have a full effect. Sulfasalazine is a tablet that is usually taken every day. The number and time to take your tablet will be explained to you by your doctor. The tablet has a special coating which means it dissolves more slowly, passing beyond the stomach before releasing its contents. This can help reduce nausea and stomach irritation associated with other treatments. You will need to have frequent blood tests for the first three months of taking the drug, followed by regular tests every three months, to monitor liver function and check for infections. You may also need an annual flu jab. Sulfasalazine may also turn your urine orange or dark yellow and your tears may be discoloured. This is nothing to worry about, however if you use extended wear contact lenses tell your doctor as they may develop an orange stain. Do check with your doctor before taking other over-the-counter or prescribed medication, or herbal remedies. Also check with your doctor or on the treatment PIL for information relating to alcohol and pregnancy whilst taking sulfasalazine.

Leflunomide (also referred to by its commercial name Arava)
Leflunomide, like methotrexate was initially developed for use in the treatment of cancer. Leflunomide is an anti-T cell medication and as such is thought to control inflammation by interfering with T cell production of cytokines, similar to some of the biologics. It acts to suppress the overactive immune system, causing damage and pain to the joints. Leflunomide is a tablet that is taken every day. Like other DMARDs, leflunomide does not work immediately – it may be up to six weeks before you feel any effect and as long as six months before you feel the full benefit. The potential side effects of leflunomide are similar to methotrexate and so you will have regular blood and blood pressure tests, and may need an annual flu jab. Do check with your doctor before taking other over-the-counter or prescribed medication, or herbal remedies. Also check with your doctor or on the treatment PIL for information relating to alcohol and pregnancy whilst taking leflunomide.

Apremilast (also referred to by its generic name Otezla)
The Scottish Medicines Consortium (SMC) has accepted Otezla for use in people with moderate to severe psoriasis and/or active psoriatic arthritis, in Scotland. The National Institute for Health and Care Excellence (NICE) published a positive ‘final appraisal determination’ for the use of Otezla to treat active psoriatic arthritis in England and Wales in December 2016. It is not known exactly how Otezla works in psoriasis or psoriatic arthritis. However, it is known that Otezla inhibits (ie. stops it from working as it usually does) an enzyme known as phosphodiesterase 4, or PDE4. PDE4 controls the inflammatory action within a cell, which can affect the level of inflammation associated with psoriasis or psoriatic arthritis. Helping to control this inflammation can lead to an improvement in symptoms for people with psoriasis or psoriatic
arthritis. Otezla is taken orally in tablet form twice a day. The dose is gradually increased over the first five days, until the patient is taking the full 30mg twice a day from day six onwards.

**Biologic Treatments**

A number of biologic treatments have been issued National Institute for Health and Clinical Excellence (NICE) guidance for treating PsA. NICE recommends that the TNF-alpha inhibitor biologics Enbrel, Humira, Remicade or Simponi should be offered as a treatment when:-

The person has arthritis with **three or more** tender joints and **three or more** swollen joints, and at least **two other** DMARDs, given on their own or together, haven’t worked. Treatment should normally be started with the least expensive drug (taking into account drug administration costs, required dose and product price per dose). This may need to be varied for individual patients because of differences in the method of administration and treatment schedules.

There is no NICE guidance specifically for the use of Cimzia in PsA, but its Marketing Authorisation (licence) was extended to cover PsA in 2013. It is a TNF-alpha inhibitor and the criteria for its use is usually the same as for the other TNF-alpha inhibitor biologics.

NICE recommends that Stelara should be offered as a treatment when the above criteria applies and a previous TNF-alpha inhibitor biologic has not worked or is not suitable.

The SMC has accepted Cosentyx for use in psoriatic arthritis when previous DMARD treatment has not worked. This is currently only available for people with psoriatic arthritis who live in Scotland.

The following treatments work in similar ways– by suppressing a specific chemical called tumour necrosis factor-alpha (TNF-alpha) that is involved in triggering inflammation.

**Cimzia** is taken in two injections at weeks 0, 2 and 4, and then in one injection every two weeks. Treatment may be stopped if no significant results are seen within 12 weeks.

**Enbrel** is usually taken once or twice a week by injection. Again, treatment may be stopped if no significant results are seen within 12 weeks.

**Humira** is usually taken once every two weeks by injection. Again, treatment may be stopped if no significant results are seen within 12 weeks.

**Remicade** is given in hospital using an intravenous drip into a vein (an infusion). Initially the infusions are given once at the beginning of treatment, after two weeks, and then after another four weeks. You will then need an infusion (which takes between one and two hours) every eight weeks. Again, treatment may be stopped if no significant results are seen within 12 weeks.

**Simponi** is taken once a month by injection, on the same date each month. Again, treatment may be stopped if no significant results are seen within 12 weeks.
Stelara works in a slightly different way – by slowing down the activity of interleukin 12 (IL-12) and interleukin 23 (IL-23), chemical ‘messengers’ in the immune system that signal other cells to cause inflammation. It is usually taken by injection at week 0, week 4, and then every 12 weeks after that. Treatment may be stopped if no significant results are seen within 24 weeks.

Cosentyx also works on interleukin activity – it binds to interleukin 17A (IL-17A) to inhibit (ie. stop it from working as it usually does) its inflammatory action. It is usually taken by two injections given at the same time, weekly for the first four weeks, and then monthly after that.

This is not a complete list of the second line treatments a Rheumatologist may prescribe for you; other treatments that are usually used for other forms of inflammatory arthritis may be prescribed on a case-by-case basis.

More in-depth information on the treatments featured in this resource, and on first line treatments for psoriatic arthritis, is available from the Psoriasis Association.

For more information, or for a list of resources used in the production of this information sheet, please contact the Psoriasis Association.

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