



# Rheumatoid Arthritis Medications and Their Side Effects

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## Understanding Rheumatoid Arthritis Medications

*With contributions from Krystina and Effie.*

If you've recently been diagnosed with rheumatoid arthritis (RA) or are struggling with your treatment plan, the medication options can be confusing. There are various drug classes and they work in different ways to treat your rheumatoid arthritis symptoms or slow the progression of the condition.

### What Are the Goals of Rheumatoid Arthritis Treatment?

Conventional treatment for rheumatoid arthritis often has several goals.

- Reducing joint pain, inflammation, and stiffness.
- Preventing joint damage or deformities, and organ damage.
- Reduce any potential long-term complications.
- Relieve the symptoms of rheumatoid arthritis.
- Improve overall quality of life and daily living.
- Stop or slow the progression of rheumatoid arthritis.

Depending on your symptoms and the progression of your rheumatoid arthritis, your doctor and rheumatologist may focus on three different types of treatment strategies: early and aggressive treatment, remission targetting, or firm disease control.

Early and aggressive treatment focuses on ending or reducing the levels of inflammation caused by your rheumatoid arthritis as soon as possible.

Remission targetting concentrates on stopping inflammation or any related-rheumatoid arthritis disease activity and getting it to a remission state. This state means minimalizing signs or symptoms of active inflammation.

The last treatment strategy is firm disease control and it focuses on keeping rheumatoid arthritis progression and its symptoms at a minimal or nonexistent in order to prevent any long-term complications, such as joint and organ damages.

### Rheumatoid Arthritis Medications 101

There are five drug classes that are typically used to treat rheumatoid arthritis. Although they can each be used separately, they are often most helpful when used in conjunction with one another to produce the best results. Keep on reading to learn about these common rheumatoid arthritis medications.

#### Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

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A drug from the DMARD category is often selected shortly after diagnosis. DMARDs are known to slow or even halt the progression of rheumatoid arthritis.

DMARDs work by stopping the immune response that causes inflammation. However, they can take several months to be effective.

Though they are often effective on their own, at least initially. Sometimes it's used in correlation with a glucocorticoid, or an NSAID to control pain.

Like all medications, DMARDs are not without their side effects. Because their action is to block immune response, they may actually reduce immunity, which can lead to increased risk of infections and subsequent illnesses.

For some people, DMARDs may also be hurtful to organs such as the kidneys and liver, so routine blood testing is crucial.

### **Conventional DMARDs**

Conventional DMARDs include methotrexate, hydroxychloroquine, sulfasalazine and leflunomide.

There are various side effects that may be associated with these drugs, including stomach upset, sore mouth, increased risk of infections, liver damage and bleeding (methotrexate), damage to the retina of the eye (hydroxychloroquine), rash, hair loss, liver damage, weight loss, diarrhea (leflunomide), orange tinge of the urine, tears and sweat, and sensitivity to light and headaches (sulfasalazine).

Rheumatoid arthritis and hair loss (along with several other of the symptoms) is common, so it can be difficult to distinguish whether it is caused by rheumatoid arthritis or by the medication.

### **Biologic Response Modifiers**

Biologic response modifiers, or "biologics," are a subcategory of DMARDs. They are intravenous medications that are given as an infusion.

An advantage to biologics is that, unlike DMARDs, which can decrease immune function, biologics work by targeting a specific immune response. This means that the risk of lowered immunity and subsequent illness is much lower.

Examples include adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade) and rituximab (Rituxan).

The potential side effects can be serious and include infections with bacteria and fungi, nerve disorders (including multiple sclerosis) and heart failure.

In addition, there is an increased risk of allergic reactions, including the most severe form – anaphylaxis, when taking infliximab.

### **JAK Inhibitors (or Targeted Synthetic DMARDs)**

JAK inhibitors are a new subcategory of DMARDs. This new medication specifically blocks the Janus kinase (JAK) pathway, which is involved in immunity.

An example of a JAK inhibitor is tofacitinib, which has an advantage over biologics, as it can be taken orally.

Side effects that have been associated with it include various bacterial infections, anemia, headaches, high blood pressure, liver damage (including fatty liver) and in rare cases cancer.

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## **Glucocorticoids (Steroids)**

Glucocorticoids, also known as corticosteroids, can be used for rheumatoid arthritis treatment but are often used on a short-term basis, when symptoms flare up or when initiating treatments that may take several months to take effect.

Steroids are potent anti-inflammatory drugs that are available in pill or injection form. They also help decrease joint pain and stiffness and are recommended to treat rheumatoid arthritis flare-ups. They have many possible side effects, including RA weight gain, aggravation of diabetes, cataracts, osteoporosis and increased risk of infections.

Glucocorticoids are quick acting and are effective in reducing inflammation. They reduce inflammation by decreasing the activity of the immune system. They also reduce the production of chemicals that cause inflammation, which lowers overall tissue damage.

If possible, glucocorticoids should be used on a short-term basis. This is because the serious side effects are tied to the dosage and duration the drug is administered.

*Next page: More information on additional rheumatoid arthritis medications and combination therapy.*

## **Glucocorticoids (Steroids)**

The higher the milligrams, the risk for decreased bone mass and increased fractures rises. These are two main side effects your doctor should and will look out for if you have been on the medication for months or years at a time.

In order to test how your bone mass is the rheumatologist or physician, will order a DEXA scan (dual-energy x-ray absorptiometry). This is simply two X-ray beams that are aimed at the bones and is a painless procedure. The spine and hips are the typical areas of the body looked at. No matter if you are taking the lowest dose possible or the highest, your rheumatologist will still order this for precautionary measures.

Along with undesirable side effects, such as increased appetite with subsequent weight gain, difficulty sleeping, acne and anxiety, they can have much more serious side effects, such as elevated blood sugar levels, high blood pressure, glaucoma and increased risk for infection.

Examples of glucocorticoids include prednisone, prednisolone, and methylprednisolone.

## **Nonsteroidal Anti-Inflammatory Medications (NSAIDs) and Analgesics**

Unlike the previously listed drug classes, NSAIDs will not treat rheumatoid arthritis specifically but will treat the symptoms associated with the condition. This class of drugs includes about 20 drugs – from the over-the-counter ibuprofen and naproxen to the prescription drug Celecoxib.

NSAIDs are used to treat pain associated with RA; in fact, they block an enzyme that increases inflammation so they actually cause a reduction in inflammation — hence the name. Although they reduce pain and inflammation, they cannot reduce damage already done to the joints.

They are taken in conjunction with other rheumatoid arthritis medications that are used to specifically treat the symptoms and progression of RA. It may need to be limited in certain patient populations, such as those with kidney or liver disease, so discussing with your physician prior to taking an NSAID is recommended.

These drugs can affect the cardiovascular system (causing high blood pressure and heart diseases), the digestive system (stomach upset/irritation, peptic ulcers, bleeding), cause liver and kidney damage and ringing in the ears.

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All these symptoms can be avoided with careful patient selection and usage of the drug. Following the dosage instructions is crucial in order to protect the organs. Taking over the recommended amount or overusing, is when problems can occur rapidly.

Two drugs from this group (Rofecoxib and Valdecoxib) had been removed from the market after being linked with increased risk of heart attacks and strokes. NSAIDs interact with many drugs including blood thinners and some anti-seizure drugs. Examples include Celebrex, ibuprofen and diclofenac.

As with NSAIDs, analgesics treat pain associated with RA. However, they do not treat inflammation so they will not reduce swelling of the joints. As with NSAIDs, they should not be used alone and should be used in conjunction with other RA treatments.

NSAIDs may be purchased over-the-counter or also may be given as a prescription, depending on the severity of the pain. Examples of analgesics include acetaminophen, tramadol, oxycodone and hydrocodone.

### **How Combination Therapy Leads to Better Results**

As a patient, it is normal to feel unease when a doctor suggests combining more than one rheumatoid arthritis medication. There are several reasons why this approach is helpful.

The two most popular drug classes, biologics and DMARDs come with a list of side effects. For instance, methotrexate has been one of the first class of DMARDs to be administered to patients with rheumatoid arthritis for over forty years.

Many find the side effects of such as hair thinning and loss or fatigue to be unbearable, leading patients no choice but to switch to another DMARD or the next step up which is a biologic.

Depending on the person's specific situation, a rheumatologist may decide to begin a treatment with a DMARD or two and corticosteroids such as prednisone or local joint injections.

While the patient is monitored with regular bloodwork, x-rays and examinations during follow-up appointments, the rheumatologist can then assess whether or not if it's appropriate to add another line of defense.

Methotrexate, in this case, is often taken alongside the medication called Hydroxychloroquine (Plaquenil), another DMARD. Studies show that combining these two pharmaceuticals, it can help those who are experiencing bad side effects from methotrexate. In fact, Plaquenil is known to protect you from the negative aspects of methotrexate and allow it to work better.

The severity of the patient's disease activity and markers also play a crucial role in deciding if two or three rheumatoid arthritis medications will be prescribed at once.

To treat aggressive RA, one biologic or DMARD is often not enough. In these cases, the best outcomes for protecting joints from irreversible damage, joint deformities and other complications is to treat the disease equally as aggressive. This is because patients find then with one biologic or DMARD, they are still experiencing morning stiffness, pain, swelling or fatigue, with the effects of the medication diminishing after several months or years.

Interestingly enough, studies have found something called "triple therapy" which is a combination of Plaquenil, sulfasalazine and methotrexate, has been shown to work similar to the combination of methotrexate (DMARD) and Etanercept (Enbrel). Enbrel being the strongest of all four medications.

Mild forms of rheumatoid arthritis, respond well to one or two DMARDs often bringing patients into complete remission or a low state of disease activity fairly quickly.

Whether you are living with a mild, moderate or severe form of rheumatoid arthritis doesn't matter. What matters is to look at the big picture that the disease can cause irreversible damage at any form or stage, and early

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detection but aggressive treatment is key to a successful outcome.

The only downside that doctors are finding is that while they know patients can respond well to one biologic or DMARD alone, there are no distinctive tests made to show who is in need of more. This leads patients down the road of trial and error, and going on and off various rheumatoid arthritis medications and combinations for months or years before they find one that works to bring the body back into a state of balance, remission or low disease activity.

### **The Takeaway**

Remember that everyone who has rheumatoid arthritis has their own treatment plan that is individualized by their physician. Your treatment plan will likely look different than someone else's.

Also keep in mind that if one medication does not work for you, there are a multitude of other options available — and there is further research being done every day to better the lives of RA sufferers.

Lastly, don't hesitate to talk to your physician and rheumatologist about all the rheumatoid arthritis medication options available now. Establishing a positive doctor-patient relationship, yields to good rapport and understanding of your health goals and what you are willing to try out moving forward.