Pfizer

# Rheumatoid Arthritis

Keep active in life.

FÜR PATIENTEN

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# Dear Patient,

"Knowledge is power," as the saying goes, and this is particularly true when it comes to a chronic disease like rheumatoid arthritis. The inflammation associated with this disease can cause a variety of symptoms, ranging from persistent morning stiffness though painful and swollen finger or toe joints, to severe limitation of mobility. Even internal organs, such as the heart or lungs, can be affected in rare cases.

But knowledge is also the best antidote to fear and feeling at the mercy of an illness. Therefore, anyone affected by this disease needs a lot of information – on the triggers for immune system symptoms, on the full range of modern treatment options, and also on opportunities for exchanging experiences with other patients in support groups. Those who are well-informed are best able to learn to manage their illness and to actively and purposefully

overcome the associated symptoms and limitations, e.g. by responding more quickly to certain events.

This brochure is intended to provide you with information. It contains many important and up-to-date facts about rheumatoid arthritis.

A final word in conclusion: Thanks to medical research, the treatment of rheumatoid arthritis has made a huge step forwards in the last few decades. Particularly since the therapeutic introduction of biologic drugs, and more recently, the new JAK inhibitors, disease activity is often able to be brought to a standstill nowadays. This prevents damage, but also significantly improves severe illness. Thus, the information in this brochure should not only expand your knowledge about the disease, but should also give you the courage to expect more from modern rheumatoid therapy and not to settle for modest improvements!

Your Pfizer Inflammation Team wishes you an interesting read and a speedy recovery.

# Information on the disease

**Key information about rheumatoid arthritis clearly summarized.**

## What is rheumatoid arthritis?

Rheumatoid arthritis (abbreviation: RA) is a chronic inflammatory disease that can affect multiple organs or organ systems. This is why it is referred to as a systemic disease. However, as the name suggests, it is mainly the joints that are affected: arthritis means inflammation of the joints.

The former name “chronic polyarthritis” suggests that many (“poly”) joints are usually affected.

In addition, a wide range of other manifestations are possible. RA belongs to a group of chronic inflammatory (joint) diseases, often referred to under the umbrella term of “rheumatism”.

## How common is rheumatoid arthritis?

RA is the most common inflammatory joint disease; it affects approximately 0.5 - 1 % of the adult population in Europe and North America. This corresponds to approximately 330,000 - 660,000 patients in Germany. Each year, new disease onset can be expected in 30 out of 100,000 inhabitants.

## Who is affected?

Generally speaking, RA can occur for the first time at any age. Women most often develop the disease between the ages of 50 and 60, men from the age of 70 . However, RA can also occur in children and adolescents. This form is termed juvenile (= adolescent) idiopathic arthritis. Women are affected about three times more often than men. The cause of this imbalance is unknown.

## How does rheumatoid arthritis develop?

The causes and development of RA are not fully understood to date. However, there are various pointers. A disorder of the immune system is thought to be the cause. RA is considered an autoimmune disease. This means that the immune system, which normally acts to defend against infectious agents and other foreign bodies, also classifies the body's own tissues as "foreign" and produces antibodies against them. Thus, the body attacks itself in certain areas, such as the inner lining of the joints, which can cause inflammation, swelling, pain, and tissue damage. Studies of affected families have shown that a hereditary predisposition plays a role, meaning that the risk of disease is increased if a close relative already has the disease. But external influences also seem to be important as possible triggers. These include, above all, infections with viruses or bacteria, which often precede the development of RA.

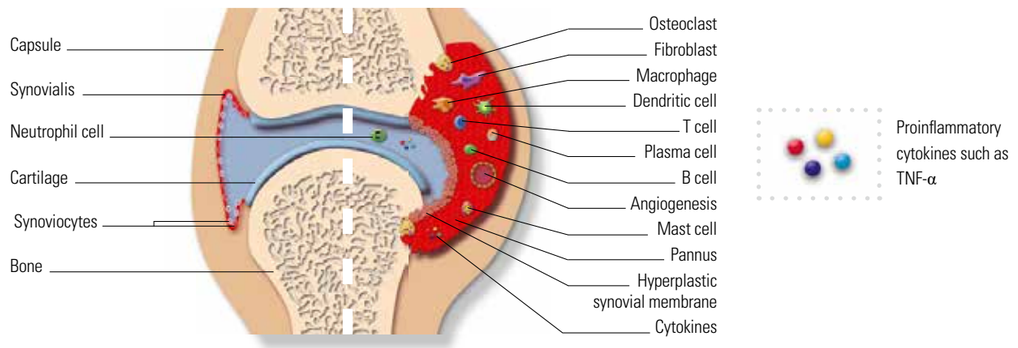
## What happens in the joints?

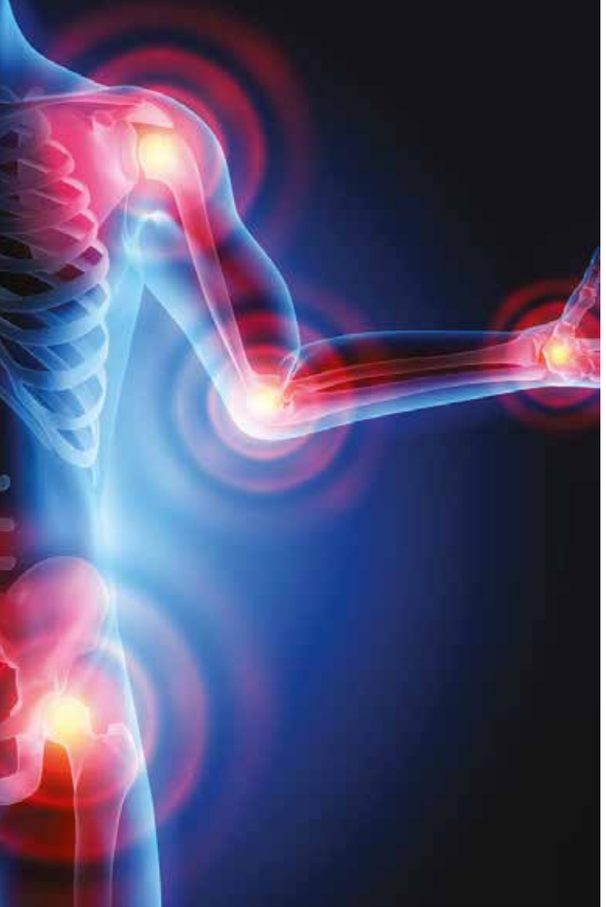
In RA, the affected joints (also called synovial joints) are those in which the involved bone surfaces are covered with a layer of articular cartilage and surrounded by a fluid-filled cavity (joint cavity). The joint cavity is lined by the synovial membrane (synovium), a thin layer of connective tissue. This synovium produces the viscous synovial fluid (synovia), which serves as a lubricant to reduce friction between bones.

As the disease progresses, the proliferating connective tissue (pannus) then progressively spreads to the cartilage of the joints, eventually causing permanent damage to the cartilage and adjacent bones.

## What is the role of the messenger TNF-α and other pro-inflammatory cytokines?

The tumor necrosis factor alpha (TNF-α and other pro-inflammatory cytokines) is a naturally occurring messenger substance (cytokine) of the immune system, which plays an essential role in the inflammatory processes of RA and other inflammatory rheumatic diseases. It has a variety of effects but is primarily pro-inflammatory. In RA, TNF-α (and other pro-inflammatory cytokines) is detectable in large amounts in the affected joints. There it is produced by certain types of cells (macrophages, lymphocytes) that perform special tasks in the immune system.





## What are the typical symptoms of the disease?

In RA, multiple joints are usually inflamed at the same time. It typically affects small joints, particularly the base and middle joints of the fingers, and the base joints of the toes. In principle, however, any joint can be affected. Very rarely, the finger joints are affected.

Over time, there is usually progression of the disease, with an increase in the number of affected joints. The inflammation then often spreads to the larger joints of the hands, arms (elbows, shoulders), feet, and legs (ankles, knees, hips). Usually, the joints or joint regions on both sides of the body are affected simultaneously; this is called a symmetrical pattern of involvement.

Inflammatory damage to the joint cartilage and bone can eventually lead to deformity of the joint and to limitations and even loss of mobility, if treatment is delayed or inadequate.

## INFO

**In RA, inflammation of the synovial membrane occurs in the joint, causing an accumulation of "inflammatory cells" and other cells of the immune system that produce numerous cytokines/messengers.**

**The inflammation leads to increased growth of cells and blood vessels with increasing thickening of the synovium, as well as an abnormally increased secretion of synovial fluid. The result is joint swelling and pain. Fortunately, the possibility of treatment is good nowadays.**

Typical symptoms include pain and swelling in the affected joints, although the soft tissues adjacent to the joint may also be swollen. Patients often also experience hyperthermia and burning in the joints. Exposure to cold (e.g., under cold water) leads to improvement. Typically, symptoms tend to occur at rest and improve with exercise.

In some patients small palpable lumps are found under the skin, particularly in the elbow area and wrists. These so-called rheumatoid nodules have become less frequent due to the improving therapies and are caused by inflammation of the connective tissue, providing an important diagnostic pointer.

As a disease of the entire body, RA can be accompanied by fatigue, exhaustion, a general feeling of illness, loss of appetite, weight loss, and listlessness to depression. Especially acute attacks with high disease activity are often also accompanied by elevated body temperature or even mild fever.

In addition to the joints, other organs or organ systems may also be affected; these are also referred to as extra-articular manifestations, i.e. manifestations outside the joints. They often include inflammation of parts of the musculoskeletal system (tendon sheaths, bursae) and, less commonly, of internal organs such as the heart and lungs, the hematopoietic system, lymph vessels, nerves, or blood vessels. This can cause significant complications.

**INFO**

**Historically, rheumatoid arthritis was often only recognized at a very late stage, for several reasons: In the early phase, it is often accompanied by a less typical manifestation. The patient is more likely to be troubled by general symptoms and possibly symptoms of jumping joints. Here, the notion of RA is not very obvious to either the patient or to the primary care physician.**

## What is the course of rheumatoid arthritis?

The onset and course of RA vary greatly from patient to patient. The onset of the disease can be sudden with acute symptoms, but also gradual and with very non-specific symptoms that are not necessarily typical for RA.

For the majority of people, the disease is progressive and episodic, meaning the symptoms increase over the years. In between, there may be periods of varied length during which the disease activity is reduced.

It is impossible to predict for certain how (severely) the disease will progress in an individual patient. The only way to positively influence the course of the disease and its possible late effects is by early diagnosis and correspondingly rapid, targeted treatment.

In recent years, the success of treatment has improved significantly. Thanks to modern, effective treatment approaches, there is now a good chance of achieving a return to a largely and, in the best case, even completely symptom-free state (remission).

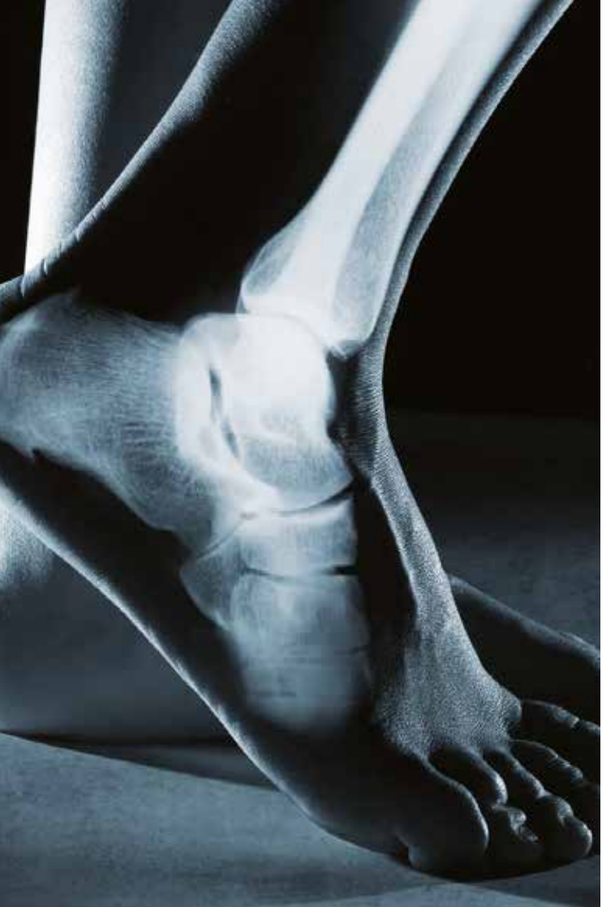
## Important criteria that may indicate the presence of rheumatoid arthritis

For a patient with at least one swollen joint that cannot be explained by an alternative diagnosis, doctors determine the likelihood of rheumatoid arthritis based on the:

+ number and location of affected joints
+ laboratory findings (presence of rheumatoid factors, antibodies to citrullinated proteins and inflammatory parameters)
+ duration of symptoms.

### INFO

**A typical characteristic is also “morning stiffness” in the joints: In the morning or after prolonged immobilization, the joints appear stiff and immobile. This condition can last from a few minutes to several hours.**

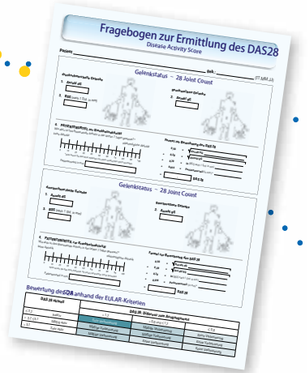


## How is rheumatoid arthritis diagnosed?

Even for an experienced rheumatologist, it is not always easy to diagnose RA with certainty, particularly at the onset of the disease and if the clinical picture is very uncharacteristic. At the beginning, some typical laboratory values are still unremarkable. Diagnosis of RA is based mainly on the following three pillars:

+ **In-depth questioning (medical history)**
+ **General and targeted physical examination by the doctor, with special attention to joint status**
+ **Examinations by means of imaging methods**
+ **Laboratory tests**

Key criteria for the diagnosis of RA were already compiled by experts in 1987 and renewed in 2010 (see page 18). However, diagnostic possibilities have been expanded by additional procedures in the meantime. The most important examination options are briefly explained below.




## INFO

**The joint status is used to record and classify the disease activity based on the so-called Disease Activity Score (DAS). The DAS28 is derived from the number of tender and swollen joints (of a total of 28 joints examined, hence DAS28), the ESR (erythrocyte sedimentation rate) after one hour, and a scale-defined value for the assessment of disease activity by the patient.**

**DAS28 values below 3.2 indicate well-controlled disease activity. Values above 5 indicate increased disease activity. In such a case, the possibility of intensifying therapy should be discussed with the doctor. However, the goal is remission, that is a DAS28 < 2.6.**

## Lab values

### + Blood (erythrocyte) sedimentation rate (ESR)

This refers to the speed at which the blood corpuscles (blood cells) drop in a vertical measuring tube filled with blood. After one or two hours, a reading is taken to see how many millimeters per hour the blood cells have dropped. An increased ESR indicates that an acute or chronic inflammatory process is taking place somewhere in the body.

However, this is a very non-specific measurement because it is not possible to identify where the inflammation is taking place, and the value can also be elevated in other inflammatory diseases. ESR is usually, but not always, elevated in RA.

### + C-reactive protein (CRP)

This is a protein whose concentration in the blood serum can increase up to 1,000-fold within a few hours during certain inflammatory processes. The level of serum CRP is characteristic of the extent of inflammation and the course of the disease. When it improves, it quickly decreases again and thus also indicates the success of a therapy. This measurement is also very non-specific. The CRP value can also be elevated in other inflammatory diseases, but it is not always elevated in RA.


### + Rheumatoid factor (RF)

Rheumatoid factors are antibodies directed against the body's own antibodies (immunoglobulins); this is why they are also called autoantibodies. They can be detected in serum (positive) in some but not all chronic rheumatic diseases. In RA, RF is positive in about half of patients in the first six months, and then in about two thirds of patients later.

However, the rheumatoid factor is, to some extent, also non-specifically detectable in healthy individuals or in patients with liver disease.

### + Anti-CCP (anti-cyclic citrullinated peptide antibody)

The determination of these proteins is a relatively new procedure that is very specific for RA, especially in connection with the detection of RF, and can already be detected in early stages of the disease.

The detection is very specific to RA but cannot be equated to the disease. Low titer anti-CCP is also common among smokers, for example.

## Imaging procedures

### + X-ray

Conventional x-rays of the joints can be used to show the most important changes or damage to the bone, such as bone defects (erosions) and narrowing of the joint space between the bones involved in the joint. However, changes in the surrounding soft tissues are barely visible.

### + Joint ultrasound (arthrosonography)

This ultrasound-based procedure is a very good way to assess inflammatory processes, but also to detect erosions. It is a readily available procedure that is usually equivalent to MRI.

### + Magnetic resonance imaging (MRI, magnetic resonance imaging)

MRI, which can be carried out with or without contrast agent, can show all structures of the inflammatory tissue, including the soft tissues (e.g., synovial membrane, tendons). Early changes, in particular, can be better or earlier detected than through X-rays.

**INFO**

**Any persistent joint swelling and any permanent joint pain, as well as a reduction in general well-being, should no longer be accepted in the future, but should instead prompt the patient to see a doctor.**

## What other disease may be similar?

Especially because the clinical picture of RA is often very non-specific at the beginning, numerous other diseases may also be considered as the cause of the symptoms. It is the doctor's job to differentiate between the various clinical pictures, taking into account all available information and diagnostic indications, in order to reach the correct diagnosis as early as possible.

The most important diseases to differentiate from RA include degenerative joint disease (arthrosis), gout, ankylosing spondylitis (Bechterew's disease), psoriatic arthritis, joint inflammation caused by infections (e.g., Lyme arthritis), and many other inflammatory or chronic diseases of the joints and connective tissue.

# Information on treatment.

**Find out what is possible today.**

The main treatment goals for RA are to relieve pain, stop joint destruction, and maintain joint functionality. While it was possible to achieve alleviation of symptoms in the past, there is now, thanks to modern treatment options, a good chance of achieving extensive or even complete regression of disease symptoms (remission) and thus a symptom-free state.

During the course of treatment, certain check-ups should be performed at regular intervals to identify possible side effects and/or to determine whether the patient is responding to the therapy. Particularly important for monitoring and checking therapeutic success are the physical examination, the laboratory chemistry tests, the recording of scores such as the DAS28 and, if necessary, the addition of imaging procedures.

If a treatment does not show sufficient efficacy after several months, the doctor must change the therapy.

The treatment generally consists of several different therapeutic procedures, the most important of which are explained below.

**INFO**

**Doctors and patients must consider the therapeutic goal of remission at every point of the disease. A patient who has significant symptoms or who tolerates their medication poorly is not well treated.**

**The treatment regimen must be reconsidered and changed in this case.**

## Medicinal treatment

Because RA is a disease that can affect the whole body, drugs are usually given internally (systemically) to achieve an effect throughout the body, if necessary. In addition, local treatment measures can be helpful on the joints.

Here you can basically distinguish between two approaches: Drugs that only treat symptoms, e.g. swelling and pain (cortisone and cortisone-free anti-inflammatory drugs), and drugs that also interfere with the disease process or have a beneficial effect on the course of the disease (disease-modifying drugs or basic therapeutics).

+ **1. Symptomatic therapy with cortisone-free anti-inflammatory drugs**
+ **2. Glucocorticoids**
+ **3. Basic therapeutics**
  - **3a. Conventional synthetic basic therapeutics**
  - **3b. Basic biological therapeutics**
  - **3c. Targeted synthetic basic therapeutics JAK inhibitors**

### + 1. Symptomatic therapy with cortisone-free anti-inflammatory drugs*

Cortisone-free non-steroidal anti-inflammatory drugs (NSAIDs) primarily have an anti-inflammatory and pain-relieving (analgesic) effect, i.e. they affect inflammatory symptoms such as joint swelling, hyperthermia and stiffness, as well as the pain caused by inflammation. However, they only affect the symptoms and not the causes.

Some substances in this drug class (e.g., acetylsalicylic acid, ibuprofen, diclofenac) are known to cause gastrointestinal symptoms (nausea, bleeding, etc.) as typical side effects. Newer representatives of this drug class are the so-called COX-2 inhibitors, which are better tolerated by the stomach due to a more specific mode of action.

* Please refer to the information in the appropriate package leaflet

## 2. Glucocorticoids (cortisone)*

Cortisone is an artificially (synthetically) produced derivative of cortisol, a natural hormone of the adrenal cortex. It has a variety of effects in the human body. Cortisone preparations (e.g., prednisolone) are also known in medical lingo as glucocorticoids, corticoids, or steroids. They are used for many diseases including RA, mainly because of their strong anti-inflammatory effect.

They affect both local inflammation and systemic inflammation in the body. Therefore, they not only have beneficial effects on the pain caused by inflammation, but also on the general symptoms of the disease and on the signs of inflammation that can be measured in the blood.

The effect of cortisone begins within a few days and is thus significantly faster than with basic therapeutics (see the following chapter). However, the symptoms and inflammatory changes in the blood may return after discontinuation. In addition, cortisone alone is not able to stop the changes in chronic inflammation at the joint cartilage or bones. Due to side effects, cortisone preparations can only be used in high doses for a short time (e.g., during a flare-up or at the start of therapy). They are dosed at very low doses in long-term use. According to current therapy recommendations, glucocorticoids should initially be administered as a supplement to classic basic therapeutics.

In the case of acute and severe inflammation of a joint, glucocorticoids can be injected directly into the joint (i.e., intra-articularly) in the form of a so-called crystal suspension to provide rapid relief of pain and swelling. However, this procedure is only suitable for individual joints.

* Please refer to the information in the appropriate package leaflet

## 3. Basic therapeutics

Active substances in this group are also known as long-acting antirheumatic drugs or disease-modifying substances (Anglo-American DMARDs = Disease Modifying Antirheumatic Drugs). The active substances differ from cortisone-free anti-inflammatory drugs and glucocorticoids in that they are able to stop or at least significantly reduce damage caused by chronic inflammation of the articular cartilage or bones.

The most commonly used conventional basic therapeutics currently used in rheumatology are methotrexate, sulfasalazine, hydroxychloroquine and leflunomide.

All basic therapeutics relieve the pain caused by inflammation and result in a regression of the local signs of inflammation. However, in contrast to the drug classes mentioned so far, this only applies to medium-term and long-term use. Similar to cortisone, disease-modifying substances also work against systemic inflammation, resulting in a normalization of the signs of inflammation measurable in the blood.

Long-acting antirheumatic drugs should be used as early as possible after a confirmed diagnosis, in order to stop imminent bone destruction or organ changes. The choice of medication must be made on a case-by-case basis. Patient co-morbidities and inflammatory activity are considered. Most preparations can be used as monotherapy (only one active substance) or in combination with one or more other active substances.

With basic therapeutics, it is only after weeks to months that an assessment can be made on how effective they are. Therefore, it is important not to stop taking them, even if no noticeable success can be seen at the beginning. If, despite a sufficient duration of therapy, no satisfactory effect is achieved or if the therapy is associated with undesirable side effects, the doctor will decide whether it makes sense to change the active substance or to combine it with another medicinal product.

For all long-acting antirheumatic drugs, treatment must be continued for a long time and only works if the drug is taken regularly. This also means that therapy must be continued even if improvement occurs, or should be continued for as long as an effect can be seen. Otherwise, a flare-up or worsening may occur again after discontinuation.

As with any effective treatment, undesirable effects can also occur with basic therapeutic agents. If you notice any unusual symptoms during therapy, you should inform your doctor as soon as possible. In order to detect in a timely manner any side effects that may occur, and in order to take the necessary measures, regular check-ups with the doctor are necessary. The doctor will perform a physical examination of you and, depending on the type of medication, will arrange for certain laboratory values to be checked and, if necessary, further tests.

Some basic therapeutics must not be used during pregnancy and breastfeeding. Women of childbearing potential who are taking basic therapy, and in some cases, also afterwards, must use reliable contraception and first talk to their doctor about the available options before planning a pregnancy.

Men who are taking basic therapy should also talk to their doctor about their desire to have children. This also means that you should inform your doctor at an early stage if you wish to have children. The most important basic therapeutics are explained below. Only the most important information is listed.

**INFO**

**If you are taking any of these medications, you should consult your doctor for more information about what to consider specifically when using these medications.**

## 3a. Conventional basic therapeutics

### + Methotrexate*

Methotrexate (MTX) is a drug with various effects. At high doses, it inhibits the proliferation of cells – an effect that is used in cancer therapy. At low doses, it has an anti-inflammatory effect and influences immunological processes. In RA, MTX is given at low-doses and works by interfering with the inflammatory process and inhibiting excessive immune responses.

MTX is administered once a week. It is available in tablet form. Other pharmaceutical forms are the pre-filled syringe and pen, which can be used to administer a subcutaneous injection (i.e., under the skin – like an insulin injection) by the doctor or patient themselves.

The effect of MTX can generally be noticed after approximately four to eight weeks. If therapy is unsuccessful, the dose is often increased first.

The most common side effects are changes in the liver and blood count. To protect the liver, patients should only use alcohol with caution during MTX treatment. In addition, intense exposure to sunlight should be avoided.

Please read the package leaflet or ask your treating doctor about any side effects that may occur. Administering folic acid 24 hours after MTX may counteract some of the side effects.

* Please refer to the information in the appropriate package leaflet

### + Sulfasalazine*

Sulfasalazine has a weaker effect compared to MTX. It is usually taken in tablet form twice a day. The dose is initially low and is gradually increased over the first few weeks. The onset of action is expected after approximately four to twelve weeks. Only after a total of six months can it be safely assessed whether sulfasalazine is sufficiently effective.

Please read the package leaflet or ask your treating doctor about any side effects that may occur. Most undesirable effects occur mainly during the first few weeks of treatment.

### INFO

**MTX has been used successfully for several decades for the treatment of RA and other inflammatory rheumatic diseases.**

**It is the most commonly prescribed basic therapeutic agent in RA. Numerous scientific studies prove the efficacy and applicability of MTX, both as a single agent and in combination with other drugs.**

### + Leflunomide*

Leflunomide works in RA by inhibiting inflammation, impaired immune system responses, and increased tissue proliferation. It is usually taken in tablet form once a day. The effect occurs after about four to six weeks. The success of therapy can only be reliably assessed after four months at the earliest.

Please read the package leaflet or ask your treating doctor about any side effects that may occur.

### + Antimalarials: Chloroquine, hydroxychloroquine*

The two substances chloroquine and hydroxychloroquine are also used to prevent and treat the tropical disease malaria. In RA, they work by weakening immunological reactions. They are used primarily in combination with other basic therapeutics. The effects are expected after three to four months, and sometimes only after six months. Both drugs are only available in tablet form. Dosing is based on body weight.

Most side effects occur mainly during the first few weeks of treatment. Please read the package leaflet or ask your treating doctor about any side effects that may occur. You must avoid intense sun exposure during treatment. At the start of treatment, vision problems, such as blurred vision, sensitivity to light, or color vision disorders sometimes occur. These changes are harmless and disappear after a short time. During treatment, retinal changes can develop very rarely, but the ophthalmologist can detect these in good time before permanent damage occurs.

### + Other basic therapeutics*

Other commonly used conventional basic therapeutics are either no longer available today (gold as an injectable pharmaceutical form) or are only used in exceptional cases (azathioprine, cyclosporine A).

* Please refer to the information in the appropriate package leaflet

## 3b. Basic biological therapeutics*

The so-called biologics (biologicals) are a new generation of medicines developed for a wide range of diseases. They are distinct, genetically produced proteins that achieve their therapeutic effect by promoting or inhibiting the activity of naturally occurring substances. They are made from living cells, using biotechnological methods.

Essentially, they are monoclonal, i.e., antibodies that are derived from a cell and have a uniform structure, cell messengers, or other proteins called fusion proteins. The biologics were developed to specifically intervene at different levels in the disturbed immunological processes that play a role in the development of RA and other chronic inflammatory diseases. They work by inhibiting growth and inflammation-promoting messenger substances, thereby preventing interaction between the cells involved in the development of pathological states.

Important targets include, for example, the messenger substances tumor necrosis factor-alpha (TNF-α) or interleukin (IL)-6. These messenger substances act on different cells by attaching to specific protein structures on the cell surface, which are known as receptors. These receptors transmit critical signals to the cell. Some biologics work by blocking the messenger substances themselves, while others occupy their receptors, thereby also preventing the messenger substances from taking effect.

**INFO**

**Modern therapy with biologics and JAK inhibitors intervenes in the inflammatory process in a more targeted and effective way than was possible with the previous basic medications. It has a stronger anti-inflammatory effect and is also well tolerated.**

**Studies have now reliably proven that the combination of traditional basic medications with the new biologics provides the best therapeutic results.**

* Please refer to the information in the appropriate package leaflet

Most preparations are injected under the skin (subcutaneously) and can also be self-administered by the patient following appropriate instructions.

Since biologics have a very targeted effect, they appear to have less of an impact on normal (physiological) processes in the body and have fewer side effects than conventional medicines. In the most favorable case, some substances can trigger repair processes and support the regression of the resulting changes, even when joint damage has already occurred. Please read the package leaflet or ask your treating doctor about any side effects that may occur.

As with basic therapeutics, biologics must not be used during pregnancy and breastfeeding. Women of childbearing potential who are under therapy with biologics, and in some cases, also afterwards, must use reliable contraception and first talk to their doctor about the available options before planning a pregnancy.

Because the development and production of these substances are very complex, their use is expensive compared to conventional therapies.

Therefore, the biologics are primarily an option for the treatment of patients with progressive forms of RA who fail to respond adequately to conventional basic therapeutics, or for whom the latter are unable to be used due to contraindications or side effects. Even in very severe cases, significant improvements can still be achieved. An effect generally occurs within a few weeks.

**INFO**

**Certainly, many patients with early rheumatoid arthritis (which has been present for no more than two years) achieve the desired remission with biologics therapy. The response to high inflammatory activity is also good.**

**However, the experience of the last few years has shown that patients with long-standing RA can also still derive significant benefit from therapy with TNF-α antagonists.**

## 3c. Targeted synthetic basic therapeutics – JAK inhibitors*

The latest medications available for the treatment of RA are JAK inhibitors. The JAK inhibitors are so-called “small molecules”; they are synthetically manufactured substances that are much smaller than the monoclonal antibodies presented in the previous chapter. These are inhibitors of a group of proteins involved in the transfer of information into the cell, otherwise known as Janus kinases (JAK). JAKs transmit the effect of different cytokines in the cell. By inhibiting them, the signals of several cytokines are inhibited, unlike the biologics that block one cytokine at a time. Depending on the preparation (there are already several JAK inhibitors and others are in development), the effects of various cytokines are inhibited at varying degrees. This means that different JAK inhibitors can also have different effects in individual patients.

Overall, JAK inhibitors are characterized by a relatively rapid onset of action. JAK inhibitors are taken by mouth and are used in combination with methotrexate or alone as a long-term background therapy. As with all immunosuppressants, particular attention must be paid to infections during use, and regular laboratory tests (blood draws) must be carried out. Please read the package leaflet or ask your treating doctor about any side effects that may occur.

* Please refer to the information in the appropriate package leaflet

## Other treatment options

### + Physical treatment measures

In order to maintain the functionality of the joints, physical treatment measures that consist of various procedures are necessary in addition to drug therapy for pain relief and suppression of inflammation. They should be tailored to each patient. Examples include cold or heat therapy, baths, massages, and electrotherapy. They serve to relieve pain, reduce inflammation, and promote muscle relaxation and blood circulation.

Cold therapy is particularly useful for acute joint inflammation because it reduces swelling and inflammation. Cold can be applied locally (cryotherapy, e.g. ice packs) or throughout the body (cold chamber).

It is particularly important to adapt physical therapy to the particular stage of the disease, with the aim of restoring or maintaining the best possible mobility.

Special movement exercises are carried out under professional guidance. Many of these exercises can also be performed regularly at home once they have been properly learned.

Occupational therapy can also be helpful. It is designed to help improve or relearn restricted movement sequences through exercises. This strengthens the patient's independence in the private and professional environments. Sometimes medical aids are also necessary.

These measures may help to preserve function (for longer) and to improve the ability to deal with any limitations in daily life or to better overcome the problems these cause.  The occupational therapists also provide advice on aids for everyday life and how to use them correctly.

## Surgical procedures

Sometimes RA also requires surgical intervention, both to prevent joint destruction and, much more commonly, to preserve the function of the joints. In the case of individual or few joints, the pathologically altered synovial tissue can be removed by endoscopic surgery (i.e., joint endoscopy). Such a procedure is called a synovectomy.

If damage to the joint or tendons has already occurred, reconstructive, i.e. restorative surgery may improve function. An arthrodesis or fitting of a joint replacement (endoprosthesis) is sometimes necessary.

Whether and when such surgery makes sense depends on many circumstances, such as the type and function of the joint, the stage of the disease, and the extent of destruction.

## Radiosynoviorthesis

In order to completely remove any residual tissue that may still be present after surgical removal of the synovium, for example, a radiosynoviorthesis is usually performed in addition some time after the procedure. This involves a radioactive substance being injected into the joint and leads to the destruction of the inflammatory abnormal tissue.

## Other concomitant measures

The treatment procedures described above may be supported by additional measures as needed. These can also be easily combined with conventional drug treatment.

Various methods can be helpful, such as behavioral therapy, relaxation exercises, meditation, yoga, or Tai Chi. They enable better stress management and pain management, and lead to an improved quality of life and to a better disease course in the long term. Finally, these methods can also help to better manage mental health problems related to the disease, such as symptoms of depression or fatigue.

You share responsibility here too: not all symptoms caused by RA can be made to “magically disappear” with medication. You are making a massively important contribution through the mentioned exemplary measures.

You will need to find out over time which method is right for you and suits you best. Because not every procedure is suitable for all patients. Of course, you can also consult your doctor or therapist.

## INFO

**Since RA not only leaves a physical mark on affected individuals, but also causes great psychological burden, accompanying psychotherapy and/or psychosocial care can often be of great help to better manage the many problems associated with the disease.**

**Pain reactions can also be influenced favorably by targeted strategies.**

## Alternative treatment

There is a wealth of medicines and procedures from the field of “alternative medicine” for the (supportive) treatment of rheumatic diseases. The so-called “complementary” procedures include therapies with bioresonance, Bach’s flowers, autologous blood or urine therapy, oscillation, and much more. They are not used in classical medicine because their efficacy has not been clearly proven.

Many herbal active substances (phytotherapy) are said to have an anti-inflammatory or cortisone-like effect. However, none of these substances were tested according to the criteria of “traditional medicinal substances”. Herbal products may also have side effects.

Caution should be exercised whenever a drug does not have the expected effect, even after prolonged use. These therapies in and of themselves cannot replace basic therapy!

On the contrary: Delaying or even preventing more effective measures such as basic therapy can lead to permanent joint damage.

Nevertheless, an alternative remedy may be helpful in individual cases and can support the specific therapy. If you have had good experiences with a method yourself, there is usually nothing to contraindicate its use. However, you should always discuss the use of alternative methods of treatment with your treating doctor beforehand!

### INFO

**Particularly in more severe forms of RA, “gentle” methods, such as herbal remedies, are usually not sufficient to prevent the progressive destruction of joints.**

# Living with rheumatoid arthritis.

## Tips for self-help and lifestyle management in everyday life.

### Tips for self-help and lifestyle assistance in everyday life

For a long time, rheumatism was considered a fate you had to accept without being able to do much about it. Thankfully, these times are over: Thanks to modern treatment options, it is now increasingly possible to halt or significantly slow down the progression of destructive disease processes and to achieve a state of being largely or even completely free of symptoms.

Nonetheless, living with a chronic, incurable illness can be stressful and burdensome. In addition, treatment and supportive care often require a lot of effort and additional time. The following tips may help you to live and better cope with the disease, and show you how to contribute to the success of the treatment yourself.

+ **Try to think positively** and not to dwell too much on your fate. With a positive and confident attitude, you can better cope with many of the stresses and impairments associated with the disease and therapy.

+ **Don't allow the illness to impact too much on your everyday,** but try to structure life in such a way that you can continue to enjoy it, finding pleasure in things and undertaking leisure activities, travel, etc. with your family or friends.

+ **Be informed about your disease**, and get help and advice from experts and other people affected, e.g. through patient organizations. A worry shared is a worry halved, which is why support groups are so important. You know you are not alone in your problems and will also receive a range of support.

+ Even if each treatment or additional procedure requires extra time and commitment, you should make the effort in the interest of your health.

**INFO**

**An optimistic attitude is desirable, but not always easy to maintain in everyday life. Pertinent to this is the fact that according to modern understanding, a patient with rheumatoid arthritis is able to lead a close to normal life in all spheres, and he/she should also actively strive to do so.**

**TIP**

**Support groups are very useful for patients with chronic illnesses. They provide important help and perform a variety of tasks. By talking to other people, the person affected can learn new information, perhaps find encouragement, and possibly even make friends. Support groups also represent the interests of patients in public life and politics.**

## Physical exercise and sport

"A rolling stone gathers no moss" – this is especially true for rheumatism patients. Through targeted training, blood flow and nutrition is improved to parts of the musculoskeletal system (bones, cartilage, muscles), thus improving muscle strength and endurance. This helps to maintain physical and emotional well-being. Not insignificantly, physical activity also has very positive psychological effects.

As with physical therapy, each training session must be adapted to the individual patient's health and training status. Sometimes only passive exercises are possible, e.g. where there is particularly pronounced disease activity or acute relapses. With low disease activity and good health status, targeted endurance and/or strength training is also feasible. However, such activities should be discussed with the doctor or physical therapist beforehand.

Strength training adapted to the overall condition is also particularly beneficial as part of osteoporosis prophylaxis or in cases of already known osteoporosis.

Exercises that put little strain on the joints are recommended. These include swimming (especially backstroke), cycling, (Nordic) walking, or cross-country skiing. On the other hand, you should avoid sports that can lead to overexertion, faulty loading and damage to the joints. These include, but are not limited to, sports with abrupt movements and sudden stops, such as tennis, squash, soccer or other ball sports. Seek advice from a physical therapist in this regard.

It is best to have them create a customized training program that is tailored to your needs and that you can follow independently and on a regular basis.

**INFO**

**Regular exercise is particularly necessary and useful for rheumatism, helping to prevent stiffening of the joints, to strengthen muscles and tendons (relieving pressure on the joints), and to prevent bad posture. This also applies to joints that have already been affected by the disease.**

## Dietary tips

To date, there is no scientifically proven evidence that diet has a decisive impact on the development or course of RA. Therefore, there is no special rheumatism diet. Nevertheless, some patients with rheumatism observe a connection between the consumption of certain foods and a deterioration (or even improvement) of their symptoms. For example, sometimes nuts, dairy products, sweets, fatty foods, or meats, especially in larger amounts, are not tolerated. There is no patent remedy here. See for yourself what you are eating or not eating, or how your body reacts to eating certain foods. If you clearly notice a deterioration in your condition after several attempts, it makes sense to avoid the food in question.

A balanced, wholesome diet is generally recommended. This includes plenty of fresh fruits and vegetables, salads, cereals (whole grain products), legumes and low-fat dairy products. In addition, the following tips may be helpful:

+ **Prioritize plant-based foods.** Reduce your consumption of meat and sausage products to a maximum of two meals per week. Replace animal fats largely with vegetable oils.

+ **Eat more fish.** The unsaturated omega-3 fatty acids contained in fish oilsare
known to have anti-inflammatory effects. They can be found mainly in fatty sea fish, such as salmon or mackerel. We therefore recommend one to two meals with sea fish per week. Afterconsulting a doctor, appropriate nutritional supplements of omega-3 fatty acids (salmon oil capsules) can also be taken.

+ **Be sure to avoid being overweight**, as this puts extra stress on the joints. However, if you lose weight, you should only lose the weight slowly.

+ **Moderate fasting can reduce disease activity.** However, it should be discussed with the doctor and should under no circumstances lead to being underweight or to an impairment in your health.

+ **Avoid excessive alcohol consumption,** as this may cause inflammation.

+ **Be sure to stop smoking.** Smokers are at increased risk of more severe disease, cardiovascular complications, and development of rheumatoid nodules.

### INFO

**For more information on eating and drinking with rheumatism, read our booklet.**

# Glossary

## A

**Analgesic (plural: analgesics)**
Pain medication

**Anamnesis**
Medical history

**Ankylosing spondylitis (= Bechterew's disease)**
Specific form of chronic inflammatory joint disease

**Ankylosis**
Bony stiffening

**Antagonist**
Substance directed against a particular effect or structure (e.g. receptor)

**Antibody (= immunoglobulin)**
Protein (protein molecule) produced as a response to the immune system and that specifically targets a particular substance or structure (antigen)

**Antigen**
Foreign (or own) substance that can trigger an immune reaction

**Anti-inflammatory**
Antiphlogistic

**Antiphlogistic**
Anti-inflammatory

**Antirheumatic drug (plural: antirheumatics)**
Drugs for the treatment of rheumatic diseases, with different modes of action

**Arthritis**
Inflammation of a joint

**Arthrodesis**
Immobilization of a joint

**Arthropathy**
(inflammatory or degenerative) disease of a joint

**Arthroscopy**
Joint endoscopy

**Arthrosis**
Chronic degenerative joint change (due to overuse or overloading)

**Autoantibody**
Antibody against the body's own tissue; autoantibodies can be detected in autoimmune diseases

## B

**Balneotherapy**
Treatment with baths

**Basic therapeutic agent (DMARD = Disease Modifying Antirheumatic Drug)**
Long-acting disease-modifying antirheumatic drug

**Bechterew's disease**
See Ankylosing spondylitis; Morbus (Latin) = disease

**Biologic (plural: biologics, biologicals)**
Active substances produced by biotechnological processes, "biological substances"

**Blood (cell) sedimentation rate (ESR)**
Speed at which the blood cells (erythrocytes) settle to the bottom of a tube due to gravity if you allow a blood sample (with an anticoagulant) to stand for one or two hours. Increased ESR may indicate acute or chronic inflammation in the body.

**Blood count**
Collective term for laboratory tests in which the quantity of the cell components of the blood (blood cells, blood pigment) is determined

## C

**Cortisone**
Artificially-produced derivative of cortisol, a hormone produced in the adrenal gland; belongs to the glucocorticoids

**C-reactive protein (CRP)**
Protein, whose concentration in the blood serum can increase up to 1,000 times within a few hours during certain inflammatory processes

**Crohn's disease**
Chronic inflammatory bowel disease

**Cyclooxygenase (COX)**
Enzyme complex that plays a key role in prostaglandin production

**Cytokine**
An umbrella term for numerous body-produced messenger substances that transmit signals between cells of the immune system and other cells, thereby playing an important role in immune responses. Among other things, cytokines have numerous pro-inflammatory, immunoregulatory, and hematologic functions. Cytokines include, for instance, interleukins or TNF-α .

## D

**Dactylitis**
Inflammation and swelling of an entire finger or toe

**Dermatology**
Field of medicine that deals with diseases of the skin, of skin appendages and of mucous membranes

**Differential diagnosis**
Differentiation and profile of similar diseases

**DMARD**
See basic therapeutic agent

## E

**Effusion**
Accumulation of fluid, e.g. in the joint; usually visible externally as swelling, which can also be painful due to pressure on neighboring nerves

**Endoprosthesis**
Part made of foreign material to replace a body part, e.g. joint replacement

**Enthesitis**
Inflammation of a tendon attachment

**Extra-articular**
Organ(s) (organ system(s)) other than the joints

## G

**Glucocorticoids (cortico(stero)ids)**
Group of drugs that are derived from cortisone and have predominantly anti-inflammatory effects but also have a range of other effects

## H

**HLA system (= Human leukocyte antigen system)**
System of human tissue antigens found on the cells of almost all tissues and detected particularly well on leukocytes

## I

**Immune system**
Defense system; totality of all structures (cells, antibodies, messenger substances, etc.) in the body that are responsible for defending against foreign substances (antigens) or abnormally produced cells (cancers) of the body

**Immunology**
The study of the structure and function of the immune system

**Immunosuppressant (plural: immunosuppressants)**
Drug that suppresses or weakens the immune system's reactions

**Immunosuppressive**
Suppressing or debilitating the immune response

**Interleukins (IL)**
Messenger substances produced by leukocytes (white blood cells) that mediate the transfer of information within the immune system, activate other cells, and also have hormone-like effects; depending on type (IL-1, IL-6 TNF-α, etc.), the interleukins exert a variety of effects

**Intra-articular**
In or within the joint

**Iritis**
Inflammation of the iris of the eye

## J

**JAK-I**
The JAK inhibitors are so-called "small molecules"; synthetically manufactured substances that are much smaller than monoclonal antibodies.

**Juvenile idiopathic arthritis**
Form of chronic joint inflammation that mainly affects children and/or adolescents

## L

**Leukocyte**
White blood cell

**Lymphocyte**
Subtype of white blood cell (leukocyte) that plays an important role in defense

## M

**Macrophage**
Subtype of white blood cells (leukocytes) that are part of the immune system; macrophages can "digest" foreign substances and are therefore also referred to as scavenger cells

**Mediators**
Messenger substances that help the communication between cells

**Mon(o)arthritis**
Inflammation of a (single) joint

**Mon(o)articular**
Affecting a (single) joint

**Monoclonal**
Derived or formed from one cell

**Monotherapy**
Treatment with only one medication or active substance

## N

**Non-steroidal anti-inflammatory drug (NSAID)**
Active substance not derived from cortisone (steroid), with pain-relieving and anti-inflammatory effect, based on inhibition of prostaglandin production

## O

**Oligoarthritis**
Inflammation of a few joints (usually 1 to 3 joints)

**Oligoarticular**
Affecting few joints

**Oral**
In the/by mouth

**Osteoporosis**
Disease of the bones with loss or reduction of bone substance, resulting in an increased risk of fractures

## P

**Pannus**
Cellular mass that invades and destroys cartilage and bone; characteristic feature of RA

**Parenteral**
Bypassing the digestive tract

**Pathogenesis**
Origin and development of diseases

**Phototherapy**
Treatment by natural or artificial light rays

**Pitted nails**
Nail changes typical of psoriasis and psoriatic arthritis, with small (up to the size of a pinhead), dimple-shaped depressions in the nail plate caused by a nail growth disorder

+ **Placebo**
Sham drug

+ **Plaque**
On the skin: flat raised, plate-like skin lesions, typical of psoriasis

+ **Polyarthritis**
Inflammation of several or many joints

+ **Polyarticular**
Affecting many joints

+ **Prognosis**
Assessment of the foreseeable outcome of a disease or condition

+ **Progression**
Progression of a disease or a change

+ **Progressive**
Advancing, progressing

+ **Pro-inflammatory**
Causing inflammation

+ **Prosthesis**
Artificial replacement of body parts

+ **Psoriatic arthritis**
Chronic inflammatory joint disease, which is usually associated with psoriasis (scaly psoriasis) of the skin and/or nails

+ **Protein**
Protein substance

+ **PUVA (= Psoralen + UVA)**
UVA radiation with the addition of Psoralen to increase light sensitivity (photochemotherapy); Psoralen can be given in tablet form or applied topically. A special form is PUVA bathing therapy, in which the substance is added to the bath water.

## R

+ **Receptor**
Structure of a cell, usually located on the cell surface, which can pick up the signals transmitted by messenger substances and forward them to the nucleus; receptors specialize in certain messenger substances and enable the cell to react to this messenger

+ **Rehabilitation**
Recovery, reintegration or even prevention to eliminate health disorders

+ **Remission**
Permanent or temporary disappearance of symptoms of the disease; symptom-free state

+ **Rheumatoid arthritis (RA), chronic polyarthritis**
Chronic inflammatory disease of the joints; colloquially also called rheumatism

+ **Rheumatoid factor (RF)**
Antibody against the body's own proteins; it can be detected in the blood serum ("positive") in some chronic rheumatic diseases, especially in the majority of patients with rheumatoid arthritis, and rarely also in healthy individuals

## S

+ **Spondylitis**
Inflammation in the area of the spinal column

+ **Spondyloarthropathy (spondyloarthritis)**
Inflammatory rheumatic disease, predominantly with changes in the spine

+ **Steroid**
See Corticosteroids

+ **Subcutaneous (SC)**
Under the skin

+ **Synovial fluid = synovium**
Viscous fluid contained in the joint cavities (= synovial cavities) that helps reduce friction between the bone surfaces

+ **Synovial joint**
Joint in which the involved bone surfaces are covered with a layer of articular cartilage, and which has a synovial cavity that is filled with synovial fluid and lined with a synovial membrane and reinforced by a connective tissue capsule and ligaments

+ **Synovial membrane (= synovium)**
The inner skin of the joint capsule that lines the joint cavity and produces synovial fluid

+ **Synovitis (= synovialitis)**
Inflammation of the synovial membrane

+ **Systemic**
An entire organ system or (in the broader sense) multiple organ systems, i.e. affecting the entire organism

## T

+ **Tumor necrosis factor-alpha inhibitor**
(TNF-α inhibitor) Naturally occurring messenger substance (cytokine) of the immune system with diverse influences, playing, among other things, a central role in a large number of inflammatory processes

## U

+ **Ulcerative colitis**
Chronic inflammatory bowel disease

# Additional information.

Knowledge is power.
Be smart and strong
about your disease.

## Support groups

+ **Deutsche Rheuma-Liga Bundesverband e.V.**
**[German Rheumatism League]**
Maximilianstr. 14
D-53111 Bonn
Tel.: 02 28 / 766 70 80
Fax: 02 28 / 766 06 20
**www.rheuma-liga.de**

The Deutsche Rheuma-Liga is the largest support organization in the health sector, with approximately 300,000 members. The organization provides, among other things, help and support for those affected, exercise programs, education of the public, and representation of the interests of people suffering from rheumatism.

## Consulting services online

+ **www.rheumanet.org**
The Deutsche Rheumahaus [German Rheumatology House] offers a range of information and links on rheumatic diseases.
+ **www.rheuma-online.de**
A to Z information on rheumatism; current news about the disease and treatment options, opportunity to exchange experiences with those affected
+ **www.rhzm.de**
Rheumazentrum München [Munich Rheumatology Center]: Rheumatism from A to Z, with numerous photos of psoriatic arthritis and the option to search for a doctor
+ **https://dgrh.de/Patienten.html**
Deutsche Gesellschaft für Rheumatologie e.V.
[German Society for Rheumatology]

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