



Annex 3: Patient information document. Use of **Tocilizumab to Treat Rheumatoid Arthritis**

Evidence Based Medicine

Official recommendations

Expert opinion

To give you a good understanding of the benefits and specificities of tocilizumab treatment, this document supplies you with practical answers to ten questions.

Tocilizumab therapy may require changes in the dosage of other medications. When you receive your first tocilizumab injection, and when you stop tocilizumab therapy, remember to give your doctor the full list of medications you are taking. Your doctor will be able to determine whether you need adjustments in the doses.

What is tocilizumab?

Tocilizumab is a medication that treats rheumatoid arthritis by regulating your immune system in order to alleviate your symptoms such as joint pain and swelling. This medication may also improve your ability to go about your daily activities. The objective of tocilizumab therapy is to halt the progression of your disease by diminishing your risk of experiencing further joint damage (joint space narrowing and bone erosions).

Why did your rheumatologist suggest tocilizumab treatment?

Your rheumatologist suggested tocilizumab because this medication has been proven effective in patients with rheumatoid arthritis. Tocilizumab is used in adults who have active moderate-to-severe rheumatoid arthritis and who did not respond adequately to earlier treatments. Tocilizumab was granted a marketing licence (AMM) in 2009 in France. You and your rheumatologist have decided together to use tocilizumab to treat your disease, based on the features of your disease and on your own characteristics (past medical history, infections, allergies ...).

How does tocilizumab work?

Tocilizumab is one of the “biotherapies” or “biologics”. These names mean that tocilizumab specifically acts to prevent the stimulation of a biological component of your immune system. More specifically, tocilizumab is a monoclonal antibody that blocks the effects of a specific protein (a cytokine) called interleukin-6. This protein is involved in the inflammatory processes that take place in the body, and blocking it is an effective way of combating inflammation.

What are the risks of tocilizumab therapy?

The main risk is the occurrence of infections that may develop because tocilizumab blunts the immune responses of the body. The most common infections affect the lungs, lower airways, and urinary tract. Most of them are non-serious infections that are easy to treat.

Tocilizumab may induce complications that can be diagnosed only by blood tests (decrease in the number of white blood cells in blood, known as neutropenia or leukopenia; decrease in the number of platelets, known as thrombocytopenia; increase in the cholesterol level; and abnormalities in liver function tests known as cytolysis). For this reason, your doctor will monitor you during and after the treatment, and you will have blood samples drawn. You must inform your doctor of any symptoms you may experience.

How is tocilizumab used?

Tocilizumab can only be given in hospitals. Your doctor will refer you to a hospital department where the specialists have acquired experience with tocilizumab and are accredited to use it. Tocilizumab must be given as an intravenous infusion once every 4 weeks. The infusion contains only tocilizumab and requires 1 hour to administer on a day-hospital basis.

You will continue your other treatments for rheumatoid arthritis. In particular, methotrexate is useful, as it increases the effectiveness of tocilizumab. Do not change your treatment without first talking to your doctor. In some cases, however, tocilizumab may be used alone, if your doctor feels that methotrexate therapy is not appropriate.

What will happen before the first tocilizumab infusion?

Your doctor will ask questions about several important points.

- You must be aware of all the medications that you take, as their effectiveness may in some cases be affected by the addition of tocilizumab. Therefore, it is important that you give your doctor the full list of all the medications you use so that he/she can adjust their dosages if needed.
- You must have detailed information on your medical history. In particular, it is important to know whether you have a history of
 - infections
 - viral hepatitis (B or C)
 - tuberculosis
 - diverticulitis or intestinal ulcers. The symptoms may consist of abdominal pain and of an unexplained change in bowel habits with a fever.
 - heart disease, hypertension, or too much cholesterol
 - lung disease or any other chronic disease
 - allergies to medications or foods

- You must check that you are properly immunised against tetanus and polio, and your doctor may recommend that you receive vaccines against influenza and pneumococcal disease. If your immunisations are not up to date, you will have to receive new shots.
- If you are a woman, you must make sure that you are not pregnant, and if you have just had a baby, you will not be able to breast-feed, since the effects of tocilizumab during pregnancy and breast-feeding are not known.
- Whether you are a woman or a man, you must use effective contraception throughout the treatment with tocilizumab. If you want a baby, you must discuss your plans with your doctor before stopping your contraception.

If you have any questions before the first tocilizumab infusion, feel free to discuss them with your doctor.

What will happen during the rituximab infusion?

You will be expected at the hospital early in the morning. The infusion will last about 1 hour. You can eat breakfast before leaving home except if you are scheduled to have blood drawn for a cholesterol test. Remember to bring the things you might need (such as books, drinks, your phone...).

If you have an infection of any kind (even a simple cold) on the day your infusion is scheduled, the infusion can be postponed until you feel better. Feel free to contact your doctor or the day-hospital nurse before the infusion to tell them about the infection.

You will be comfortable during the infusion. You will be able to read, listen to music, or watch television.

During the infusion, pay attention to any abnormal symptoms that might indicate a reaction to the medication. Such reactions are rare with tocilizumab.

These symptoms may consist of trouble breathing, swelling of your tongue or lips, a headache, a feeling of warmth and/or shivering, redness or itching of the skin, nausea and/or vomiting, itchiness inside your nose and/or sneezing, itchiness in your throat, pain in your chest, and/or an abnormally fast heartbeat.

You must report all your symptoms to the nurse in charge of monitoring you. If you experience symptoms of any kind, the nurse will stop or slow the infusion and call the doctor working in the hospital department. If your symptoms resolve rapidly, the doctor may decide to continue the infusion. Severe reactions that require permanent discontinuation of the infusion are very rare.

If you experience any symptoms during the infusion, you will be monitored at the hospital for at least 2 hours before going home.

What will happen after the infusion?

If the infusion went well, you will return home. You may leave with a family member or friend or ask us to help you find an appropriate means of transportation.

Between the infusions, you will go on with your life normally.

Pay attention to any possible symptoms during the first few hours and days following the infusion, although delayed allergic reactions are exceedingly rare.

Until the next infusion, pay attention to any symptoms that may indicate an infection. These symptoms may consist of a fever, chills, a sore throat or bad cold, an unusual cough and/or trouble breathing, a burning sensation during urination, back pain, weight loss, spots on your skin (redness, swelling, blisters) or breaks in your skin, or marked weakness.

Patients who are taking tocilizumab may experience a form of abdominal infection known as diverticulitis, although this is uncommon. Obtain advice from a doctor immediately if you have stomach pains or abdominal cramps or if you pass blood through your rectum.

Feel free to contact your rheumatologist if you notice anything that is unusual, or talk to your primary doctor if needed. It is better to ask questions right away than to wait. Do not take any medications without first talking to your doctor.

How and when will you notice the effects of the treatment?

Tocilizumab has been proven effective in rheumatoid arthritis. Tocilizumab improves not only the pain and fatigue, but also the joint swelling. You should be aware, however, that the full effect often requires several weeks to develop. You will objectively document your improvements with your doctor, who will perform a physical examination and order blood tests to evaluate the degree of inflammation (based on the erythrocyte sedimentation rate [ESR] and/or C-reactive protein [CRP] level). The longer-term effectiveness of the treatment will be assessed by obtaining radiographs of your hands and feet about 1 year after the first infusion.

How long should tocilizumab be used?

Tocilizumab therapy may induce a remission, but the disease relapses if the treatment is stopped. Therefore, if tocilizumab is effective and well tolerated, it should be continued. The maximum treatment duration is unknown, but some patients will require tocilizumab for several years at least.

Your rheumatologist will see you at least once every 6 months to perform a physical examination, ask questions, and order blood tests for monitoring the degree of inflammation. You will discuss further tocilizumab therapy with your rheumatologist.

In the intervals between rheumatologist visits, you will see your primary doctor if needed, according to the course of your joint disease and to whether you have other health problems that require attention, such as infections that may be precipitated by the treatment.

We hope this information was helpful.

If you have any questions, feel free to discuss them with your doctor or the other healthcare professionals.