It's time to FIGHT BACK

For moderate to severe Rheumatoid Arthritis (RA)

What is ORENCIA?
ORENCIA (abatacept) is a prescription biologic medicine used to reduce signs and symptoms of moderate to severe Rheumatoid Arthritis (RA) in adults 18 years and older. Taking ORENCIA may prevent further damage to your bones and joints, and may help your ability to perform daily activities. ORENCIA may help those who are not getting the results they need with other medicines for RA.

In adults, ORENCIA may be used alone or with other RA treatments, but should not be used with TNF-blockers (also called Tumor Necrosis Factor antagonists). TNF-blockers are a type of RA medication, and include such treatments as Enbrel® (etanercept), Humira® (adalimumab), and Remicade® (infliximab).

Please read the Important Facts About ORENCIA on pages 20-25.
Don’t wait to talk to your doctor
For adults with moderate to severe Rheumatoid Arthritis (RA), joint damage is progressive and may be permanent. If symptoms still hold you back despite your current treatment, it may be time to consider a change. Early diagnosis and appropriate treatment are an important part of preventing further joint damage.

Fight back with ORENCIA
• Reduces the pain and swelling of moderate to severe RA in adults
• Can help stop further joint damage
• Works differently by targeting a source of RA early in the inflammation process
• Has helped new RA patients and those not helped enough by other RA treatments, including Enbrel® (etanercept), Humira® (adalimumab), and Remicade® (infliximab)
• Prescribed by rheumatologists for 12 years and counting

Selected Important Facts About ORENCIA
Serious side effects
Serious side effects are those that may require medical treatment or hospitalization, cause permanent damage, or be life-threatening or sometimes even fatal. Talk to your healthcare provider about any concerns you may have.

• Infections. ORENCIA can make you more likely to get infections or make the infections that you have worse. In some cases, these infections have been fatal. Symptoms of an infection include:
  • Fever
  • Cough
  • Warm, red, or painful skin
  • Feeling very tired
  • Flu-like symptoms

Call your healthcare provider right away if you feel sick or have any of the symptoms of an infection.

“I first realized how effective ORENCIA was for me when I was able to make plans for something I wanted to do.”

Betsy, actual ORENCIA® (abatacept) patient.

*Individual results may vary.*
Moderate to severe Rheumatoid Arthritis (RA) can be such a difficult disease because it keeps you struggling to do the everyday things that you really want to and have to do.

One of the hardest things is that your RA may not be obvious to your friends and loved ones. The next few pages were designed as a visual tool that you can use to learn more about RA, and talk to those that are closest to you.

**What is RA, and what causes it?**

RA is an autoimmune disease, meaning your immune system becomes overactive and mistakenly attacks the healthy tissues in your own body. In RA, a key target of the overactive immune system is the lining of the joints, also known as the synovium.

The exact cause of RA is unknown. RA may be influenced by many risk factors, including:

- Genes
- Infection
- Hormonal changes
- Environmental factors

**What's happening on the inside?**

The pain and swelling occurs because the lining of your joint, called the synovium, becomes swollen or inflamed. The synovium is an important part of the capsules that support and protect your joints. Lining the inside of the capsules, a healthy synovium produces fluid that lubricates and nourishes your joints. RA affects joints that have a synovium, such as fingers, knees, and hips.

**What does this mean for me?**

RA is chronic, which means it doesn’t go away. Moderate to severe RA can result in joint stiffness and reduced mobility, and can make daily activities like getting ready in the morning difficult. Early diagnosis and appropriate treatment are an important part of preventing further joint damage. The treatment goals for each patient may be different, but can include:

- Decreasing pain
- Reducing inflammation
- Stopping/slowing further joint damage
- Improving physical function

Work with your rheumatologist to find the right treatment for you.

*Please read the Important Facts About ORENCIA on pages 20-25.*
How ORENCIA® (abatacept) works

In order to understand how ORENCIA works, it’s helpful to take a closer look at some of the cells of the immune system that are particularly important to the inflammation that happens in Rheumatoid Arthritis (RA).

The Science Behind ORENCIA

T cells play a key role in your immune system, and are particularly important in the chain of events that are believed to lead to the inflammation in RA.

In RA, your immune system confuses some of your own cells as foreign invaders, and T cells may be mistakenly activated.

Activated T cells send signals to the other inflammatory cells of the immune system, calling them into action.

These other inflammatory cells send out signals of their own. These signals are thought to be linked to inflammation in RA.

ORENCIA works by targeting a source of RA early in the inflammation process

ORENCIA is a biologic DMARD (disease-modifying antirheumatic drug) that works early in the chain of events leading to inflammation in RA. It works by getting in the way of T-cell activation, reducing the amount of signals that can be sent.

Many other DMARDs work by getting in the way of the signals that have been sent to wake up other inflammatory cells in the immune system.

Anti-inflammatories decrease inflammation.

See the science in action at ORENCIA.com/MOA

Selected Important Facts About ORENCIA

Serious side effects

- **Allergic reactions.** Allergic reactions can happen with ORENCIA. Symptoms of an allergic reaction may include:
  - Hives
  - Swollen face, eyelids, lips, or tongue
  - Trouble breathing

Seek urgent medical attention if you have any of the symptoms of an allergic reaction.

See the glossary on pages 16-19 for key terms.
ORENCIA has been studied in approximately 2,000 patients to see how well it would work in people with moderate to severe Rheumatoid Arthritis (RA) who have not been helped enough by the treatments they have taken.

Clinical Trial 1 studied how well ORENCIA intravenous (IV) infusion worked in patients with moderate to severe RA, who haven’t been helped enough by MTX.

At 6 months, patients’ signs and symptoms were measured, and at 1 year, their physical function and joint damage were assessed.

On average, the ORENCIA IV group saw:

- Greater improvement in pain as measured at 6 months
  - ORENCIA IV group: 42% improvement
  - Control group: 3% improvement

- Greater improvement in physical function as measured at 1 year
  - ORENCIA IV group: 37% improvement
  - Control group: 20% improvement

Physical function is assessed using a patient questionnaire about dressing and grooming, arising, eating, walking, hygiene, reach, grip, and common daily activities.

Clinical Trial 2 studied how well ORENCIA intravenous (IV) infusion worked in patients with moderate to severe RA, who haven’t been helped enough by TNF-blockers.

At 6 months, patients’ signs and symptoms as well as physical function were measured.

On average, the ORENCIA IV group saw:

- Greater improvement in pain as measured at 6 months
  - ORENCIA IV group: 28% improvement
  - Control group: 6% improvement

- Greater improvement in physical function as measured at 6 months
  - ORENCIA IV group: 25% improvement
  - Control group: 5% improvement

It is important to note that every patient is different. How you respond to treatment may vary from how other patients respond.

Selected Important Facts About ORENCIA

Most common side effects
Clinical studies looked at 1,955 patients who took ORENCIA. The most commonly reported side effects occurred in 10% or more of patients.

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These are not all of the possible side effects of ORENCIA. If you have any questions or want more information about side effects, ask your rheumatologist or healthcare provider. If you experience any side effects and would like to report them to the FDA, you can call 1-800-FDA-1088.

How to read this page: Choose the treatment history closest to yours and follow the dotted line to learn about the trial results that are most relevant to you.

Please read the Important Facts About ORENCIA on pages 20-25.
Trial data: What about a self-injectable option?

ORENCIA® (abatacept) is also available as a once-weekly self-injection

Clinical Trial 3 compared ORENCIA IV and ORENCIA self-injection in patients who weren’t helped enough by methotrexate (MTX).

Clinical Trial 3 showed that the improvement in signs and symptoms and reported side effects were similar for ORENCIA IV and ORENCIA self-injection.

Selected Important Facts About ORENCIA

Serious side effects

- If you are receiving or are scheduled to receive vaccinations, it is important to know that:
  - You should not receive live vaccines while taking ORENCIA and for 3 months after ending treatment, as it may cause serious side effects.
  - ORENCIA may also cause some other vaccinations to be less effective.

Talk to your rheumatologist about your vaccination plans.

Trial data: What were the common side effects?

The safety of ORENCIA was studied across all the clinical trials. Here are the side effects that occurred in at least 3% of patients who took ORENCIA, and at least 1% more frequently in ORENCIA-treated patients across all trials.

- Headache
  - ORENCIA + DMARDs (1955 patients): 18% vs. DMARDS only (989 patients): 13%
- Nasopharyngitis*
  - ORENCIA + DMARDs (1955 patients): 12% vs. DMARDs only (989 patients): 9%
- Dizziness
  - ORENCIA + DMARDs (1955 patients): 9% vs. DMARDs only (989 patients): 7%
- Cough
  - ORENCIA + DMARDs (1955 patients): 8% vs. DMARDs only (989 patients): 7%
- Back pain
  - ORENCIA + DMARDs (1955 patients): 7% vs. DMARDs only (989 patients): 6%
- Pain in extremity
  - ORENCIA + DMARDs (1955 patients): 3% vs. DMARDs only (989 patients): 2%
- Rash
  - ORENCIA + DMARDs (1955 patients): 4% vs. DMARDs only (989 patients): 3%
- Urinary tract infection
  - ORENCIA + DMARDs (1955 patients): 6% vs. DMARDs only (989 patients): 5%
- Heartburn
  - ORENCIA + DMARDs (1955 patients): 6% vs. DMARDs only (989 patients): 4%
- High blood pressure
  - ORENCIA + DMARDs (1955 patients): 7% vs. DMARDs only (989 patients): 4%
- Difficulty sleeping
  - ORENCIA + DMARDs (1955 patients): 7% vs. DMARDs only (989 patients): 6%

* Nasopharyngitis: Inflammation of the nose and throat (characterized by sneezing, stuffy nose, cough, sore throat).
ORENCIA® (abatacept) offers three administration options

ORENCIA is the only biologic for moderate to severe Rheumatoid Arthritis (RA) that offers three administration options.

ORENCIA IV Infusion
- An IV (through a vein) infusion of ORENCIA is given in your arm by a healthcare professional. This once-a-month procedure at the doctor’s office or infusion center usually takes about 30 minutes.*

* Dosing at Days 1, 15, and 29 and every 4 weeks thereafter.

ORENCIA Prefilled Syringe
- A self-injection (under the skin) is something you can do yourself after initial training at your doctor’s office. This once-weekly procedure can also be done in the comfort of your home.

ORENCIA ClickJect™ Autoinjector
- ORENCIA’s newest dosing technology, the ClickJect™ Autoinjector, is an accurate and easy-to-use self-injector designed with RA patients in mind.
- The non-slip grip and lightweight, ergonomic design of the ClickJect™ Autoinjector helps with handling and control.
- The large viewing window and blue indicator help confirm the full dose of ORENCIA has been injected.

To learn more about ORENCIA dosing options, including instructions for use, visit ORENCIA.com/dosing

Education is everything
When you’re educated about your moderate to severe RA, you feel empowered as a patient. Staying well-informed and up to date can help you get the best treatment results.

Here are some helpful resources:
Arthritis Foundation
http://www.arthritis.org

Creaky Joints: Arthritis Resource Community
https://www.creakyjoints.org

American College of Rheumatology (ACR)
http://www.rheumatology.org (See “Patient Information”)

This list of resources is provided as a convenience. Bristol-Myers Squibb does not endorse and is not responsible for information provided by third-party organizations.

Selected Important Facts About ORENCIA

Serious side effects
- If you have Chronic Obstructive Pulmonary Disease (COPD), you may experience breathing problems more often while taking ORENCIA. Call your healthcare provider if you experience any of the following:
  - Worsened COPD
  - Cough
  - Trouble breathing

Visit ORENCIA.com for all things ORENCIA.
Answer the questions below and discuss your responses with your rheumatologist:

- On a scale of 1-10, how satisfied are you with your current moderate to severe Rheumatoid Arthritis (RA) treatment?

- What RA treatment are you taking now?

- Is it providing enough relief? Yes  No

- How often do you experience pain on average?

- Where are you currently experiencing pain and swelling? Circle all that apply.

- What everyday activities are you struggling with? (Climbing stairs, turning doorknobs, getting dressed, etc.)

- Which administration option would you like to discuss with your rheumatologist? An ORENCIA 30-minute monthly infusion* or weekly self-injection?

*Dosing at Days 1, 15, and 29 and every 4 weeks thereafter.

Selected Important Facts About ORENCIA

Serious side effects

- Certain kinds of cancer (malignancies) have been reported in people using ORENCIA. It is not known if ORENCIA increases your chances of developing certain kinds of cancer.
T Cells

T cells are a type of white blood cell, and are part of your immune system.

T cells are normally activated when they find a sign of a foreign invader. When this happens, they send signals to wake up other parts of your immune system to deal with the foreign invaders.

T-Cell Activation

T cells can be activated by Antigen-Presenting Cells (APCs). An APC's job is to present T cells with parts of foreign invaders (antigens) that they have collected in the body.

APCs activate T cells through two signals, 1 and 2.

Once activated, T cells send out signals that affect other parts of the immune system. T cells cannot be activated without either of these signals.

Selected Important Facts About ORENCIA

Most common side effects

Clinical studies looked at 1,955 patients who took ORENCIA. The most commonly reported side effects occurred in 10% or more of patients.

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These are not all of the possible side effects of ORENCIA. If you have any questions or want more information about side effects, ask your rheumatologist or healthcare provider.

If you experience any side effects and would like to report them to the FDA, you can call 1-800-FDA-1088.

Disease-Modifying Antirheumatic Drugs (DMARDs)

Disease-modifying antirheumatic drugs (DMARDs) are a group of medications that help calm the overactive immune system and inflammatory activities in the body. There are two categories of DMARDs: biologic (created to be similar to proteins found in the body) and non-biologic. The following is a list of examples:

<table>
<thead>
<tr>
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<th>Non-biologic DMARDs</th>
</tr>
</thead>
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<tr>
<td>TNF-blockers:</td>
<td>methotrexate</td>
</tr>
<tr>
<td>Enbrel® (etanercept)</td>
<td>hydroxychloroquine</td>
</tr>
<tr>
<td>Humira® (adalimumab)</td>
<td>leflunomide</td>
</tr>
<tr>
<td>Simponi® (golimumab)</td>
<td>sulfasalazine</td>
</tr>
<tr>
<td>Cimzia® (certolizumab pegol)</td>
<td>JAK-inhibitor:</td>
</tr>
<tr>
<td>Remicade® (infliximab)</td>
<td>Xeljanz® (tofacitinib citrate)</td>
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How ORENCIA® (abatacept) works

ORENCIA works early in the inflammation process, at the point where APCs activate T cells.

T cells need two signals, 1 and 2, from APCs to become activated. ORENCIA interrupts signal 2, blocking T-cell activation.
**What does ‘improvement in pain’ mean?**

A patient’s assessment of their pain levels is a core part of the American College of Rheumatology (ACR) criteria. The ACR criteria are a well-accepted measure of patient improvement in clinical trials.

**How ‘improvement in pain’ is calculated**

‘Improvement in pain’ is calculated by comparing patients’ pain levels at the beginning of the trial to patients’ pain levels at a set time in the trial (eg, at 6 months).

**How physical pain is measured**

Physical pain is measured by having patients pick a relative pain level along a ‘visual analog scale’ (VAS) from 0 to 100.

![VAS scale](image)

**What does ‘improvement in physical function’ mean?**

A patient’s assessment of their physical function is a core part of the American College of Rheumatology (ACR) criteria. The ACR criteria are a well-accepted measure of patient improvement in clinical trials.

**How ‘improvement in physical function’ is calculated**

‘Improvement in physical function’ is calculated by comparing patients’ Health Assessment Questionnaire Disability Index (HAQ-DI) score at the beginning of the trial to patients’ physical function at a set time in the trial (eg, at 6 months).

**How physical function is measured**

Physical function is determined by the HAQ-DI questionnaire that patients fill out. A score is calculated based on questions about the difficulty patients had in the past week with activities in eight categories, and what kind of aids they may be using for each. Scores can range from 0 to 3.

**Categories**

1. Dressing and grooming
2. Arising*
3. Eating
4. Walking
5. Hygiene
6. Reach
7. Grip
8. Common daily activities

**Difficulty**

- 0: Without ANY difficulty
- 1: With SOME difficulty
- 2: With MUCH difficulty
- 3: UNABLE to do

*Arising: standing up from a straight chair, getting in and out of bed.
What should I discuss with my rheumatologist before starting ORENCIA?

Talk to your rheumatologist about all of your medical conditions, including if:

- You have any kind of infection, as you may have a higher chance of getting serious side effects from an infection while taking ORENCIA. Infections include:
  - Small infections (such as an open cut or sore) to whole body infections (such as the flu).
  - Any infection that will not go away or a history of infections that keep coming back.
  - Viral hepatitis, a viral infection that affects the liver.
  - Tell your rheumatologist if you have or have ever had viral hepatitis. Before starting ORENCIA, your rheumatologist may examine you for hepatitis.
  - Tuberculosis (TB), a type of lung infection. Tell your rheumatologist if you have ever had TB or a positive skin test for TB, or have recently been in close contact with someone who has ever had TB. Before starting ORENCIA, your rheumatologist may check you for TB or do a skin test. Call your rheumatologist if you notice any symptoms of TB, including: a cough that does not go away, weight loss, fever, or night sweats.

- You have allergies to the ingredients of ORENCIA. For a list of ingredients, see What are the ingredients in ORENCIA? in the Patient Information section of the Full Prescribing Information.

- You have Chronic Obstructive Pulmonary Disease (COPD), a type of lung disease.

- You have diabetes. Your healthcare provider may tell you to use a different way to monitor your blood sugar levels on the day that you receive ORENCIA IV infusion. ORENCIA IV contains maltose, which can alter the blood sugar readings with certain types of blood glucose monitors.

Tell your rheumatologist about all of your medical treatments, including if:

- You are scheduled to have surgery.
- You recently received or are scheduled to receive vaccinations.
- You are taking:
  - Other medications for RA.
  - Prescription medications or over-the-counter medications.
  - Vitamins or herbal supplements.

Please read the Important Facts About ORENCIA continued on the following pages.
What are the possible side effects of ORENCIA? (continued)

Serious side effects
Serious side effects are those that may require medical treatment or hospitalization, cause permanent damage, or be life-threatening or sometimes even fatal. Talk to your healthcare provider about any concerns you may have.

- **Infections.** ORENCIA can make you more likely to get infections or make the infections that you have worse. In some cases, these infections have been fatal. Symptoms of an infection include:
  - Fever
  - Cough
  - Warm, red, or painful skin

Call your healthcare provider right away if you feel sick or have any of the symptoms of an infection.

- **Allergic reactions.** Allergic reactions can happen with ORENCIA. Symptoms of an allergic reaction may include:
  - Hives
  - Swollen face, eyelids, lips, or tongue
  - Trouble breathing

Seek urgent medical attention if you have any of the symptoms of an allergic reaction.

- **If you have the hepatitis B virus,** talk to your healthcare provider as hepatitis B can become an active infection while you use ORENCIA. Your rheumatologist may do blood tests before treatment with ORENCIA to check if you have hepatitis B.

- **If you are receiving or are scheduled to receive vaccinations,** it is important to know that:
  - You should not receive live vaccines while taking ORENCIA and for 3 months after ending treatment, as it may cause serious side effects.
  - ORENCIA may also cause some other vaccinations to be less effective.
What are the possible side effects of ORENCIA? (continued)

- If you have Chronic Obstructive Pulmonary Disease (COPD), you may experience breathing problems more often while taking ORENCIA. Call your healthcare provider if you experience any of the following:
  - Worsened COPD
  - Cough
  - Trouble breathing

- Certain kinds of cancer (malignancies) have been reported in people using ORENCIA. It is not known if ORENCIA increases your chances of developing certain kinds of cancer.

Most common side effects

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If you experience any side effects and would like to report them to the FDA, you can call 1-800-FDA-1088.

How will I receive ORENCIA?

ORENCIA is available in two forms, as intravenous (IV) infusions and as subcutaneous (SC) injections. Work with your rheumatologist to determine the right treatment plan for you.

- **ORENCIA IV infusion** is given by a healthcare provider through a vein in your arm.
  - You will receive your first three infusions 2 weeks apart from each other (weeks 0, 2, and 4). After that, you will receive an infusion every 4 weeks.
  - Each infusion takes about 30 minutes, though actual time in the clinic will be longer.

- **ORENCIA SC injection** is a shot that is given just under your skin. It is available as a prefilled syringe or ClickJect™ Autoinjector. If your rheumatologist decides that your injections can be given at home, you or your caregiver will receive training on how to prepare and inject ORENCIA. Do not try to inject ORENCIA until you have been shown the right way by your rheumatologist or healthcare provider.
  - You will use ORENCIA SC injection once weekly.
  - For more information about preparing and giving ORENCIA SC injections at home, see Instructions for Use in the Patient Information section of the Full Prescribing Information.

Please click here to read the Patient Information in the Full Prescribing Information for ORENCIA.
FIGHT BACK with support on your side.
Managing your moderate to severe Rheumatoid Arthritis (RA) can be challenging. You may have lots of questions about the disease, ORENCIA insurance coverage, or co-pay assistance. Whether you’re looking to change your treatment or currently taking ORENCIA, On Call™ is here to help.

ORENCIA On Call™ provides free services, including:
• 24/7 personal Care Counselors and nurse support*†
• Help understanding your ORENCIA insurance coverage
• Educational materials that may help you throughout your treatment

Enrolling is easy.
Call 1-800-ORENCIA
(1-800-673-6242)
Visit ORENCIA.com

ORENCIA® (abatacept) On Call™
Comprehensive support. Human connection.

The ORENCIA Co-pay Assistance Program offers savings to eligible patients who self-inject ORENCIA
• $5 out-of-pocket drug cost per one-month supply
• No monthly benefit limit
• 12 uses per calendar year, maximum benefit $15,000
Eligibility requirements and Terms and Conditions apply. Please see Terms and Conditions in pocket.

“My outlook now is I have RA, but RA doesn’t have me. I need to live my life.”
Callia, actual ORENCIA® (abatacept) patient.
Individual results may vary.

Selected Important Facts About ORENCIA
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Learn more at [ORENCIA.com](http://ORENCIA.com)

Please click here to read the Patient Information in the Full Prescribing Information for ORENCIA.