Package leaflet: Information for the patient
ORENCIA 250 mg powder for concentrate for solution for infusion
abatacept

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What ORENCIA is and what it is used for

ORENCIA contains the active substance abatacept, a protein produced in cell cultures. ORENCIA lessens the immune system's attack on normal tissues by interfering with the immune cells (called T lymphocytes) that contribute to the development of rheumatoid arthritis. ORENCIA selectively modulates the activation of T cells involved in the immune systems' inflammatory response.

ORENCIA is used to treat rheumatoid arthritis and psoriatic arthritis in adults and also polyarticular juvenile idiopathic arthritis in children 6 years of age and older.

Rheumatoid Arthritis
Rheumatoid arthritis is a long-term progressive systemic disease that, if untreated, can lead to serious consequences, such as joint destruction, increased disability and impairment of daily activities. In people with rheumatoid arthritis the body's own immune system attacks normal body tissues, leading to pain and swelling of the joints. This can cause joint damage. Rheumatoid arthritis (RA) affects everyone differently. In most people, joint symptoms develop gradually over several years. However, in some, RA may progress rapidly and yet other people may have RA for a limited period of time and then enter a period of remission. RA is usually a chronic (long-term), progressive disease. This means, even if you're on treatment, whether or not you're still having symptoms, RA could be continuing to damage your joints. By finding the right treatment plan for you, you may be able to slow down this disease process, which may help reduce long-term joint damage, as well as pain and fatigue and improve your overall quality of life.

ORENCIA is used to treat moderate to severe active rheumatoid arthritis when you do not respond well enough to treatment with other disease-modifying medicines or with another group of medicines called 'tumour necrosis factor (TNF) blockers'. It is used in combination with a medicine called methotrexate.
ORENCIA can also be used with methotrexate to treat highly active and progressive rheumatoid arthritis without previous methotrexate treatment.

Psoriatic Arthritis
Psoriatic arthritis is an inflammatory disease of the joints, usually accompanied by psoriasis, an inflammatory disease of the skin. If you have active psoriatic arthritis you will first be given other medicines. If you do not respond well enough to these medicines, you may be given ORENCIA to:
- Reduce the signs and symptoms of your disease.
- Slow down the damage to your bones and joints.
- Improve your physical function and your ability to do normal daily activities.

ORENCIA is used to treat psoriatic arthritis alone or in combination with methotrexate.

Polyarticular Juvenile Idiopathic Arthritis
Polyarticular juvenile idiopathic arthritis is a long-term inflammatory disease affecting one or more joints in children and adolescents.
ORENCIA powder for concentrate for solution for infusion is used in children and adolescents aged 6 to 17 years when a previous disease-modifying medicine has not worked well enough or is not suitable for them. ORENCIA is usually used in combination with methotrexate, although ORENCIA may also be used alone in case of intolerance to methotrexate or if treatment with methotrexate is inappropriate.

ORENCIA is used to:
- slow down the damage to joints
- improve physical function
- improve other signs and symptoms of polyarticular juvenile idiopathic arthritis

2. What you need to know before you are given ORENCIA

You should not be given ORENCIA
- **if you are allergic** to abatacept or any of the other ingredients of this medicine (listed in section 6).
- **if you have a severe or uncontrolled infection**, do not start treatment with ORENCIA. Having an infection could put you at risk of serious side effects from ORENCIA.

Warnings and precautions
Talk to your doctor, pharmacist or nurse:
- **if you experience allergic reactions** such as chest tightness, wheezing, severe dizziness or lightheadedness, swelling or skin rash **tell your doctor immediately**.
- **if you have any kind of infection**, including long-term or localised infection, if you often get infections or **if you have symptoms of infection (e.g. fever, malaise, dental problems), it is important to tell your doctor.** ORENCIA can lower your body's ability to fight infection and the treatment can make you more likely to get infections or make any infection you have worse.
- **if you have had tuberculosis (TB)** or have symptoms of tuberculosis (persistent cough, weight loss, listlessness, mild fever) **tell your doctor**. Before you are given ORENCIA, your doctor will examine you for tuberculosis or do a skin test.
- **if you have viral hepatitis** tell your doctor. Before you are given ORENCIA, your doctor may examine you for hepatitis.
- **if you have cancer,** your doctor will decide if you can still be given ORENCIA.
- **if you recently had a vaccination** or are planning to have one, **tell your doctor**. Some vaccines should not be given while you are receiving ORENCIA. **Check with your doctor before you are given any vaccines.** It is recommended that patients with polyarticular juvenile idiopathic arthritis, if possible, be brought up to date with all immunisations in agreement with current immunisation guidelines prior to starting ORENCIA therapy. Certain vaccinations may cause infections from the vaccine. If you received ORENCIA while you were pregnant, your baby may be at a higher risk for getting such an infection for up to approximately 14 weeks after the last dose you received during pregnancy. It is important that you tell your baby’s doctors and other health care professionals about your ORENCIA use during your pregnancy so they can decide when your baby should receive any vaccine.
- **if you are using a blood glucose monitor** to check your blood glucose levels. ORENCIA contains maltose, which is a type of sugar that can give falsely high blood glucose readings with certain types of blood glucose monitors. Your doctor may recommend a different method for monitoring your blood glucose levels.

Your doctor may also do tests to examine your blood values.

Children and adolescents
ORENCIA powder for concentrate for solution for infusion has not been studied in children and adolescents under 6 years of age, therefore ORENCIA powder for concentrate for infusion is not recommended for use in this patient population.
ORENCIA solution for injection pre-filled syringe is available for subcutaneous administration for paediatric patients 2 years of age and older.

Other medicines and ORENCIA
Tell your doctor if you are taking, have recently taken or might take any other medicines.
ORENCIA should not be used with biological medicines for rheumatoid arthritis, including TNF-blockers like adalimumab, etanercept, and infliximab; there is not enough evidence to recommend its being given with anakinra and rituximab.

ORENCIA can be received with other medicines commonly used to treat rheumatoid arthritis, such as steroids or painkillers, including non-steroidal anti-inflammatories such as ibuprofen or diclofenac. Ask your doctor or pharmacist for advice before taking any other medicine while using ORENCIA.

Pregnancy and breast-feeding
The effects of ORENCIA in pregnancy are not known, so you should not be given ORENCIA if you are pregnant unless your doctor specifically recommends it.

- if you are a woman who could become pregnant, you must use reliable contraception (birth control) while using ORENCIA and up to 14 weeks after the last dose. Your doctor will advise you on suitable methods.
- if you become pregnant while using ORENCIA, tell your doctor.

If you received ORENCIA during your pregnancy, your baby may have a higher risk for getting an infection. It is important that you tell your baby's doctors and other health care professionals about your ORENCIA use during your pregnancy before the baby receives any vaccine (for more information see section on vaccination).

It is not known whether ORENCIA passes into human milk. **You must stop breast-feeding** if you are being treated with ORENCIA and for up to 14 weeks after the last dose.

Driving and using machines
The use of ORENCIA is not expected to affect the ability to drive, cycle or use machines. However, if you are feeling tired or unwell after receiving ORENCIA, you should not drive, cycle or operate any machinery.

ORENCIA contains sodium
This medicine contains 34.5 mg sodium (main component of cooking/table salt) per maximum dose of 4 vials (8.625 mg sodium per vial). This is equivalent to 1.7% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use ORENCIA

ORENCIA will be given to you under the supervision of an experienced doctor.

Recommended dose in adults
The recommended dose of abatacept for adults with rheumatoid arthritis or psoriatic arthritis is based on body weight:

Your weight	Dose	Vials
Less than 60 kg	500 mg	2
60 kg - 100 kg	750 mg	3
More than 100 kg	1,000 mg	4

Your doctor will advise you on the duration of treatment and what other medicines, including other disease-modifying medicines, if any, you may continue to take while on ORENCIA.

ORENCIA can be used by adults over 65 with no change in dose.

Use in children and adolescents
For children and adolescents aged 6 to 17 years with polyarticular juvenile idiopathic arthritis who weigh less than 75 kg, the recommended dose of intravenous abatacept is 10 mg/kg. Children weighing 75 kg or more should be administered ORENCIA powder for concentrate for solution for infusion following the adult dosing regimen.

How ORENCIA is given to you
ORENCIA is given to you into a vein, usually in your arm, over a period of 30 minutes. This procedure is referred to as an infusion. Healthcare professionals will monitor you while you receive your ORENCIA infusion.
ORENCIA is supplied as a powder for solution for infusion. This means that before ORENCIA is given to you, it is first dissolved in water for injections, then further diluted with sodium chloride 9 mg/mL (0.9%) solution for injection.

How often ORENCIA is given to you
ORENCIA should be given to you again, 2 and then 4 weeks after the first infusion. After that you will receive a dose every 4 weeks. Your doctor will advise you on the duration of treatment and what other medicines you may continue to take while on ORENCIA.

If you are given more ORENCIA than you should
If this happens, your doctor will monitor you for any signs or symptoms of side effects, and treat these symptoms if necessary.

If you forget to receive ORENCIA
If you miss receiving ORENCIA when you are supposed to, ask your doctor when to schedule your next dose.

If you stop using ORENCIA
The decision to stop using ORENCIA should be discussed with your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
The most common side effects with ORENCIA are infections of the upper airway (including infections of the nose and throat), headache and nausea, as listed below. ORENCIA can cause serious side effects, which may need treatment.

Possible serious side effects include serious infections, malignancies (cancer) and allergic reactions, as listed below.

Tell your doctor immediately if you notice any of the following:
- severe rash, hives or other signs of allergic reaction
- swollen face, hands or feet
- trouble breathing or swallowing
- fever, persistent cough, weight loss, listlessness

Tell your doctor as soon as possible if you notice any of the following:
- feeling generally unwell, dental problems, burning sensation during urination, painful skin rash, painful skin blisters, coughing

The symptoms described above can be signs of the side effects listed below, all of which have been observed with ORENCIA in adult clinical trials:

Very common (may affect more than 1 in 10 people):
- infections of the upper airway (including infections of the nose, throat and sinuses).

Common (may affect up to 1 in 10 people):
- infections of lungs, urinary infections, painful skin blisters (herpes), flu
- headache, dizziness
- high blood pressure
- cough
- abdominal pain, diarrhoea, nausea, upset stomach, mouth sores, vomiting
- rash
- fatigue, weakness
- abnormal liver function tests

Uncommon (may affect up to 1 in 100 people):
- tooth infection, nail fungal infection, infection in the muscles, blood stream infection, collection of pus under the skin, kidney infection, ear infection
- low white blood cells count
- skin cancer, skin warts
- low blood platelet count
- allergic reactions
- depression, anxiety, sleep disturbance
- migraine
- numbness
- dry eye, reduced vision
- eye inflammation
- palpitation, rapid heart rate, low heart rate
- low blood pressure, hot flush, blood vessels inflammation, flushing
- difficulty in breathing, wheezing, shortness of breath, acute worsening of a lung disease called chronic obstructive pulmonary disease (COPD)
- throat tightness
- rhinitis
- increased tendency to bruise, dry skin, psoriasis, skin redness, excessive sweating, acne
- hair loss, itching, hives
- painful joints
- pain in the extremities
- absence of menstruation, excessive menses
- flu-like illness, increased weight, infusion-related reactions

Rare (may affect up to 1 in 1,000 people):
- tuberculosis
- inflammation of uterus, fallopian tubes and/or ovaries
- gastrointestinal infection
- cancer of white blood cells, lung cancer

<u>Children and adolescents with polyarticular juvenile idiopathic arthritis</u>

The side effects experienced in children and adolescents with polyarticular juvenile idiopathic arthritis are similar to those experienced in adults as described above, with the following differences:

Common (may affect up to 1 in 10 people):
- upper airway infection (including infections of nose, sinus and throat)
- fever

Uncommon (may affect up to 1 in 100 people):
- blood in urine
- ear infection

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

5. How to store ORENCIA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C).

Store in the original package in order to protect from light.

After reconstitution and dilution, the infusion solution is stable for 24 hours in a refrigerator, but for bacteriological reasons, it is to be used immediately.

Do not use this medicine if you notice opaque particles, discolouration or other foreign particles present in the infusion solution.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What ORENCIA contains
- The active substance is abatacept. Each vial contains 250 mg of abatacept.
- After reconstitution, each mL contains 25 mg of abatacept.

- The other ingredients are maltose, sodium dihydrogen phosphate monohydrate and sodium chloride (see section 2 "ORENCIA contains sodium").

What ORENCIA looks like and contents of the pack
ORENCIA powder for concentrate for solution for infusion is a white to off-white powder that can appear solid or broken into pieces.
ORENCIA is available in packs of 1 vial and 1 silicone-free syringe, and in multipacks containing 2, or 3 vials and 2, or 3 silicone-free syringes (2 or 3 packs of 1).

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Bristol-Myers Squibb Pharma EEIG
Plaza 254
Blanchardstown Corporate Park 2
Dublin 15, D15 T867
Ireland

Manufacturer

Swords Laboratories Unlimited Company t/a Bristol-Myers Squibb Cruiserath Biologics
Cruiserath Road, Mulhuddart
Dublin 15
Ireland

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The following information is intended for healthcare professionals only

Reconstitution and dilution should be performed in accordance with good practices rules, particularly with respect to asepsis.

Dose selection: see section 3 'How to use ORENCIA' of the Package Leaflet

Reconstitution of vials: under aseptic conditions, reconstitute each vial with 10 mL of water for injections, using the **silicone-free disposable syringe provided with each vial** and an 18-21 gauge needle. Remove the flip-top from the vial and wipe the top with an alcohol swab. Insert the syringe needle into the vial through the centre of the rubber stopper and direct the stream of water for injections to the glass wall of the vial. Do not use the vial if a vacuum is not present. Remove the syringe and needle after 10 mL of water for injections have been injected into the vial. To minimise foam formation in solutions of ORENCIA the vial should be rotated with gentle swirling until the contents are completely dissolved. **Do not shake**. **Do not use prolonged or vigorous agitation**. Upon complete dissolution of the powder, the vial should be vented with a needle to dissipate any foam that may be present. After reconstitution the solution should be clear and colourless to pale yellow. Do not use if opaque particles, discolouration, or other foreign particles are present.

Preparation of infusion: immediately after reconstitution, dilute the concentrate to 100 mL with sodium chloride 9 mg/mL (0.9%) solution for injection. From a 100 mL infusion bag or bottle, withdraw a volume of 0.9% sodium chloride injection equal to the volume of the reconstituted ORENCIA vials. Slowly add the reconstituted ORENCIA solution from each vial to the infusion bag or bottle using the same **silicone-free disposable syringe provided with each vial**. Gently mix. The final concentration of abatacept in the bag or bottle will depend upon the amount of active substance added, but will be no more than 10 mg/mL.

Administration: when reconstitution and dilution are performed under aseptic conditions ORENCIA infusion solution can be used immediately or within 24 hours if stored refrigerated at 2°C to 8°C. However, for microbiological reasons, it is to be used immediately. Prior to administration, the ORENCIA solution should be inspected visually for particulate matter and discolouration. Discard the solution if any particulate matter or discolouration is observed. The entire, fully diluted ORENCIA solution should be administered over a period of 30 minutes and must be administered with an infusion set and a sterile, non-pyrogenic, low-protein-binding filter (pore size of 0.2 to 1.2 mcm). Do not store any unused portion of the infusion solution for reuse.

Other medicines: ORENCIA should not be mixed with other medicines or infused concomitantly in the same intravenous line with other medicines. No physical or biochemical compatibility studies have been conducted to evaluate the co-administration of ORENCIA with other medicines.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.