Patient leaflet in accordance with the
Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Orencia 250 mg

Powder for concentrate for solution for infusion

The active ingredient and its quantity:
abatacept 250 mg

For a list of inactive ingredients please see section 6 and "Important information about some of this medicine's ingredients" in section 2.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Orencia 250 mg:

- Is intended to reduce signs and symptoms, induce major clinical response, inhibit the progression of structural damage, and improve physical functioning of adult patients with moderate to severe active rheumatoid arthritis. Orencia 250 mg may be used as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs) other than tumor necrosis factor (TNF) antagonists.
- Orencia 250 mg in combination with methotrexate is intended for treating active moderate to severe polyarticular juvenile idiopathic arthritis (JIA), in patients aged 6 years and older, who have not sufficiently responded to previous treatment with other disease-modifying antirheumatic drugs (DMARDs) including treatment with at least one medicine of the TNF inhibitors group.
- Orencia 250 mg is intended to treat adult patients with active psoriatic arthritis (PsA).

Therapeutic group: Selective immunosuppressant.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient abatacept or to any of the other ingredients in this medicine. See section 6 'Additional information' for a list of the other ingredients.

Special warnings about using this medicine:

- **Before you use Orencia 250 mg, tell your doctor about all of your medical conditions, including if you:**
  - have any kind of infection, even if it is small (such as an open cut or sore), or an infection that is in your whole body (such as the flu). If you have an infection

when taking Orencia 250 mg, you have a higher chance of getting serious side effects.
- have an infection that will not go away or an infection that keeps coming back.
- have or have had inflammation of your liver due to an infection (viral hepatitis). Before you start to use Orencia 250 mg, your doctor may examine you for hepatitis.
- have had a lung infection called tuberculosis (TB), received a positive skin test for TB, or you recently have been in close contact with someone who has had TB.
  Before you start to use Orencia 250 mg, your doctor may examine you for TB or perform a skin test.
  Symptoms of TB may include: a cough that does not go away, weight loss, fever, and night sweats.
- are scheduled to have surgery.
- recently received a vaccination or are scheduled for a vaccination. While you are receiving Orencia 250 mg, and for 3 months after you stop receiving Orencia 250 mg, you must not receive live vaccines.
- have a history of a breathing problem called chronic obstructive pulmonary disease (COPD).
- have diabetes and use a blood glucose monitor to check your blood sugar (blood glucose) levels. Orencia 250 mg for intravenous infusion (given through a needle placed in a vein) contains maltose, a type of sugar, that can give false high blood sugar readings with certain types of blood glucose monitors on the day of Orencia 250 mg infusion. Your doctor may tell you to use a different way to monitor your blood sugar levels.
- are pregnant or plan to become pregnant, see the section 'Pregnancy and breastfeeding'.
- are breastfeeding or plan to breastfeed. See the section 'Pregnancy and breastfeeding'.
- Some people treated with Orencia have developed skin cancer. Tell your doctor if you have a family or personal history of skin cancer, and if you see any growths or changes in the appearance of your skin during or after your treatment with Orencia.
- you may have a higher chance of getting a serious infection if you take Orencia 250 mg with other biologic medicines for rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), or psoriatic arthritis (PsA).

Children and adolescents:
The efficacy and safety of treating children with Orencia IV 250 mg has not been established, except for treatment of active juvenile idiopathic arthritis (JIA).

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Orencia 250 mg may affect the way other medicines work, and other medicines may affect the way Orencia 250 mg works, causing serious side effects. Especially if you take other biologic medicines to treat rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), or psoriatic arthritis (PsA) that may affect your immune system, such as:
- etanercept

- adalimumab
- infliximab
- anakinra
- rituximab
- golimumab
- certolizumab pegol
- tocilizumab.

Pregnancy and breastfeeding:

Tell your doctor if you are pregnant or if you are planning a pregnancy. It is not known if Orencia 250 mg can harm your unborn baby.
If you took Orencia 250 mg during pregnancy, talk to your doctor before your baby receives any vaccines.
Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Orencia 250 mg passes into breast milk. Talk to your doctor about the best way to feed your baby if you are being treated with Orencia 250 mg.

Important information about some of this medicine's ingredients:

Orencia 250 mg contains sodium.
This medicine contains 34.5 mg of sodium (main component of cooking/table salt) in a maximum dose of 4 vials (8.625 mg sodium in each vial).
This amount is equivalent to 1.7% of the recommended maximum daily dietary intake of sodium in adults.

3. How to use this medicine?

- Orencia is given by a healthcare provider (your doctor or nurse) into a vein in your arm (IV or intravenous administration). It takes about 30 minutes to give you the full dose of medicine. You will then receive Orencia 2 weeks and 4 weeks after the first dose and then every 4 weeks.
- Always use this medicine according to the doctor's instructions.

Check with your doctor or pharmacist if you are not sure about the dosage and the treatment regimen of this medicine.
The dosage and treatment regimen will be determined by the doctor only.
Do not exceed the recommended dose.

If you have injected a higher dose of the medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

Do not take medicines in the dark! Check the label and the dose <u>each time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects:

Like with all medicines, using Orencia 250 mg may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Orencia 250 mg may cause serious side effects, including:

- **Infections.** Orencia 250 mg may make you more likely to get infections or make the infection that you have get worse. Some people have died from these infections. Contact your doctor right away if you have any symptoms of an infection. Symptoms of an infection may include:
    - fever
    - feeling very tired
    - cough
    - flu-like symptoms
    - warm, red, or painful skin.

  The most common side effects resulting in clinical intervention (changes in treatment or discontinuation of ORENCIA treatment) in medicine administration, were due to infection.

  The most commonly reported infections resulting in changes in the medicine dose were upper respiratory tract infection, bronchitis, and herpes zoster.

  The most common infections resulting in discontinuation of treatment with the medicine were pneumonia, localized infections, and bronchitis.

  The most commonly reported infections were upper respiratory tract infection, inflammation of the throat and nose (nasopharyngitis), sinusitis, urinary tract infection, flu and bronchitis.

  Other infections reported were rhinitis, herpes simplex, and pneumonia.

  The most common serious infections reported were pneumonia, soft tissue infection (cellulitis), urinary tract infection, bronchitis, diverticulitis, and acute pyelonephritis.

- **Allergic reactions.** Allergic reactions can happen to people who use Orencia 250 mg. Contact your doctor or go to the emergency room right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction may include:
    - allergic rash (hives)
    - swollen face, eyelids, lips, or tongue
    - trouble breathing
    - hypotension.
- **Hepatitis B infection in people who carry the virus in their blood.** If you are a carrier of the hepatitis B virus (a virus that affects the liver), the virus can become active while you use Orencia 250 mg. Your doctor may do blood tests before you start treatment with Orencia 250 mg.
- **Vaccinations.** You should not receive Orencia 250 mg with certain types of vaccines (live vaccines). You can receive non-live vaccines, such as pneumococcal and inactivated influenza (flu) vaccines. Orencia 250 mg may also cause some vaccinations

to be less effective.
Talk to your doctor about your vaccination plans.

- **Breathing problems in people with Chronic Obstructive Pulmonary Disease - COPD.** You may get certain respiratory problems more often if you receive Orencia 250 mg and have COPD. Symptoms of problems in the respiratory system, include:
    - COPD that becomes worse
    - cough
    - rhonchi
    - trouble breathing
    - pneumonia.

- **Cancer (malignancies).** Certain kinds of cancer have been reported in patients using Orencia 250 mg. It is not known if Orencia 250 mg increases your chance of getting certain kinds of cancer. The types of cancer that have been observed include: lung cancer, lymphomas, skin cancer, breast cancer, bile duct cancer, bladder cancer, cervical cancer, endometrial cancer, melanoma, myelodysplastic syndrome, ovarian cancer, prostate cancer, kidney cancer, thyroid cancer, and uterine cancer.

Most common side effects of Orencia 250 mg include:

- headache
- upper respiratory tract infection
- nausea
- inflammation of the throat and nose (nasopharyngitis).

Additional side effects:

- headaches
- inflammation of the throat and nose (nasopharyngitis)
- dizziness
- cough
- back pain
- hypertension
- digestion problems (dyspepsia)
- urinary tract infection
- rash
- pain in the extremities.

Infusion related reactions and hypersensitivity reactions in patients receiving Orencia 250 mg intravenously:
The most frequently reported acute side effects of infusion (side effects that happen during the first hour of infusion) are dizziness, headache, and hypertension.
Other acute side effects reported include heart and lung related symptoms such as hypotension, increase in blood pressure, and breathlessness. Other symptoms include: nausea, flushing, hives (urticaria), cough, hypersensitivity, pruritus, rash, and wheezing.

Side effects in patients with polyarticular juvenile idiopathic arthritis (pJIA) patients (with damage in a number of joints) using intravenous Orencia 250 mg:
In general, the side effects seen in children and adolescents were similar in type and frequency to those seen in adult patients.

- Infections. The most common infections were upper respiratory tract infection and inflammation of the throat and nose (nasopharyngitis)
- headache
- nausea
- diarrhea
- cough
- fever
- abdominal pain
- Serious side effects:
  - acute lymphocytic leukemia
  - ovarian cyst
  - chickenpox
  - disease flare
  - joint erosion
- allergic reaction
- acute infusion-related reactions
- multiple sclerosis.

Side effects reported after the medicine was placed on the market (postmarketing experience)

- inflammation of the blood vessels (vasculitis)
- new or worsening psoriasis
- non-melanoma skin cancers (basal cell carcinoma and squamous cell carcinoma)
- fatal anaphylaxis.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health by clicking on the link: "Reporting of side effects from drug treatment", which can be found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. How to store the medicine?

- **Prevent poisoning!** To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:

- Store in the refrigerator between 2°C-8°C.
- Store in the original package to protect from light.
- Can be used up to 24 hours after dilution.

Discard expired or out-of-use medicines safely.

6. Additional information:

- **In addition to the active ingredient, this medicine also contains:**
  Maltose monohydrate; sodium dihydrogen phosphate, monohydrate; sodium chloride, hydrochloric acid, sodium hydroxide.
- **What the medicine looks like and contents of the pack:**
  Each vial contains a powder for preparation of a concentrated solution for preparation of a solution for infusion.
  The powder is white to off-white, whole or fragmented cake.
  A pack contains 1 vial and 1 syringe.
- **Registration holder's name and address:**
  Bristol-Myers Squibb (Israel) Ltd., 18 Aharon Bart St., P.O. Box 3361, Kiryat Arye, Petach Tikva 4951448.
- **Manufacturer's name and address:**
  Bristol-Myers Squibb Company, Princeton, New Jersey, 08543, USA.
- Revised in February 2021 according to MOH guidelines.
- **Registration number of the medicine in the Ministry of Health's National Drug Registry:** 143-23-31924-00