PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

This medicine is dispensed with a physician's prescription only

KINERET 100 MG SOLUTION FOR INJECTION
Pre-filled syringes

Solution for Subcutaneous Injection

Each pre-filled syringe contains:
Anakinra 100 mg per 0.67 ml (150 mg/ml)

For a list of inactive and allergenic ingredients in the medicine, see section 6 "Additional Information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, consult your physician 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.

1. What is this medicine intended for?

Kineret 100 mg solution for injection is indicated for the treatment of the signs and symptoms of Rheumatoid Arthritis (RA) in combination with methotrexate, in adult patients with an inadequate response to methotrexate alone.

Kineret 100 mg solution for injection is indicated for adults and children aged 8 months and older with a body weight of 10 kg or above for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), a group of rare autoinflammatory diseases, including:

- Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA), also called Neonatal-Onset Multisystem Inflammatory Disease (NOMID).
- Muckle-Wells Syndrome (MWS).
- Familial Cold Autoinflammatory Syndrome (FCAS).

Kineret 100 mg solution for injection is indicated for the treatment of Familial Mediterranean Fever (FMF). Kineret should be given in combination with colchicine, if appropriate.

Kineret 100 mg solution for injection is a cytokine that belongs to the immunosuppressant group of medicines and is used for the treatment of Rheumatoid Arthritis and for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS). This is a group of rare, autoinflammatory diseases including: Familial Cold Autoinflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS) and Chronic Infantile Neurological, Cutaneous, Articular Syndrome (CINCA), also called Neonatal-Onset Multisystem Inflammatory Disease (NOMID).

Cytokines are proteins that are produced by the body and coordinate communication between cells, thus assisting in cell activity control.

In Rheumatoid Arthritis and in Cryopyrin-Associated Periodic Syndromes (CAPS), the body produces an excessive amount of cytokines called interleukin-1 (IL-1), which cause harmful effects such as swelling and tissue damage.

Normally, your body produces a protein that blocks the harmful effects of interleukin-1.

The active ingredient in **Kineret 100 mg solution for injection** is called anakinra, which is produced by genetic engineering biotechnology (recombinant DNA generated from a microorganism called *E. coli*), and works in the same way that the blocking protein in your body does.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive to the active ingredient anakinra or to any of the additional ingredients that the medicine contains (please see section 6, "Additional information").
- You are allergic to other products that are produced by genetic engineering biotechnology using the microorganism *E. coli*.
- You suffer from neutropenia (low white blood cell count) determined after a blood test.

Special warnings regarding the use of the medicine
Consult your physician immediately

- If you show any of the following signs after an injection of **Kineret 100 mg solution for injection:** A rash all over your body, shortness of breath, wheezing, fast pulse or sweating. These signs may indicate that you are allergic to **Kineret 100 mg solution for injection**.
- If you have ever developed an atypical, widespread rash or skin peeling after taking **Kineret 100 mg solution for injection**.
- There is a serious skin reaction, called DRESS (drug reaction with eosinophilia and systemic symptoms), that has been reported rarely in association with **Kineret 100 mg solution for injection** treatment, predominantly in patients with systemic juvenile idiopathic arthritis (SJIA). Seek medical attention immediately if you notice an atypical, widespread rash, which may occur in conjunction with high body temperature and enlarged lymph nodes.

Before starting treatment with Kineret 100 mg solution for injection, tell your physician if:

- There is a history of recurring infections or if you suffer from asthma. Treatment with **Kineret 100 mg solution for injection** may worsen these conditions.
- You have cancer; your physician will decide whether you can be treated with **Kineret 100 mg solution for injection**.
- You have suffered in the past from increased levels of liver enzymes in your blood.
- You require vaccinations. You must not be given live vaccines while being treated with **Kineret 100 mg solution for injection**.

Children and adolescents:
Rheumatoid Arthritis – Since there is no information regarding the efficacy of treatment in children and adolescents, the medicine is not intended for this population.

Cryopyrin-Associated Periodic Syndromes (CAPS) – **Kineret 100 mg solution for injection** is not intended for use by children below the age of 8 months, since there is no information regarding its use in children below this age.

For the treatment of Familial Mediterranean Fever (FMF) – the treatment is intended for adults, adolescents and children above the age of two years.

Drug interactions:
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell your physician or pharmacist. Especially if you are taking:

- Do not take medicines that contain a TNF-α inhibitors (such as medicines containing an active ingredient called etanercept) together with **Kineret 100 mg solution for injection**, as this may increase the risk of infections.
- After starting treatment with **Kineret 100 mg solution for injection**, the chronic inflammation in your body will decrease. After this change, it may be necessary to readjust the dose of other medicines such as: warfarin/Coumadin or phenytoin.

Pregnancy, breastfeeding and fertility:
You should consult your physician before taking this medicine if you are pregnant, think you are pregnant, or are planning to become pregnant.

Kineret 100 mg solution for injection has not been tested in pregnant women. Use of **Kineret 100 mg solution for injection** is not recommended during pregnancy and in women of childbearing age not using contraception. It is important to inform your physician if you are pregnant, if you think you may be pregnant or are planning to become pregnant. Your physician will discuss with you the potential risks of taking **Kineret 100 mg solution for injection** during pregnancy.

Do not breastfeed if you are being treated with **Kineret 100 mg solution for injection**, since it is not known whether the active ingredient anakinra is excreted in breastmilk.

Important information about some of the medicine's ingredients:

- **Sodium** - this medicine contains less than 1 mmol (23 mg) sodium per 100 mg of medicine, and is therefore considered to be a "sodium free" medicine.

3. How should you use the medicine?

Always use this preparation according to your physician's instructions. If you are not sure about the dosage or treatment regimen, consult your physician or pharmacist.

The dosage and treatment regimen will be determined by your physician only. The usual dosage is generally:

For FMF:
The recommended dose for patients weighing 50 kg and over is 100 mg per day, by subcutaneous injection. For patients weighing less than 50 kg, dose in accordance with body weight, at a recommended dose of 1-2 mg per kg per day.

For other indications:
The usual dosage is generally one subcutaneous injection of **Kineret 100 mg solution for injection** once per day.

You should try to have the injection at the same time each day.

Do not exceed the recommended dose.

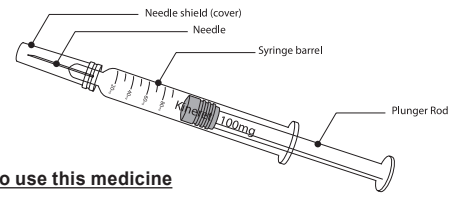
If you have accidentally taken a higher dose, no dangerous medical condition should develop, but you should contact your physician, nurse or pharmacy. If you are not feeling well, consult your physician or a nurse immediately.

If a child has swallowed the medicine, proceed immediately to a physician or a hospital emergency room and bring the package of the medicine with you.

If you have forgotten to take the medicine, consult with your physician as to when you should take the next dose of **Kineret 100 mg solution for injection.**

Self-Injection
Your physician may decide that it would be more convenient for you to inject yourself or your child with **Kineret 100 mg solution for injection**. Your physician or nurse will instruct you on how to administer the injection. Do not inject the medicine yourself without instruction.

This section of the leaflet contains information on how to self-inject **Kineret 100 mg solution for injection**. If you have any questions about how to administer the injection, consult your physician or nurse for assistance.



How to use this medicine

Equipment:
In order to perform a subcutaneous injection, you will need:

- a new pre-filled syringe of **Kineret 100 mg solution for injection**
- an alcohol pad or similar
- a sterile gauze or tissue

What should you do before a subcutaneous injection of Kineret 100 mg solution for injection?

1. Take the pre-filled syringe of **Kineret 100 mg solution for injection** out of the refrigerator.
2. Do not shake the pre-filled syringe.
3. Check the expiry date on the pre-filled syringe. Do not use after the last day of the indicated month.
4. Check the appearance of the **Kineret 100 mg solution for injection**. It must be a clear-to-white solution. There may be some translucent-to-white protein particles in the solution. The presence of these particles does not affect the quality of the medicine. The solution should not be used if it is discoloured or cloudy, or if any particles other than translucent-to-white particles are present.
5. For a more comfortable injection, leave the pre-filled syringe outside the refrigerator, at room temperature, for approximately 30 minutes, or hold the pre-filled syringe gently between your hands for a few minutes. **Do not** warm **Kineret 100 mg solution for injection** in any other way (for example, in a microwave or in hot water).
6. **Do not remove** the cover from the pre-filled syringe until you are ready to inject.
7. **Wash your hands thoroughly.**
8. Find a comfortable, well-lit place and a clean surface, where you should place all of the equipment within reach.
9. Make sure you know what dose your physician has prescribed for you or your child:
   20 mg - 90 mg, 100 mg or a higher dose.
   - If your physician has prescribed a 100 mg dose for you or your child, please see **"How to prepare a 100 mg dose for injection".**
   - If your physician has prescribed a dose lower than 100 mg for you or your child, please see **"How to prepare a 20 mg - 90 mg dose for injection".**

How to prepare a 100 mg dose for injection
Prior to injecting **Kineret 100 mg solution for injection**, you should do the following:

1. Hold the pre-filled syringe gently and remove the cover from the needle without twisting. Pull the cover straight, as shown in **Figure 1**. Do not touch the needle or push the plunger. Discard the needle cover immediately.

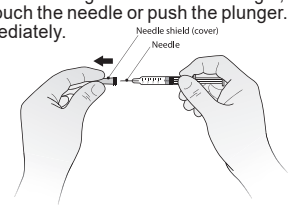


Figure 1

2. You may notice a small air bubble in the pre-filled syringe. There is no need to remove the air bubble before injecting. Injecting the solution with the air bubble is harmless.
3. You can now use the pre-filled syringe.

How to prepare a 20 mg - 90 mg dose for injection
Prior to injecting **Kineret 100 mg solution for injection**, you should do the following:

1. Hold the pre-filled syringe gently and remove the cover from the needle without twisting. Pull the cover straight, as shown in **Figure 1**. Do not touch the needle or push the plunger. Discard the needle cover immediately.
2. Hold the syringe in one hand with the needle pointing straight upwards, as shown in **Figure 2**. Place your thumb on the plunger rod and push slowly until tiny drops begin to come out of the syringe's needle.

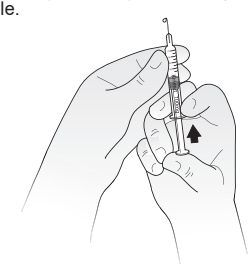


Figure 2

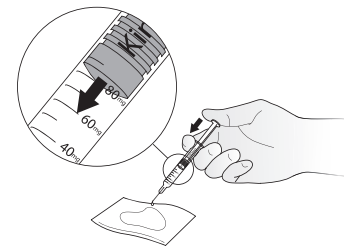


Figure 3

3. Turn the syringe so that the needle is now pointing downwards. Place a sterile gauze or tissue on a flat surface and hold the syringe above it with the needle pointing toward the gauze or tissue, as shown in **Figure 3**. Make sure the needle does not touch the gauze or tissue.
4. Place your thumb on the plunger rod and push gently until the head of the plunger reaches the scale mark on the syringe that is appropriate for your dose (your physician will tell you which dose you need). The ejected liquid will be absorbed by the gauze or tissue, as shown in **Figure 3**.
5. If you were unable to set the syringe to the correct dose, dispose of the syringe and use a new one.
6. You can now use the pre-filled syringe.

Where should you give the injection?
The most suitable places to inject are:

- the upper thigh
- the abdomen, except for the area around the navel
- the upper outer areas of the buttocks
- the outer area of the upper arms as shown in **Figure 4**.

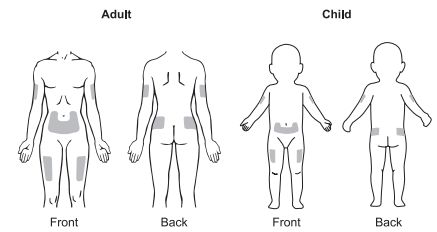


Figure 4

Change the place that you inject each time in order to prevent pain at the injection site. If someone else is injecting for you, they can also inject into the back part of your arm.

How do you give the injection?

1. Disinfect the skin by using an alcohol wipe. Pinch the skin between your thumb and forefinger, without squeezing it.
2. Insert the needle fully into the skin, as instructed by your physician or nurse.
3. Inject the liquid slowly and evenly, always keeping the skin pinched as shown in **Figure 5**.

Figure 5

4. After injecting the liquid, pull the needle out and let go of the skin.
5. Discard any unused medicine. Each syringe is intended for a single injection only. Reuse of a syringe can cause infection.

Remember!
If you experience any problems, do not hesitate to consult your physician or nurse.

Syringe and supplies disposal:

- Do not put the needle cover back on the used needle.
- Keep the used syringes out of the reach and sight of children.
- Never throw the used syringe into the household rubbish bin.
- When using a dose lower than 100 mg, it is necessary to eject liquid from the syringe on to the gauze or tissue. After the liquid is ejected, discard the gauze or tissue and clean the surface with a fresh tissue.
- The used syringes and any gauze or pads should be disposed of in accordance with local requirements. Ask the pharmacist how to dispose of medicines no longer in use. These measures will help to protect the environment.

Treatment duration and termination:
You must complete the treatment as recommended by your physician. Even if there is an improvement in your health condition, do not stop treatment with this medicine without consulting with your physician.

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

If you have further questions regarding use of the medicine, consult your physician or pharmacist.

4. Side effects

As with any medicine, the use of **Kineret 100 mg solution for injection** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Side effects are similar regardless of the indication (Rheumatoid Arthritis, Cryopyrin-Associated Periodic Syndromes or Familial Mediterranean Fever) for which the medicine is being given.

Consult your physician immediately if you experience any of the following side effects:

- **Serious infections** – such as pneumonia (respiratory tract infection) or infections of the skin can occur during treatment with **Kineret 100 mg solution for injection**. Symptoms might include high fever, shivers, cough, headache or redness and tenderness of the skin. Also persistent low-grade fever, weight loss and persistent cough can be signs of an infection.
- **Serious allergic reactions** are uncommon. However, any of the following symptoms may indicate an allergic reaction to **Kineret 100 mg solution for injection**, so you should seek immediate medical attention and not continue to inject **Kineret 100 mg solution for injection** if any of the following occur:
  - Swelling of the face, tongue or throat
  - Trouble swallowing or breathing
  - Sudden occurrence of fast pulse or sweating
  - Itchy skin or rash

Very common side effects (effects that occur in more than one user in 10):

- Redness, swelling, bruising or itching at the injection site. These symptoms are generally mild to moderate and are more common at the beginning of treatment.
- Headaches.
- Increased total blood cholesterol levels.

Common side effects (effects that occur in 1-10 in 100 users):

- Neutropenia (low white blood cell count) determined after a blood test. This condition may increase the risk of getting an infection. Symptoms of an infection might include a fever and a sore throat.
- Serious infections such as pneumonia (respiratory tract infection) or infections of the skin.
- Thrombocytopenia (low levels of blood platelets).

Uncommon side effects (effects that occur in 1-10 in 1,000 users):

- Serious allergic reactions including swelling of the face, tongue or throat, trouble swallowing or breathing, suddenly feeling fast pulse or sweating and itchy skin or rash.
- Elevated levels of liver enzymes in the blood, seen from blood tests.

Side effects whose frequency is not known (effects whose frequency has not yet been determined):

- Signs of liver disorders such as yellow skin and eyes, nausea, loss of appetite, dark-colored urine and light-colored stool.

If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult your physician.

Side effects can be reported to the Ministry of Health by clicking the link "Report Side Effects of Drug Treatment" on the homepage of the Ministry of Health website (www.health.gov.il), which will direct you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. How should the medicine be stored?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a closed place out of the reach and sight of children and/or infants, in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your physician.
- Do not use this medicine after the expiry date (exp. date) which appears on the outer package. The expiry date refers to the last day of that month. Even under the recommended packaging/storage conditions, medicines keep only for a limited time. Please take note of the medicine's expiry date! In any case of doubt, consult with the pharmacist who supplied you with the medicine.

Storage conditions:

- Store in a refrigerator, between 2-8ºC. Do not freeze.
- Store in the original package in order to protect the medicine from exposure to light.
- Do not use **Kineret 100 mg solution for injection** if you think it has been frozen. Once the pre-filled syringe has been removed from the refrigerator and has reached room temperature (up to 25°C) it must either be used within 72 hours or disposed of.
- Do not throw away medicines in wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.
- Do not store different medicines in the same package.

6. Additional information

- In addition to the active ingredient anakinra, this medicine also contains:
  Sodium chloride, Citric acid anhydrous, Polysorbate 80, Disodium EDTA dehydrate, Sodium hydroxide, Water for injections.
- **What the medicine looks like and what the package contains:**
  Graduated, pre-filled syringes containing a clear, transparent-to-white solution. The solution may contain some protein particles, imparting the solution with a translucent-to-white color. These particles do not affect the quality of the medicine.
  The syringes come in packs of 1, 7 or 28 syringes.
  Not all package sizes may be marketed.
- **Registration holder and address:**
  Megapharm Ltd., 15 Hatidhar St., Ra'ananna, Israel.
- **Manufacturer and address:** Swedish Orphan Biovitrum AB (SOBI), Stockholm, Sweden.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 145-79-33059

Updated in September 2023 in accordance with Ministry of Health guidelines.