NOVARTIS

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

The medicine is dispensed with a doctor's prescription only.

Ilaris 150 mg/ml Solution for Injection

Active ingredient:
Each vial contains 150 mg Canakinumab in 1 mL solution.

Inactive and allergenic ingredients: see section 6 "Further 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, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Ilaris contains the active substance canakinumab, a monoclonal antibody that belongs to a group of medicines called interleukin (IL) inhibitors. It blocks the activity of a substance called interleukin-1 beta (IL-1 beta), which is present at increased levels in inflammatory diseases.

- Periodic fever syndromes:
  Ilaris is indicated for the treatment of the following autoinflammatory diseases in adults, adolescents and children from the age of 2 and above:
  - Cryopyrin-associated periodic syndromes (CAPS)
    Cryopyrin-associated periodic syndromes (CAPS) in adults, adolescents and children from the age of two and above and weighing 7.5 kg or more. Including:
    - Muckle-Wells syndrome (MWS),
    - Neonatal-onset multisystem inflammatory disease (NOMID)/ chronic infantile neurological, cutaneous, articular syndrome (CINCA),
    - Severe forms of familial cold auto-inflammatory syndrome (FCAS)/ familial cold urticaria (FCU) presenting with signs and symptoms beyond cold-induced urticarial skin rash.
  - Tumour necrosis factor receptor associated periodic syndrome (TRAPS)
    Ilaris is indicated for the treatment of tumour necrosis factor receptor associated periodic syndrome (TRAPS)
  - Hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD)
    Ilaris is indicated for the treatment of hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD)
  - Familial Mediterranean fever (FMF)
    Ilaris is indicated for the treatment of FMF in patients with a contraindication for use of colchicine, an intolerance to colchicine or colchicine does not provide an adequate response, despite administration of the maximum tolerated dose.
    Ilaris can be given as a monotherapy or in combination with colchicine.

  In patients with periodic fever syndromes (HIDS/MKD, TRAPS, CAPS, and FMF), the body produces high levels of IL-1 beta. This may cause fever, headache, fatigue, skin rash, or joint and muscle pain. By blocking the activity of IL-1 beta, Ilaris may improve these symptoms.
- Gout:
  Ilaris is indicated for the treatment of the symptoms of frequent gout attacks in adults (at least three attacks in the past 12 months), in whom use of nonsteroidal anti-inflammatory drugs and colchicine is contraindicated, who are intolerant to these medicines or in whom these medicines did not bring about an adequate response and in whom retreatment with corticosteroids is not suitable.
  Gout is caused by the formation of urate crystals. These crystals cause excessive production of IL-1 beta, which may lead to sudden and severe pain, redness, warmth and swelling in the joints (known as a gout attack). By blocking IL-1 beta, Ilaris may improve these symptoms.
- Still's disease:
  Ilaris is indicated for the treatment of active Still's disease, including adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older, who did not respond well enough to previous treatment with non-steroidal anti-inflammatory drugs (NSAID's) and to systemic administered steroids. Ilaris can be administered as treatment on its own or in combination with methotrexate.
  Still's disease, including systemic juvenile idiopathic arthritis (SJIA) and adult-onset Still's disease (AOSD) is an inflammatory disease that can cause pain, swelling and inflammation of one or more joints, as well as rash and fever. A pro-inflammatory protein called interleukin-1-beta (IL-1 beta) plays an important role in the inflammation that characterizes Still's disease. Ilaris blocks the activity of interleukin-1-beta (IL-1 beta), which may improve the signs and symptoms of the disease.

Therapeutic group: Interleukin (IL) inhibitors

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient canakinumab, or to any of the additional ingredients contained in the medicine (appearing in section 6).
- you have or suspect you have an active and severe infection.

Special warnings regarding use of the medicine

Before treatment with the preparation, tell the doctor if any of the following conditions apply to you:
- If you currently have an infection or if you have had repeated infections or a condition such as a known low white blood cell count which increases your risk of getting infections.
- If you have or have ever had tuberculosis or direct contact with a person with an active tuberculosis infection. Your doctor may check whether you have tuberculosis using a specific test.
- if you have signs of a liver disorder such as yellow skin and eyes, nausea, loss of appetite, dark-colored urine and light-colored stools.
- If you need to get any vaccination. Avoid being vaccinated with a live vaccine during treatment with Ilaris (also see reference below under "Drug interactions").

Contact your doctor immediately:
- If you have ever developed an atypical, widespread rash or peeling of the skin after administration of Ilaris. The serious skin reaction, DRESS (drug reaction with eosinophilia and systemic symptoms), has been reported rarely in association with Ilaris treatment, particularly in patients with SJIA. Seek medical attention immediately if you notice an atypical, widespread rash which may occur in conjuction with high body temperature and enlarged lymph nodes.

Still's disease
- Patients with Still's disease may develop a condition called macrophage activation syndrome (MAS), which can be life-threatening. Your doctor will monitor you for potential triggering factors of MAS that include infections and re-activation of the disease (flare-up).

Children and adolescents
- **Periodic fever syndromes (CAPS, TRAPS, HIDS/MKD, FMF) and systemic juvenile idiopathic arthritis (SJIA):** Ilaris can be used in children aged 2 years and above.
- **Gout:** Ilaris is not intended for children and adolescents under 18 years of age.

Drug interactions
If you are taking, or have recently taken, or may take, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist, particularly if you are taking:
- Live vaccines: Avoid being vaccinated with a live vaccine during treatment with Ilaris. Your doctor may want to check your vaccination history and give you vaccinations that you missed before starting treatment with Ilaris. If you are supposed to receive a live vaccine after starting treatment with Ilaris, discuss it with your doctor. A live vaccine should normally be given 3 months after the last injection of Ilaris and 3 months before the next injection.
- Medicines called TNF (tumor necrosis factor) inhibitors, such as etanercept, adalimumab or infliximab. These medicines are used mainly in rheumatic diseases (diseases related to the joints, soft tissues and connective tissues) and autoimmune diseases. These medicines should not be used with Ilaris because they may increase the risk of infections.

Pregnancy, breastfeeding and fertility
- If you are pregnant or breastfeeding, think you are pregnant or planning to become pregnant, consult your doctor before taking the medicine. Avoid becoming pregnant and you must use appropriate contraception while taking Ilaris and for at least three months after the last Ilaris treatment. It is important to tell your doctor if you are pregnant, if you think you may be pregnant or are planning to become pregnant. Your doctor will discuss with you the potential risks of use of Ilaris during pregnancy.
- If you received canakinumab while you were pregnant, it is important that you inform the baby's doctor or nurse before any vaccinations are given to your baby. Your baby should not receive live vaccines until at least 16 weeks after you received the last dose of canakinumab before giving birth.
- It is not known whether Ilaris passes into breast milk. Your doctor will discuss with you the potential risks of taking Ilaris before breastfeeding.

Driving and operating machinery
Ilaris treatment may cause you to have a spinning sensation (dizziness or vertigo) or intense tiredness. This may affect your ability to drive or operate tools or machinery. If you feel a spinning sensation or feel tired, do not drive or use any tools or machines until you feel normal again.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
Keep your doctor informed of your condition and of any symptoms before Ilaris is injected (see section 2).
Your doctor may decide to delay or interrupt the treatment, but only if necessary.
Ilaris is intended for subcutaneous injection. This means that it is injected through a short needle into the fatty tissue just under the skin.

Ilaris will be injected by a medical healthcare provider only.

The dosage and treatment regimen will be determined by the doctor only. The recommended dosage is generally:

Cryopyrin-associated periodic syndromes (CAPS)
The recommended starting Ilaris dosage is:
- Adults and children aged 4 years or above:
  - 150 mg for patients who weigh more than 40 kg
  - 2 mg/kg for patients who weigh between 15 kg - 40 kg
  - 4 mg/kg for patients who weigh between 7.5 kg and less than 15 kg
- Children aged 2 to 3 years
  - 4 mg/kg for patients with body weight of 7.5 kg or more

Ilaris is injected every 8 weeks as a single dose.
- If you have not responded well enough to the treatment after 7 days, your doctor may give you another dose of 150 mg or 2 mg/kg.
- If you respond well enough to the second dose, your treatment will be continued with 300 mg or 4 mg/kg every 8 weeks.
- If you do not respond well enough to the second dose, a third dose of Ilaris 300 mg or 4 mg/kg may be given.
- If you respond well enough to the third dose, your treatment will be continued at 600 mg or 8 mg/kg every 8 weeks.

For children receiving a starting dosage of 4 mg/kg and who have not responded well enough after 7 days, the doctor may give a second dose of 4 mg/kg. If the child responds to it well enough, treatment may be continued with a dosage of 8 mg/kg every 8 weeks.

Tumour necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) and familial Mediterranean fever (FMF)
The recommended starting dosage of Ilaris is:
- Adults and children aged 2 years or above
  - 150 mg for patients who weigh more than 40 kg
  - 2 mg/kg for patients who weigh between 7.5 kg and less than 40 kg.

Ilaris is injected every 4 weeks as a single dose.
- If you have not responded well enough to the treatment after 7 days, your doctor may give you another dose of 150 mg or 2 mg/kg.
- If you respond to this well enough, your treatment will be continued with 300 mg or 4 mg/kg, every 4 weeks.

Still's disease (SJIA and AOSD)
The recommended starting dosage of Ilaris for patients with Still's disease with body weight of 7.5 kg and above is 4 mg/kg (up to a maximum of 300 mg). Ilaris is injected every 4 weeks as a single dose.

Gout
Your doctor will discuss with you the need to start or adjust treatment to lower the uric acid level in your blood.
The recommended starting dosage of Ilaris for adult gout patients is 150 mg, which is given as a single dose at the time of a gout attack. Treatment should be received as close as possible to the onset of the attack in order to derive the most benefit from it.
If you need another treatment with Ilaris, and got relief from the last dose, wait at least 12 weeks before the next dose.

For instructions for the healthcare professional on how to use Ilaris injections, please see "Instructions for use for healthcare professionals" section, written in English at the end of the leaflet.

How long to use Ilaris
- **Cryopyrin-associated periodic syndromes (CAPS), tumour necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD), familial Mediterranean fever (FMF) or Still's disease (SJIA or AOSD):** Continue treatment with Ilaris for as long as the doctor instructs you to.
- **Gout:** If you have a gout attack, you will be given a single dose of Ilaris. If you experience a new attack, your doctor may consider giving you a new dose of Ilaris, but not earlier than 12 weeks from the previous dose.

Do not exceed the recommended dose.

If you accidentally take a higher dosage
If a higher than recommended dose of Ilaris was injected, it is unlikely to be serious, but you should inform your doctor, nurse or pharmacist as soon as possible.

If you forget to take the medicine
If you have CAPS, TRAPS, HIDS/MKD, FMF or Still's disease (SJIA and AOSD) and you forget to come to get your injection, get the next injection as close as possible to the time that you remembered. Then, talk to your doctor about when to inject your next dose. Afterwards, continue with the injections at the previously recommended intervals.

Adhere to the treatment regimen recommended by the doctor.

If you stop taking Ilaris
Stopping treatment with Ilaris may cause your condition to worsen. Do not stop taking Ilaris, unless your doctor has told you to do so.

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

4. SIDE EFFECTS

As with any medicine, use of Ilaris may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Some side effects may be serious. Refer to a doctor immediately, if you notice any of the side effects listed below:
- Fever lasting longer than 3 days or any other symptom that might indicate a serious infection, including shivering, chills, malaise, lack of appetite, body aches, typically in connection with a sudden onset of illness, sore throat or mouth ulcers, cough, phlegm, chest pain, breathing difficulties, ear pain, prolonged headaches or localized redness, warmth or swelling of your skin or inflammation of connective tissue (cellulitis). These symptoms could be due to a serious infection, an unusual infection (opportunistic infection) or be related to a low level of white blood cells (called leukopenia or neutropenia). Your doctor may instruct you to perform blood tests regularly, if necessary.
- Allergic reaction with rash and itching and possibly also hives, difficulty breathing or swallowing, dizziness, unusual awareness of your heart beat (palpitations) or low blood pressure.

Other side effects of Ilaris include:
Very common side effects (may affect more than 1 in 10 patients):
- Any kind of infection. Can include:
  - Respiratory infections such as chest infection, flu, sore throat, runny nose, blocked nose, sneezing, feeling of pressure in pain in the cheeks or forehead, with or without fever (pneumonia, bronchitis, influenza, sinusitis, runny nose, pharyngitis, tonsillitis, nasopharyngitis, upper respiratory tract infection).
  - Other infections such as ear infection, skin infection (cellulitis), stomach pain and nausea (gastroenteritis) and frequent and painful urination, with or without fever (urinary tract infection).
- Upper abdominal pain.
- Joint pain.
- Drop in level of white blood cells (leukopenia).
- Abnormal kidney function test results (decreased creatinine renal clearance, proteinuria).
- Injection site reaction (such as redness, swelling, warmth and itching).

Common side effects (may affect up to 1 in 10 patients):
- Candida - vaginal fungal infection.
- Feeling dizzy or a spinning sensation (dizziness or vertigo).
- Pain in the back or muscles.
- Feeling weak or very tired.
- Drop in level of white blood cells which help prevent infection (neutropenia).
- Abnormal levels of triglycerides in the blood (blood lipid disorder).
- Abnormal liver function test results (increased transaminases) or high level of bilirubin in the blood, with or without yellow skin and eyes (hyperbilirubinaemia).

Uncommon side effects (may affect up to 1 in 100 patients):
- Heartburn (gastroesophageal reflux disease GERD).
- Drop in level of blood cells that help to prevent bleeding (platelets).

Tell your doctor or your child's doctor immediately if you notice any of these symptoms.

Reporting side effects
If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" 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 SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe 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 the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- **Storage conditions:**
  Store refrigerated (2°C-8°C). Do not freeze.
  Store in the original package to protect from light.
  After piercing the rubber stopper of the vial to prepare the injection, the medicine is intended for immediate use.
- Do not use the medicine if you notice that the solution is not clear to opalescent, or if it contains particles.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Water for injection, Mannitol, L-Histidine/L-Histidine hydrochloride monohydrate, Polysorbate 80 low peroxide.

What the medicine looks and the contents of the package:
1 ml transparent to slightly yellowish-brown solution, packaged in a transparent 2 ml glass vial with a gray rubber stopper, covered with an aluminum plastic seal.

Registration Holder and Importer and its address: Novartis Israel Ltd., P.O.B 7126, Tel Aviv.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 161 35 35349

Revised in July 2021 according to MOH guidelines.

ILR SOL APL July21 V3

הוראות שימוש לצוות הרפואי
تعليمات الاستعمال للطاقم الطبي

Instructions for use of Ilaris solution for injection by Health Care Professionals

These instructions are intended for health care professionals only.
Read all the way through these instructions before injecting.

Essential preparation

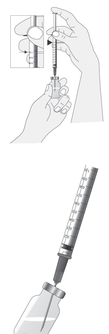
- Find a clean place suitable for injection.
- Wash your hands with soap and water, then dry them on a clean towel.
- After removing the vial from the refrigerator, check the expiry date on the vial. Do not use after the expiry date which is stated on the label and carton. The expiry date refers to the last day of that month.
- Let the vial stand unopened for 10 minutes to bring the contents to room temperature. Do not try to heat the vial. Let it warm up on its own.
- Always use new, unopened needles and syringes. Do not touch the needles or the top of the vial.

- **Gather together the necessary items**

Included in the pack
- one vial of Ilaris solution for injection (keep refrigerated)

Not included in the pack
- one 1.0 ml syringe
- one needle (such as 18 G or 21 G x 2 inch or similar, as available on the market) to draw up the solution from the vial ("withdrawal needle").
- one 27 G x 0.5 inch (or similar, as available on the market) needle for injecting ("injection needle")
- alcohol swabs
- clean, dry cotton swabs
- an adhesive bandage
- a proper disposal container for used needles, syringe and vial (sharps container)

Preparing the injection



1. Take off the protective cap from the Ilaris vial. Do not touch the vial stopper. Clean the rubber stopper of the vial with an alcohol swab.

Open the wrappers containing the syringe and the withdrawal needle.
- Put the withdrawal needle on the syringe.
- Take off the cap from the withdrawal needle.
- Push the withdrawal needle into the vial of Ilaris solution through the centre of the rubber stopper

2. Tip the vial to ensure that the required amount of solution can be drawn into the syringe. NOTE: The required amount depends on the dose to be administered. The patient's healthcare provider will instruct on the right amount for the patient.

3. Slowly pull the syringe plunger up to the correct mark (amount to be given as per healthcare provider's instructions), filling the syringe with Ilaris solution. If there are air bubbles in the syringe, remove bubbles. Ensure that the correct amount of solution is in the syringe.

4. Remove the syringe and withdrawal needle from the vial. (There may be solution remaining in the vial.) Recap the withdrawal needle. Remove the withdrawal needle from the syringe and place it in the sharps container.

5. Open the wrapper containing the injection needle and attach the needle to the syringe. Immediately proceed to administering the injection.

Giving the injection

6. Choose an injection site on the upper thigh, abdomen, upper arm or buttocks. Do not use an area that has a rash or broken skin, or is bruised or lumpy. Do not inject into scar tissue as this may mean the patient does not get all of the medicine. Avoid injecting into a vein.

7. Clean the injection site with a new alcohol swab. Allow the area to dry. Uncap the injection needle. Administer the injection.

8. Afterward, dispose of the needle and syringe in the sharps container without recapping or removing the needle.

After the injection

9. If bleeding occurs, apply a clean, dry cotton swab over the area, and press gently for 1 to 2 minutes, or until bleeding stops. Then apply an adhesive bandage

10. Safely dispose of needles and syringe in the sharps container.
Never re-use syringes or needles.

11. Properly dispose of vials containing remaining Ilaris solution (if any). Any unused product or waste material should be disposed of in accordance with local requirements. Never re-use the leftover solution.

Keep the sharps container out of reach of children.

Dispose by appropriate procedure in accordance with the local requirements.