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

The medicine is dispensed with a physician's prescription only

Nucala Solution for Injection

Solution for injection in pre-filled pen

Mepolizumab 100 mg/ml

Each 1 mL pre-filled pen contains 100 mg of mepolizumab.
For a list of inactive and allergenic ingredients in the preparation, see section 2 – "Important information about some of the ingredients of the medicine" and section 6 "Further information".

Read the 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 physician or pharmacist.
This medicine has been prescribed for you. 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?

This medicine is used for the treatment of:

→ adult patients with **severe eosinophilic asthma** that does not respond to other treatments, in combination with additional medicines.

→ adult patients with **severe chronic rhinosinusitis with nasal polyps (CRSwNP)**, for whom corticosteroid treatment and surgery within the past ten years did not provide adequate control of the disease.
The medicine is given together with intranasal corticosteroids.

→ adult patients with **eosinophilic granulomatosis with polyangiitis (EGPA)** – Churg-Strauss Syndrome.

→ adult patients with **hypereosinophilic syndrome (HES)** that is not adequately controlled, with no secondary non-hematological cause. The medicine is given together with other medicines.

Therapeutic group
Monoclonal antibody, medicines for obstructive airway diseases.

Nucala Solution for Injection contains the active ingredient **mepolizumab**, a *monoclonal antibody*, a type of protein designed to recognize a specific target substance in the body.

Mepolizumab, the active ingredient in Nucala Solution for Injection, blocks a protein called interleukin-5. By blocking the activity of this protein, mepolizumab limits the production of eosinophils in the bone marrow and reduces the number of eosinophils in the circulation and lungs.

- Some people with severe asthma have too many *eosinophils* (a type of white blood cell) in the blood and lungs. This condition is called *eosinophilic asthma* –

the type of asthma Nucala Solution for Injection can treat.

If you are already being treated with medicines such as high dose inhalers but your asthma is not well controlled, Nucala Solution for Injection can reduce your number of attacks.

If you are taking medicines called *oral corticosteroids*, Nucala Solution for Injection can also help reduce the daily dose you need to control your asthma.

- **Chronic rhinosinusitis with nasal polyps (CRSwNP)** is a condition in which people have too many *eosinophils* (a type of white blood cell) in the blood and tissue lining the nose and sinuses. This condition can cause symptoms such as a blocked nose, loss of smell, and soft jelly-like growths inside the nose (called nasal polyps).

  Nucala Solution for Injection reduces the number of eosinophils in the blood and can reduce the size of the polyps, relieve nasal congestion and help prevent surgery for nasal polyps.

  Nucala Solution for Injection can also help reduce the need for *oral corticosteroids* to control your symptoms.
- **Eosinophilic granulomatosis with polyangiitis (EGPA)** is a condition where people have too many *eosinophils* (a type of white blood cell) in the blood and tissues and also have vasculitis. This condition most commonly affects the lungs and sinuses but often affects other organs such as the skin, heart and kidneys.

  Nucala Solution for Injection can help control and delay a flare-up of these EGPA symptoms. This medicine can also help your physician to reduce the daily dose of *oral corticosteroids* you need to control your symptoms.
- **Hypereosinophilic syndrome (HES)** is a condition in which there is a high number of *eosinophils* (a type of white blood cell) in the blood. These cells can damage organs in the body, particularly the heart, lungs, nerves and skin.

  Nucala Solution for Injection helps reduce the symptoms and prevent flares. If you are taking *oral corticosteroids*, Nucala Solution for Injection can also help reduce the daily dosage needed to control your HES symptoms/flares.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (**allergic**) to the active ingredient (mepolizumab) or any of the additional ingredients contained in the medicine (detailed in section 6).

→ **Check with your physician** if you think this applies to you.

Special warnings regarding use of the medicine

Talk to your physician before using Nucala Solution for Injection.

Worsening asthma

There are some people who experience asthma-related side effects or whose asthma may become worse during treatment with Nucala Solution for Injection.

→ **Tell your physician or nurse** if your asthma is uncontrolled, or gets worse, after

you start treatment with Nucala Solution for Injection.

Allergies and injection site reactions

Medicines of this type (*monoclonal antibodies*) can cause severe allergic reactions when injected (see section 4 “Side Effects”).

If you may have had a similar reaction to any type of injection or medicine,

→ **Tell your physician before receiving Nucala Solution for Injection.**

Infections caused by a parasite

Nucala Solution for Injection may weaken your resistance to infections caused by parasites. If you already have an infection caused by a parasite, it should be treated before you start treatment with Nucala Solution for Injection. If you live in a region where these infections are common or if you are travelling to such a region:

→ **Check with your physician** if you think any of these may apply to you.

Children and adolescents

This medicine is not intended for use **in children or adolescents below the age of 18.**

Drug interactions

If you are taking, have recently taken or are beginning to take other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist. In particular if you are taking:

Other medicines for the treatment of asthma, CRSwNP, EGPA or HES.

Consult with the physician before discontinuing other medicines to treat asthma, CRSwNP, EGPA or HES when beginning treatment with Nucala Solution for Injection. These medicines (especially medicines called *oral corticosteroids*) should be stopped only by your physician’s instruction, gradually, under your physician’s close supervision and dependent on your response to Nucala Solution for Injection.

Pregnancy and breastfeeding

If you are pregnant, think you are pregnant or planning to become pregnant, **consult with your physician** before using the medicine.

It is not known whether the ingredients of Nucala Solution for Injection can pass into breast milk. **If you are breastfeeding, you must check with your physician** before using Nucala Solution for Injection.

Driving and using machinery

The possible side effects of Nucala Solution for Injection are unlikely to affect your ability to drive or use machinery.

Important information about some of the ingredients of the medicine

Nucala Solution for Injection contains sodium.

The medicine contains less than 1 mmol sodium (23 mg) per 100 mg dose, and is therefore considered to be essentially sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions. Check with the physician or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined by the doctor only.

Nucala Solution for Injection is given by injection under the skin (subcutaneous injection).

Your nurse or physician will decide if you can inject yourself or if your caregiver can give you the injection.
If needed, they will provide you with training to show you or your caregiver the correct way to use Nucala Solution for Injection.

The usual dose is generally:

- **For the treatment of severe eosinophilic asthma – 100 mg, one subcutaneous injection every 4 weeks.**
- **For the treatment of severe chronic rhinosinusitis with nasal polyps (CRSwNP) – 100 mg, one subcutaneous injection every 4 weeks.**
- **For the treatment of eosinophilic granulomatosis with polyangiitis (EGPA) – 300 mg (3 subcutaneous injections of 100 mg) once every 4 weeks.**
- **For the treatment of hypereosinophilic syndrome (HES) – 300 mg (3 subcutaneous injections of 100 mg), once every 4 weeks.**

  Injection sites must be at a distance of at least 5 cm from each other.

Do not exceed the recommended dosage.

The instructions for using the pre-filled pen are found at the end of this leaflet.

If you use more Nucala Solution for Injection than you should
If you think you have injected too much Nucala Solution for Injection, **contact the physician** and consult with him.
If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to the hospital emergency room, and bring the package of the medicine with you.

If you missed a dose of Nucala Solution for Injection
If you missed a dose of Nucala Solution for Injection, you or your caregiver should inject the next dose of Nucala Solution for Injection as soon as you remember.
If you do not notice that you have missed a dose until it is already time for your next dose, then just inject the next dose as planned. If you are not sure what to do, consult with the physician, pharmacist or nurse.

Adhere to the treatment regimen as recommended by the physician.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the physician.
Do not stop injections of Nucala Solution for Injection unless your physician advises you to.
Interrupting or stopping the treatment with Nucala Solution for Injection may cause the symptoms and attacks of your illness to come back.

If the symptoms of your illness get worse while receiving injections of Nucala Solution for Injection

→ **Contact your physician.**

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.
If you have further questions regarding use of the medicine, consult the physician or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Nucala Solution for Injection 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.
The side effects caused by Nucala Solution for Injection are usually mild to moderate but can occasionally be severe.

Allergic reactions
Some people may have allergic or allergic-like reactions. These reactions may be common (they can affect **up to 1 in every 10 people**). They usually occur within minutes to hours after the injection, but sometimes symptoms can appear up to several days later.
Symptoms can include:

- chest tightness, cough, difficulty breathing
- fainting, dizziness, feeling lightheaded (due to a drop in blood pressure)
- swelling of the eyelids, face, lips, tongue or mouth
- hives
- rash

→ **Seek medical assistance immediately** if you think you may be having an allergic reaction.

If you may have had a similar reaction to any type of injection or medicine,

→ **Tell the physician** before you receive Nucala Solution for Injection.

Additional side effects

Very common side effects
May occur in **more than 1 in every 10 people**:

- headache

Common side effects
May occur in **up to 1 in every 10 people**:

- chest infection – symptoms may include cough and fever (high temperature)
- urinary tract infection (blood in urine, pain upon urination and increased frequency of urination, fever, pain in lower back)
- upper abdominal pain (stomach pain or discomfort in the upper area of the stomach)
- fever (high temperature)
- eczema – itchy red patches on the skin

- injection-site reactions (pain, redness, swelling, itching, and burning sensation of the skin in the area close to the injection site)
- back pain
- pharyngitis (sore throat)
- nasal congestion (stuffy nose)

Rare side effects

These may occur in **up to 1 in every 1,000 people**:

- severe allergic reactions (*anaphylaxis*)

→ **Tell your physician or a nurse immediately** if you develop any of these symptoms.

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 with the physician, pharmacist or nurse.

Reporting side effects

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, should 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 physician.
- 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.
- Keep refrigerated (2°C-8°C).
- Do not freeze.
- Store in the original package in order to protect from light.
- If necessary, it can be removed from the refrigerator and kept in the unopened package for up to 7 days at room temperature (up to 30°C), protected from light, and no later than the expiry date of the preparation. Discard if left out of the refrigerator for more than 7 days.
- For use within 8 hours of opening the carton package. Discard if not used within 8 hours.

6. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
  Sucrose, sodium phosphate dibasic heptahydrate, citric acid monohydrate, polysorbate 80, EDTA disodium dihydrate, water for injection.
- **What the medicine looks like and the contents of the package**

Nucala Solution for Injection is supplied in a single use pre-filled pen containing 1 mL of a clear to opalescent, colorless to pale yellow to pale brown solution.
Each package contains 1 pre-filled pen or 3 pre-filled pens.
Not all package sizes may be marketed.

- **License Holder:** GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- **Manufacturer:** Glaxo Operations UK Ltd., Barnard Castle, England.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 168-06-36652.
- Revised in May 2022 according to MOH guidelines.

7. STEP BY STEP INSTRUCTIONS FOR INJECTION USING THE PRE-FILLED PEN

Inject once every 4 weeks.

Follow the instructions below on how to use the pre-filled pen.
Failure to follow these instructions may affect the proper functioning of the pre-filled pen.
You should also undergo training on how to use the pre-filled pen.
Nucala Solution for Injection in a pre-filled pen is intended for **subcutaneous use only**.

How to store Nucala Solution for Injection

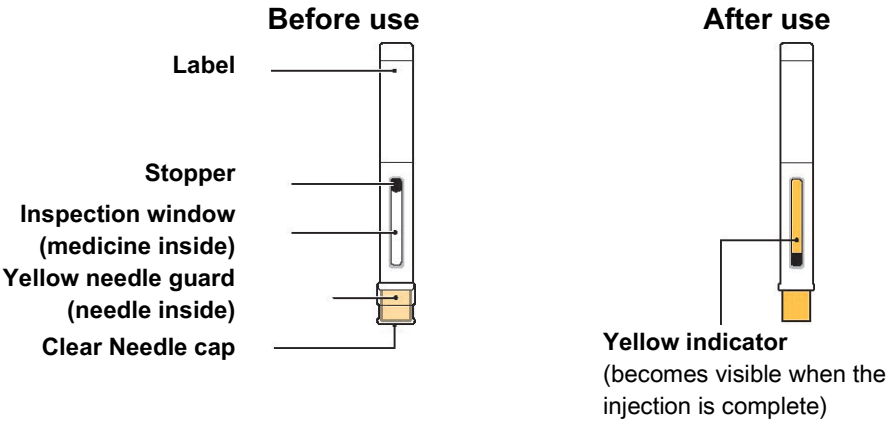
- Keep refrigerated (2°C-8°C) before use.
- Do not freeze.
- Keep in the carton package to protect from light.
- Keep out of the reach and sight of children.
- If necessary, it can be removed from the refrigerator and kept in the unopened package for up to 7 days at room temperature (up to 30°C), protected from light, and no later than the expiry date of the preparation. Discard safely if left out of the refrigerator for more than 7 days.
  Do not store at a temperature above 30°C.
- For use within 8 hours of opening the carton package. Discard if not used within 8 hours.

Before you use Nucala Solution for Injection

The pre-filled pen is intended to be used once only and should then be discarded.

- **Do not** share your Nucala Solution for Injection in pre-filled pen with another person.
- **Do not** shake the pen.
- **Do not** use the pen if dropped onto a hard surface.
- **Do not** use the pen if it appears damaged.
- **Do not** remove the needle cap until just before your injection.

Know the parts of the pre-filled pen



Prepare

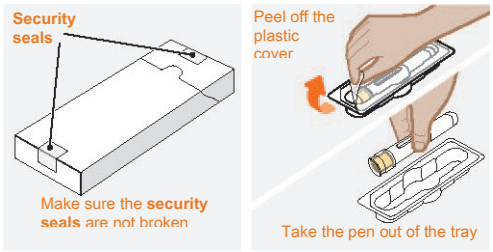
1. Prepare what you need

Find a comfortable, well-lit and clean surface. Make sure you have within reach:

- Nucala Solution for Injection in a pre-filled pen
- Alcohol wipe (not included in package)
- Gauze pad or cotton wool ball (not included in package)

Do not perform the injection if you do not have all the accessories listed above.

2. Take out the pre-filled pen

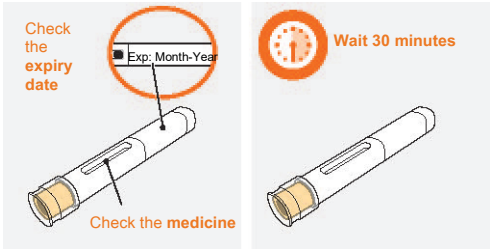


- Take the carton package out of the refrigerator. Check that the security seals are not broken.
- Remove the tray from the carton package.
- Peel back the cover from the tray.
- Holding the middle of the pen, carefully take it out of the tray.
- Place the pen on a clean, flat surface, at room temperature, away from direct sunlight and out of the reach of children.

Do not use the pen if the security seal on the carton package is broken.

Do not remove the needle cap at this stage.

3. Inspect and wait 30 minutes before use



- Check the expiry date on the label of the pen.
- Look in the inspection window to check that the liquid is clear (free from cloudiness or particles) and colorless to pale yellow to pale brown.
- It is normal to see one or more air bubbles.
- Wait 30 minutes (and no more than 8 hours) before use.

Do not use if the expiry date has passed.

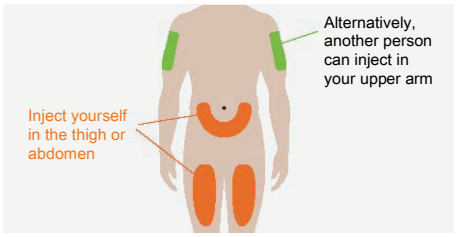
Do not warm the pen in a microwave, hot water, or direct sunlight.

Do not inject if the solution looks cloudy, discolored, or if it contains particles.

Do not use the pen if more than 8 hours have passed since opening of the carton package.

Do not remove the needle cap during this step.

4. Choose your injection site

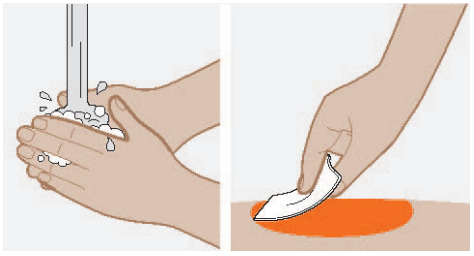


- You can inject Nucala Solution for Injection into your thigh or abdomen.
- If someone else gives you the injection, they can also inject in your upper arm.
- If you need more than one injection to reach the full dosage prescribed for you, keep a distance of at least 5 cm between injection sites.

Do not inject in places where your skin is injured, tender, red or hard.

Do not inject at a distance of less than 5 cm from your navel.

5. Clean your injection site



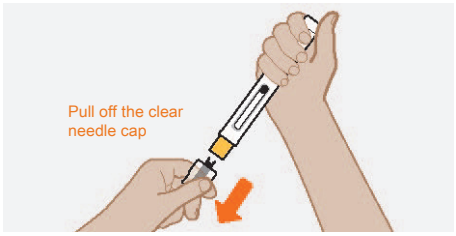
- Wash your hands with soap and water.

- Clean the injection site by wiping the skin with an alcohol wipe, and allow the skin to air dry.

Do not touch the injection site again until you have finished your injection.

Inject

6. Remove the clear needle cap

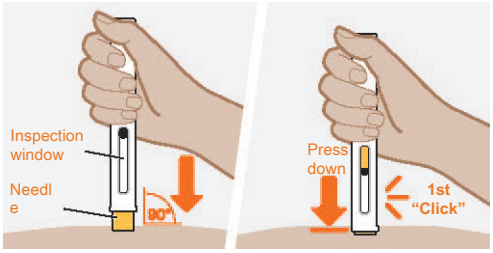


- Remove the clear needle cap from the pen by firmly pulling it straight off.
- Do not worry if you see a drop of liquid at the end of the needle. This is normal.
- Inject straight after removing the needle cap, and no more than 5 minutes after removing the needle cap.

Do not touch the yellow needle guard with your fingers. This could activate the pen too soon and may cause a needle injury.

After removal, **do not** put the needle cap back onto the pen, as it may accidentally start the injection.

7. Start your injection



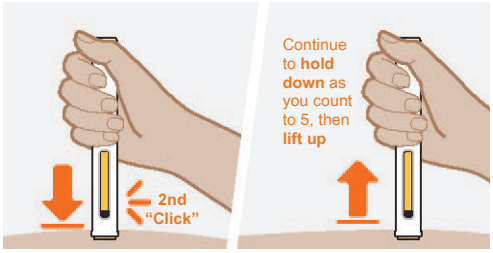
- Hold the pen with its inspection window facing towards you, so you can see it, and with the yellow needle guard facing down.
- Place the pen straight over your injection site with the yellow needle guard flat against the surface of your skin, as can be seen in the figure above.
- To start the injection, push the pen down all the way and keep it held down against your skin. The yellow needle guard will slide up into the pen.
- You should hear the 1st “click” which indicates that your injection has started.
- The yellow indicator will move down through the inspection window as you receive your dose.

Do not lift the pen from your skin at this stage, as it may mean that you might not get your full dose of medicine. The injection may take 15 seconds to complete.

Do not use the pen if the yellow needle guard does not slide up as described.

Discard it (see Step 9), and start again with a new pen.

8. Hold the pen in place to complete your injection



- Continue to hold the pen down until you hear the 2nd “click”, and the stopper and yellow indicator stop moving and fill the inspection window.
- Continue to hold the pen in place and count to 5. Then lift the pen away from your skin.
- If you **do not** hear the 2nd “click”:
  - Check that the inspection window is filled with the yellow indicator.
  - If you are not sure, hold the pen down for another 15 seconds to make sure the injection is complete.

Do not lift the pen until you are sure you have completed your injection.

- You may notice a small drop of blood at the injection site. This is normal. Press a cotton wool ball or gauze on the area for a few moments if necessary.

Do not rub the injection site.

Dispose

9. Dispose of the used pen

- Dispose of the used pen and needle cap according to guidelines. Ask your physician or pharmacist for advice if necessary.
- **Keep the used pens and needle caps out of the reach of children.**