PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE
PHARMACIST'S REGULATIONS (PREPARATIONS) - 1986
The medicine is dispensed with a physician's prescription only

Nucala Powder for Solution for Injection

Powder for solution for injection

Each vial contains 100 mg mepolizumab (100 mg/ml after reconstitution).

For a list of the 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 the 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?

The medicine is used for treatment of:

- ➔ Adult patients with **severe eosinophilic asthma**, which is not responding to other treatments, in combination with other medicines.
- ➔ Adult patients with **severe chronic rhinosinusitis with nasal polyps (CRSwNP)**, for whom corticosteroid treatment and surgery in the past ten years did not achieve adequate control of the disease. The medicine is given in combination with intranasal corticosteroids.
- ➔ Adult patients with **eosinophilic granulomatosis with polyangiitis (EGPA)** - Churg-Strauss Disease.
- ➔ Adult patients with **hypereosinophilic syndrome (HES)** that is not adequately controlled, with no non-hematological secondary cause. The medicine is given in combination with other medicines.

Therapeutic group
Monoclonal antibody, medicines for obstructive airway diseases.
Nucala Powder for 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 substance in Nucala Powder for 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 lowers the number of eosinophils in the

bloodstream and the 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 which Nucala Powder for Solution for Injection can treat it.
  If you are already being treated with medicines such as high-dose inhalers, but your asthma is not well controlled, Nucala Powder for Solution for Injection can reduce the number of asthma attacks.
  If you are taking medicines called *oral corticosteroids*, Nucala Powder for Solution for Injection can also help reduce the daily dosage needed 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 to form inside the nose (called nasal polyps).
  Nucala Powder for 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 Powder for Solution for Injection can 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 have vasculitis. This condition primarily affects the lungs and sinuses but can sometimes affect other organs such as the skin, heart and kidneys.
  Nucala Powder for Solution for Injection can help control and delay a flare-up of these EGPA symptoms. This medicine can also help your physician reduce the daily dose of oral corticosteroids you need to control your symptoms.
- **Hypereosinophilic syndrome (HES)** is a condition in which there are 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 Powder for Solution for Injection helps reduce the symptoms and prevent flare-ups. If you are taking *oral corticosteroids,* Nucala Powder for Solution for Injection can also help reduce the daily dosage you need to control your HES symptoms/flare-ups.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

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

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

Special warnings regarding use of the medicine
Speak with the physician before using Nucala Powder for Solution for Injection.

Asthma exacerbation
Some people experience asthma-related side effects, or their asthma may become worse during treatment with Nucala Powder for Solution for Injection.
→ **Tell your physician or nurse** if your asthma is uncontrolled, or worsens, after starting treatment with Nucala Powder for Solution for Injection.

Allergic and injection-site reactions
Medicines of this type *(monoclonal antibodies*) can cause severe allergic reactions when injected (see section 4 "Side effects").
If you have experienced a similar reaction to any type of injection or medicine,
→ **Tell your physician before receiving Nucala Powder for Solution for Injection.**

Parasitic infections
Nucala Powder for Solution for Injection may weaken your resistance to infections caused by parasites. If you already have a parasitic infection, it should be treated before you start treatment with Nucala Powder for Solution for Injection. If you live in a region where such 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 18 years of age.**

Drug interactions
If you are taking, if you have recently taken, or are about to start taking other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist, especially if you are taking:
Other medicines for treating asthma, CRSwNP, EGPA or HES.
Consult the physician before discontinuing other medicines for treatment of asthma, CRSwNP, EGPA or HES, once starting treatment with Nucala Powder for Solution for Injection. Stop taking these medicines gradually (especially medicines called *oral corticosteroids*) *per your physician's instructions only,* under the close supervision of your physician and depending on your response to Nucala Powder for Solution for Injection.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, **consult the physician** before using this medicine.

It is not known whether the ingredients of Nucala Powder for Solution for Injection can pass into breast milk. **If you are breast-feeding, consult the physician** before using Nucala Powder for Solution for Injection.

Driving and operating machinery
The possible side effects of Nucala Powder for Solution for Injection are unlikely to affect your ability to drive or operate machinery.

Important information about some of the ingredients of the medicine
Nucala Powder for Solution for Injection contains sodium
- This medicine contains less than 1 mmol of sodium (23 mg) in each dose (100 mg); therefore, it can be considered sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions. Check with the physician or the pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.
The dosage and treatment regimen will be determined only by the physician.
The medicine is given by a physician, nurse or healthcare professional as an injection under the skin (subcutaneously).

The recommended dosage is generally:
- **For treatment of severe eosinophilic asthma – 100 mg, one subcutaneous injection every 4 weeks.**
- **For treatment of severe chronic rhinosinusitis with nasal polyps (CRSwNP) – 100 mg, one subcutaneous injection every 4 weeks.**
- **For treatment of eosinophilic granulomatosis with polyangiitis (EGPA) – 300 mg (3 subcutaneous injections of 100 mg), once every 4 weeks**.
- **For treatment of hypereosinophilic syndrome (HES) – 300 mg (3 subcutaneous injections of 100 mg), once every 4 weeks**.
  The injection sites must be at a distance of at least 5 cm from each other.

Do not exceed the recommended dose.

If you have taken an overdose or if a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to a hospital emergency room and bring the package of the medicine with you.

If you miss a dose of Nucala Powder for Solution for Injection
If you missed a dose of Nucala Powder for Solution for Injection, contact your physician or hospital as soon as possible to re-schedule your appointment.

Adhere to the treatment regimen as recommended by the physician.

Even if there is an improvement in your health, do not stop the treatment with the medicine without consulting the physician.
Do not stop receiving injections of Nucala Powder for Solution for Injection, unless so advised by the physician.

Stopping or interrupting treatment with Nucala Powder for Solution for Injection may cause symptoms and attacks of your ailment to return.

If the symptoms of your ailment worsen while receiving injections of Nucala Powder for Solution for Injection
→ **Call the 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 the use of the medicine, consult the physician, pharmacist or nurse.

4. SIDE EFFECTS

As with any medicine, use of Nucala Powder for Solution for Injection may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.
The side effects of Nucala Powder for Solution for Injection are generally mild to moderate, but can sometimes be severe.

Allergic reactions
Some users may suffer from allergic or allergic-like reactions. These reactions may be common (may affect **up to 1 in 10 people**). They usually occur within minutes to hours after the injection, but sometimes symptoms may 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 help immediately** if you think you may be suffering from an allergic reaction.

If you may have experienced a similar reaction to any injection or medicine,
→ **Tell the physician** before you receive Nucala Powder for Solution for Injection.

Other side effects

Very common side effects
These may occur in **more than 1 in 10 people:**
- Headache

Common side effects
These may occur in **up to 1 in 10 people:**
- Chest infection – symptoms may include cough and fever (high temperature)
- Urinary tract infection (blood in the urine, painful urination and increase in the frequency of urination, fever, pain in lower back)

- Upper abdominal pain (stomach pain or discomfort in the upper part of the stomach)
- Fever (high temperature)
- Itching (eczema, red and itchy patches on the skin)
- Injection-site reactions (pain, redness, swelling, itching and burning sensation of the skin in the area near the injection site)
- Back pain
- Pharyngitis (sore throat)
- Nasal congestion (stuffy nose)

Rare side effects
These may occur in **up to 1 in 1,000 people:**
- Severe allergic reactions (*anaphylaxis*)

→ **Refer immediately to a physician or to a nurse** if you develop any of these symptoms.

If a side effect occurred, if one of the side effects worsens or if you suffer from a side effect not mentioned in the leaflet, consult 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 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 a 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.
- Store below 25°C.
- Do not freeze.
- Store in the original package in order to protect from light.

6. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains -**
  Sucrose, sodium phosphate dibasic heptahydrate, polysorbate 80, hydrochloric acid, water for injection.
- **What the medicine looks like and the content of the package**
  Nucala Powder for Solution for Injection is supplied as a white powder, in a

clear glass vial with a rubber stopper.
Nucala Powder for Solution for Injection is available in a pack containing 1 vial or in a pack containing 3 vials.

Not all pack sizes may be marketed.

- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: GlaxoSmithKline Manufacturing S.p.A., Parma, Italy
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 157-57-34861

Revised in May 2022 according to MOH guidelines.

Nuc PT v4C

The following information is intended for healthcare professionals only:

Step-by-step instructions for use and handling, reconstitution, and administration of Nucala powder for solution for injection

Nucala is provided as a lyophilised, white powder in a single-use vial for subcutaneous injection only. Reconstitution should be carried out under aseptic conditions.

Once reconstituted, Nucala will contain a concentration of 100 mg/ml mepolizumab. The solution for injection can be stored below 30°C for no more than 8 hours. Any unused concentrate or solution remaining after 8 hours must be discarded.

Traceability

In order to improve the traceability of biological medicinal products, the name of the administered product should be clearly recorded. It is recommended to record the batch number as well.

Instructions for reconstitution for each vial

1. **Reconstitute the contents of the vial with 1.2 ml of sterile water for injections** preferably using a 2 to 3 ml syringe and a 21 gauge needle. The stream of sterile water should be directed vertically, onto the centre of the lyophilised cake. Allow the vial to sit at room temperature during reconstitution, gently swirling the vial for 10 seconds with a circular motion at 15-second intervals until the powder is dissolved.

Note: The reconstituted solution ***must not be shaken*** *during the procedure as this may lead to product foaming or precipitation. Reconstitution is typically complete within 5 minutes after the sterile water has been added, but it may take additional time.*

2. If a mechanical reconstitution device (swirler) is used to reconstitute Nucala, reconstitution can be accomplished by swirling at 450 rpm for no longer than 10 minutes. Alternatively, swirling at 1,000 rpm for no longer than 5 minutes is acceptable.
3. Following reconstitution, Nucala should be visually inspected for particulate matter and clarity prior to use. The solution should be clear to opalescent, and colorless to pale yellow or pale brown, free of visible particles. Small air bubbles, however, are expected and acceptable. If particulate matter remains in the solution or if the solution appears cloudy or milky, the solution must not be used.
4. The reconstituted solution, if not used immediately must be:

- Protected from sunlight
- Stored below 30°C, not frozen
- Discarded if not used within 8 hours of reconstitution

Instructions for administration

1. For subcutaneous administration, a 1 ml polypropylene syringe fitted with a disposable needle 21 gauge to 27 gauge x 0.5 inch (13 mm) should preferably be used.
2. Just prior to administration, remove 1 ml of reconstituted Nucala from one vial. Do not shake the reconstituted solution during the procedure as this could lead to product foaming or precipitation.
3. Administer the 1 ml injection (equivalent to 100 mg mepolizumab) subcutaneously into the upper arm, thigh, or abdomen.

If more than one vial is required for administration of the prescribed dosage, repeat steps 1 to 3. It is recommended that individual injection sites are separated by at least 5 cm.

Disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.