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

The medicine is dispensed with a doctor's prescription only

Dupixent 300 mg

Solution for injection in a pre-filled pen

Active ingredient:
Each pre-filled pen of Dupixent 300 mg contains 300 mg dupilumab.

Inactive and allergenic ingredients in the preparation: see section 2 and section 6.

Read this leaflet carefully in its entirety before using the medicine.
Keep this leaflet; you may need to read it again.
This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor, pharmacist or nurse.
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?

- Treatment of moderate-to-severe atopic dermatitis, in adults and children from six months of age and above, when inadequately controlled by prescription medicines for topical treatment or when the patient cannot use topical treatment.
  Dupixent may be used with or without topical corticosteroids.
- Maintenance treatment of moderate-to-severe asthma, in adults and children from the age of six years and above, in combination with other asthma medicines in patients whose asthma is not controlled by their asthma medications. Dupixent helps prevent severe asthma attacks and can improve breathing. Dupixent may also help reduce the amount of oral corticosteroids the patient takes, while preventing severe asthma attacks and improving breathing.
  Dupixent is not used to treat sudden breathing problems.
- Dupixent 300 mg is used with other medicines to treat chronic rhinosinusitis with nasal polyposis in adults whose disease is not controlled.
- Dupixent 300 mg is used to treat eosinophilic esophagitis in adults and children from the age of 12 years, who weigh at least 40 kg.
- Dupixent 300 mg is used to treat moderate to severe prurigo nodularis in adults eligible for systemic treatment.

Therapeutic group: Non-corticosteroid treatments for the skin and for dermatitis.

Dupixent acts by blocking two proteins that cause a type of inflammation that plays a central role in eczema/atopic dermatitis, asthma, chronic rhinosinusitis with nasal polyposis, eosinophilic esophagitis and prurigo nodularis.

2. BEFORE USING THE MEDICINE

Do not use the medicine:
if you are sensitive (allergic) to dupilumab or to any of the additional ingredients contained in the medicine (see section 6).

Special warnings regarding use of the medicine
Before treatment with Dupixent, talk with the doctor about all your medical conditions, including if:

- you have eye problems.
- you have an intestinal parasitic infection.
- you are scheduled to receive any vaccinations. You should not receive a "live vaccine" right before and during treatment with Dupixent.

Children and adolescents

- Dupixent is not intended for treatment of atopic dermatitis in children under 6 months of age.
- Dupixent is not intended for the treatment of asthma in children under 6 years of age.
- Dupixent is not intended for the treatment of chronic rhinosinusitis with nasal polyposis in children and adolescents under 18 years of age.
- Dupixent is not intended for the treatment of eosinophilic esophagitis in children under 12 years of age and who weigh at least 40 kg.
- Dupixent is not intended for the treatment of prurigo nodularis in children and adolescents under 18 years of age.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist, especially if:

- you are taking oral, topical, or inhaled corticosteroid medicines.
- you have asthma and are taking asthma medicines.
- you have atopic dermatitis, chronic rhinosinusitis with nasal polyposis, eosinophilic esophagitis or prurigo nodularis, as well as asthma.

Do not change or stop taking your corticosteroids or asthma medicines without consulting the doctor. This may cause other effects, which were already under control by the corticosteroids or asthma medicine, to recur.

Pregnancy, breastfeeding and fertility
If you are pregnant, think you may be pregnant, or are planning to become pregnant, or are breastfeeding, consult with your doctor before taking any medicine.

- The effect of this medicine on the unborn baby is unknown.
- It is not known whether Dupixent passes into breast milk.

Important information about some of the ingredients of the medicine
Dupixent contains less than 1 mmol (23 mg) sodium per 300 mg dose, i.e., it is essentially "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Thoroughly read the "Instructions for Use" provided with the leaflet for information on how to prepare and inject Dupixent, how to properly store the medicine and how to dispose of used Dupixent pens.
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.
Dupixent is given by injection under the skin (subcutaneous injection).
If your doctor or nurse decides that you or your caregiver can administer the Dupixent injection, you or your caregiver must receive training on how to properly prepare and perform the injection.
Do not attempt to inject Dupixent before being trained by the doctor or nurse.
The Dupixent pen is not intended for use in children under 6 years of age. For children 6 months to less than 6 years of age, contact a doctor who will prescribe Dupixent pre-filled syringe.
For children from age 12 years and above, it is recommended that the Dupixent injection be given by or under the supervision of an adult.
For children 6 months to 12 years of age, the Dupixent injection must be administered by a caregiver.

How much Dupixent to inject and for how long
The dosage and treatment regimen will be determined by the doctor only.
Each pen of Dupixent 300 mg contains one dose of Dupixent (300 mg).

Recommended dosage for adults with atopic dermatitis:

- Starting dose of 600 mg (two 300 mg injections).
- Thereafter, 300 mg every two weeks.

Recommended dosage for children 6 years to 17 years of age with atopic dermatitis:

Body weight	Initial loading dose	Subsequent doses
15 kg to less than 30 kg	600 mg (two 300 mg injections)	300 mg every 4 weeks
30 kg to less than 60 kg	400 mg (two 200 mg injections)	200 mg every 2 weeks
60 kg or more	600 mg (two 300 mg injections)	300 mg every 2 weeks

Recommended dosage for children 6 months to 5 years of age with atopic dermatitis:

Body weight	Initial dosage* and subsequent doses
5 kg to less than 15 kg	200 mg (one 200 mg injection) every 4 weeks
15 kg to less than 30 kg	300 mg (one 300 mg injection) every 4 weeks

*for children 6 months to 5 years of age with atopic dermatitis, an initial loading dose is not recommended.

Recommended dosage for adults and children from the age of 12 years and above with asthma:

Initial loading dose	Subsequent doses
400 mg (two 200 mg injections)	200 mg every 2 weeks
OR	
600 mg (two 300 mg injections)	300 mg every 2 weeks
Dosage for patients with asthma who are dependent on oral corticosteroids or patients with asthma and comorbid moderate-to-severe atopic dermatitis or adults with chronic rhinosinusitis with nasal polyposis	
600 mg (two 300 mg injections)	300 mg every 2 weeks

Recommended dosage for children 6 years to 11 years of age with asthma:

Body weight	Initial dose* and subsequent doses
15 kg to less than 30 kg	300 mg every 4 weeks
30 kg or more	200 mg every 2 weeks

*for children 6 to 11 years of age with asthma, an initial loading dose is not recommended.
For children 6 to 11 years of age with asthma and concomitant moderate-to-severe atopic dermatitis, follow the table showing the recommended dosage for children 6 to 17 years of age with atopic dermatitis, which includes an initial loading dose.

Dosage for adults with chronic rhinosinusitis with nasal polyposis:
The recommended dosage is 300 mg every two weeks.

Dosage for adults and children from the age of 12 years with eosinophilic esophagitis:
The recommended dosage for adults and children from the age of 12 years, who weigh at least 40 kg, is 300 mg every week.

Dosage for adults with prurigo nodularis:
The recommended dosage is an initial dose of 600 mg (two 300 mg injections) and then 300 mg every two weeks.

Do not exceed the recommended dose.

If you use more Dupixent than needed
If you used more Dupixent than needed or the dose has been given too early, get medical help right away.

If you forgot to use Dupixent
If you forgot to inject a dose of Dupixent, refer to your doctor, pharmacist or nurse.

If you stop using Dupixent
Do not stop using Dupixent without first consulting with the doctor.
Your doctor may recommend taking additional medicines together with Dupixent. Use the other medicines exactly as instructed by your doctor.

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

4. SIDE EFFECTS

As with any medicine, use of Dupixent 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.

Dupixent can cause serious side effects including:

- **Allergic reactions. Dupixent can cause allergic reactions that can sometimes be severe.**
  Stop using Dupixent and refer to your doctor or an emergency center immediately if one or more of the following signs or symptoms occur:
  Breathing problems or wheezing, swelling of the face, lips, mouth, tongue or throat, fainting, dizziness, lightheadedness, rapid heartbeat, fever, general ill feeling, swollen lymph nodes, joint pain, hives, itching, skin rash, nausea or vomiting, cramps in the area of the stomach.
- **Eye problems.** Refer to your doctor if you have a new eye problem or a worsening of a previous problem, including eye pain or vision changes, such as blurred vision. Your doctor may send you to an ophthalmologist for an eye examination, if needed.
- **Inflammation of blood vessels.** Rarely, patients suffering from asthma may develop this effect. This happens to people who are also taking an oral steroid, but who stop treatment with it or whose dosage is reduced. It is not known whether this is caused as a result of Dupixent. Tell the doctor immediately if you have: a rash, chest pain, worsening of shortness of breath, a feeling of pins and needles or numbness of your arms or legs, persistent fever.
- **Joint pains.** Joint pains can happen in people who use Dupixent. Some people had trouble walking or moving due to their joint symptoms, and in some cases, required hospitalization. Tell your doctor about new or worsening joint symptoms. Your doctor may stop Dupixent treatment if you develop joint symptoms.

The most common side effects of Dupixent:

- injection site reactions
- upper respiratory tract infections
- eye and eyelid inflammation, including redness, swelling and itching, sometimes with blurred vision
- dry eye
- herpes virus infections
- cold symptoms (upper respiratory tract infection)
- pain in the throat (oropharyngeal pain)
- cold sores in the mouth and on the lips
- high count of certain white blood cells (eosinophilia)
- dizziness
- muscle pains
- diarrhea
- trouble sleeping
- toothache
- gastritis
- joint pain
- intestinal parasitic infections

The following additional side effects have been reported:

- facial rash or redness

If a side effect occurs, if any of the side effects worsen, or when you are suffering 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:
Do not store different medicines in the same package. Store in the original package in order to protect from light.
Store in a refrigerator (2°-8°C). Do not freeze. Do not shake. Do not heat or expose the Dupixent pen to direct sunlight.

If necessary, the pens can be stored at a room temperature of up to 25°C for a maximum of 14 days. Do not store at a temperature above 25°C. If you take the carton out of the refrigerator, write the removal date on the outer package and use Dupixent within 14 days. Do not return the medicine to the refrigerator.

Do not use the medicine if it is cloudy, discolored or contains particles.
Do not discard medicines into the household waste bin. Ask your pharmacist how to dispose of medicines you no longer need. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains the following inactive ingredients:

Each Dupixent 300 mg pen contains:
Sucrose (100 mg), L-arginine monohydrochloride, L-histidine monohydrochloride monohydrate, L-histidine, polysorbate 80, glacial acetic acid, sodium acetate trihydrate, water for injections.

What the medicine looks like and the contents of the package:
Each pre-filled pen contains 300 mg dupilumab in 2 ml of clear to slightly opaque, colorless to pale yellow solution.

The package contains: 1, 2, 3 or 6 pre-filled pens with a needle shield.

Not all package sizes may be marketed.

This leaflet does not contain all the information about the medicine. If you have any question or are not sure about anything, please refer to the doctor.

License holder and importer's name and address: Sanofi Israel Ltd., Greenwork Park P.O. box 47 Yakum.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 1602235266

Revised in February 2024 according to MOH guidelines.

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INSTRUCTIONS FOR USE

Dupixent 300 mg
Single-use pre-filled pen

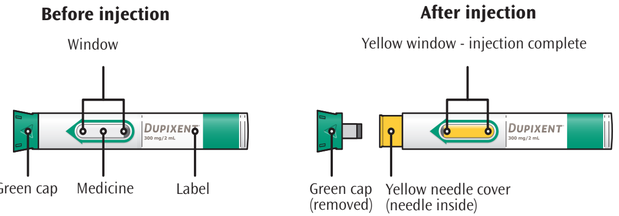
The Instructions for Use contain information explaining how to inject Dupixent.

Read the instructions before using the pen. **Do not inject yourself or anyone else until you have been shown how to inject Dupixent.** Your medical team can show you or your caregiver how to prepare and inject a dose of Dupixent before you try to do it yourself for the first time. Keep these instructions for future use. Call your medical team if you have questions.

The Dupixent pre-filled pen is intended for use in adults and children from the age of 6 years and above.

The Dupixent pre-filled pen is a single-use device. It contains 300 mg of Dupixent for injection under the skin (subcutaneous injection).

The parts of the Dupixent pre-filled pen are displayed below:



Important information

- Read all of the instructions carefully before using Dupixent pre-filled pen.
- Ask your healthcare provider how often you will need to inject the medicine.
- **In children aged 12 years and older**, it is recommended that Dupixent be administered by or under the supervision of an adult.
- **In children 6 years to 12 years of age**, the Dupixent injection must be administered by a caregiver.
- Choose a different injection site for each injection.
- **Do not** press or touch the yellow needle cover with your fingers.
- **Do not** inject through clothes.
- **Do not** remove the green cap until just before the injection.
- **Do not** try to put the green cap back on the pen.
- Throw away the used pen immediately after use.
- **Do not** re-use a Dupixent pre-filled pen.

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Storing Dupixent

- Before use, store pens in the refrigerator at a temperature between 2°C-8°C.
- Store pens in the original package in order to protect from light.
- If necessary, Dupixent pens can be stored at room temperature (up to 25°C) for **up to 14 days**.
- **Do not** store Dupixent pens at a room temperature above 25°C.
- After removing a Dupixent pen from the refrigerator, use it within 14 days or throw it away.
- **Never** shake the pen.
- **Do not** heat the pen.
- **Do not** freeze the pen.
- **Do not** put the pen into direct sunlight.
- **Keep the Dupixent pens and other medicines out of the reach and sight of children.**

A. GET READY TO INJECT

A1: Prepare supplies

Choose a clean and flat work surface.

Ensure you have the following items:

the Dupixent pen

*an alcohol wipe

*a cotton ball or gauze pad

*a puncture-resistant container (see Step D)

**These items are not included in the product package*

A2: Check the pen

Do not use the Dupixent pen if it has been damaged.

Do not use the Dupixent pen if the green cap is missing or not securely attached.

Do not use the Dupixent pen if the window is yellow before use.

A3: Look at the label

Check the preparation and the dose

- Make sure you have the correct preparation and the correct dose.

- Check the expiration date.

⚠ **Do not** use the Dupixent pen if the expiration date has passed.

A4: Check the medicine

- Look at the medicine through the window. It should be clear and colorless to pale yellow.
- Note: You may see an air bubble, this is normal.

⚠ **Do not** use the pen if the liquid is discolored or cloudy, or if it contains visible flakes or particles.

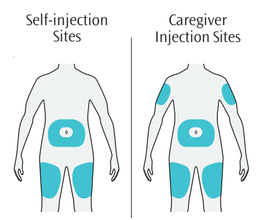
A5: Wait 45 minutes

- Place the Dupixent pen on a flat surface and let it warm up naturally at room temperature, below 25°C, for at least 45 minutes.

⚠ **Do not** heat the Dupixent pen in a microwave, hot water or direct sunlight.

B. CHOOSE AND PREPARE YOUR INJECTION SITE

B1: Wash your hands well with soap and water



B2: Choose an injection site

- **Thigh**
- **Abdomen,** except for 5 cm around your navel.
- A caregiver can also inject in the outer area of your **upper arm**.
- Choose a different injection site each time you inject Dupixent.

⚠ **Do not** inject into skin that is tender, damaged, has bruises or scars, or into areas with visible veins.

⚠ **Do not** inject through clothes.

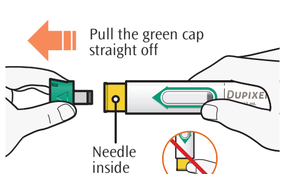
B3: Prepare the injection site

- Clean the injection site with an alcohol wipe.
- Let the skin dry before injecting.

⚠ **Do not** touch the injection site again or blow on it before the injection.

C. GIVE THE INJECTION

C1: Remove green cap



- Remove the green cap by pulling it straight off, as shown in the illustration. **Do not** twist the green cap off.
- **Do not** remove the green cap until you are ready to inject.
- **Do not** touch or press the yellow needle cover with your fingers. The needle is inside.

⚠ **Do not** put the green cap back on the pen after you have removed it.

C2: Pinch the skin and place

Pinch the skin before and during the injection.

- Hold the Dupixent pen so that you can see the window. Place the yellow needle cover on the skin.
- Place the yellow needle cover on the skin at approximately a 90-degree angle.
- Pinching of the skin is not needed for adults and children aged 12 years and older.

C3: Press down → Look at the window until it turns completely yellow → Then count to 5

Press and hold the Dupixent pen firmly against the skin **until you cannot see the yellow needle cover**.

- There will be a **"click"** when the injection starts, **and then**
- The window will start to turn yellow.
- **Keep pressing** the Dupixent pen against the skin.

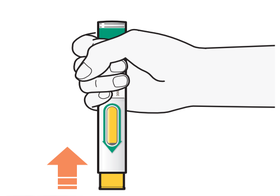
Keep pressing the Dupixent pen against the skin and **watch the window**:

- The window will turn completely yellow, **and then**
- You will hear **a second "click"**.
- **Keep pressing** the Dupixent pen against the skin.

Keep pressing the Dupixent pen against the skin **and count to 5 to make sure you get the full dose**.

Pinching of the skin is not needed for adults and children aged 12 years and older.

C4: Remove



- After you have completed the injection, pull straight up to remove the Dupixent pen from the skin. The yellow needle cover will cover the needle.
- If you see blood at the injection site, gently wipe with a cotton ball or gauze pad.

⚠ **Do not** rub the skin after the injection.

If the window does not turn completely yellow, or if it looks like medicine is still coming out of the pen, you may not have received the full dose. Dispose of the pen and contact your medical team immediately.

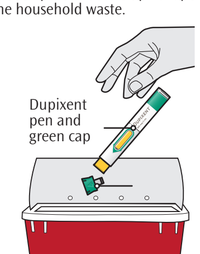
⚠ **Do not** administer a second dose without speaking to your medical team.

D. DISPOSAL OF A USED DUPIXENT PEN

How to dispose of the Dupixent pen

Dispose of used Dupixent pens and green caps in a puncture-resistant container, immediately after use.

⚠ **Do not** dispose of used Dupixent pens and green caps in the household waste.



⚠ **Do not put the green cap back on the pen.**

Keep the container out of the reach and sight of children.