

## **Patient package insert according to Pharmacists' Regulations (Preparations) – 1986**

This medicine can be sold with a physician's prescription only

### **Deximune® 25, 50, 100 mg, Capsules**

Each capsule contains: Ciclosporin 25, 50 or 100 mg respectively.

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

**Read this entire leaflet carefully before using the medicine.** This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist. This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if you think that their medical condition is the same as yours.

#### **1. What is the medicine intended for?**

- Prophylaxis of organ rejection in kidney, liver and heart transplantation in combination with corticosteroids.
- Treatment during a bone marrow transplantation.
- Treatment of eye inflammation called uveitis, which is not caused by infection (Endogenous uveitis).
- Treatment of nephrotic syndrome (MCD, Minimal Change Disease type) when conventional therapy has failed.
- Treatment of severe cases of rheumatoid arthritis, when standard treatment is ineffective or inappropriate.
- Treatment of severe cases of psoriasis, in patients above 16 years of age that do not respond to other treatment.
- Treatment of severe cases of atopic dermatitis in adults, for up to 8 weeks only, when conventional therapy is ineffective or inappropriate.

**Therapeutic group:** Immunosuppressants.

If you have undergone an organ or bone marrow transplantation, the function of **Deximune** is to regulate your body's immune system. **Deximune** prevents rejection of transplanted organs by blocking the development of special cells which would normally attack the transplanted tissue. If you suffer from a non-transplant disease, in which your body's immune response attacks the cells in your body (autoimmune disease), **Deximune** suppresses the immunoreactions in these diseases.

#### **2. Before using the medicine**

If you are taking **Deximune** after a transplant, the medicine will only be prescribed for you by a specialist experienced in transplants and/or autoimmune diseases.

The information in this leaflet may change according to the reason for which the medicine is being taken – after a transplant or for treatment of an autoimmune disease.

Follow your doctor's instructions exactly. They may be different from the general information in this leaflet.

#### **Do not use the medicine if:**

- You are hypersensitive (allergic) to the active ingredient (ciclosporin) or to any of the other ingredients this medicine contains (see section 6).
- You are taking preparations containing Hypericum perforatum (St. John's wort).
- You are taking preparations containing dabigatran etexilate (to prevent blood clots after surgery) or bosentan and aliskiren (to treat hypertension).

If these conditions apply to you, **inform the doctor without taking Deximune**. If you are not sure, consult the doctor before starting treatment with **Deximune**.

#### **Special warnings regarding the use of the medicine**

**Before and during treatment with Deximune, inform the doctor immediately if:**

- You have any signs of infection, such as fever or a sore throat. **Deximune** suppresses the immune system and may also affect your body's ability to fight infections.
- You have liver problems.
- You have kidney problems. Your doctor will carry out regular blood tests and may adjust your dose if necessary.
- You develop high blood pressure. Your doctor will check your blood pressure regularly and may give you a medicine to lower blood pressure as necessary.
- You have low magnesium levels. Your doctor may give you magnesium supplements, especially after an organ transplant operation.
- You have high blood potassium levels.
- You have gout.
- You need to get vaccinated.

If any of the above applies to you before or during treatment with **Deximune**, refer to the doctor immediately.

### **Protection from sun exposure**

**Deximune** suppresses the immune system. Therefore, it increases the risk of developing cancers, particularly cancer of the skin and lymphatic system. Limit exposure to the sun and to UV light by wearing protective clothes and frequently applying sunscreen with a high protection factor.

### **Inform your doctor before starting treatment if:**

- You have or have had problems related to alcohol dependence.
- You have epilepsy.
- You have any liver problems.
- You are pregnant.
- You are breastfeeding.
- The medicine is given to a child.

If these cases apply to you (or if you are unsure), refer to the doctor before taking **Deximune**. This is because this medicine contains an ingredient which is broken down into alcohol. See section "Important information about some of the ingredients of the medicine".

### **Tests during treatment with Deximune**

Your doctor will carry out the following tests:

- **Levels of ciclosporin in the blood** - especially if you have undergone a transplant.
- **Blood pressure** before starting treatment and regularly during treatment.
- **Liver and kidney function.**
- **Blood lipid levels.**

If you have any questions about how to use the medicine or why this medicine has been prescribed for you, refer to the doctor.

**If you are taking Deximune for non-transplant conditions** (such as: uveitis, intermediary or posterior uveitis or Behcet's uveitis, atopic dermatitis, severe rheumatoid arthritis or nephrotic syndrome), do not take **Deximune** if you have:

- Kidney problems (except for nephrotic syndrome).
- Infections which are not under control with medication.
- Any type of cancer.
- High blood pressure which is not under control with medication. If you develop high blood pressure during treatment and it cannot be controlled, your doctor should stop the treatment with **Deximune**.

Do not take **Deximune** if any of the above applies to you. If you are not sure, refer to the doctor or pharmacist before taking **Deximune**.

If you are being treated for Behcet's uveitis, the doctor will carefully monitor the course of treatment with **Deximune**, especially if you have neurological symptoms (for example: increased forgetfulness, personality changes noticed over time, psychiatric or mood disorders, "burning" sensation in limbs, decreased sensation in limbs, tingling sensation in limbs, weakness of limbs, walking disorders, headache with or without nausea and vomiting, vision disorders including

restricted movement of the eye).

If you are elderly and are being treated with **Deximune** for psoriasis or atopic dermatitis, avoid exposure to any type of UVB rays or phototherapy during the course of treatment. Your doctor will closely monitor the course of treatment.

### **Children and adolescents**

Do not give **Deximune** to children for non-transplant conditions, except for treatment of nephrotic syndrome.

### **Elderly (65 years of age and older)**

There is limited experience with administration of **Deximune** in elderly patients. Your doctor should monitor your kidney function. If you are over the age of 65 and have psoriasis or atopic dermatitis, you will only be treated with **Deximune** if your disease is particularly severe.

### **Drug interactions**

**If you are taking, or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.**

Inform the doctor or pharmacist before taking **Deximune**, especially if you are taking:

- Medicines that may affect potassium levels, such as medicines containing potassium, potassium supplements, potassium-sparing diuretics and certain medicines which lower blood pressure.
- Methotrexate. This medicine is used to treat tumors, severe psoriasis and severe rheumatoid arthritis.
- Medicines which may increase or decrease ciclosporin level (the active ingredient in **Deximune**) in the blood. The doctor might check the concentration of ciclosporin in your blood when starting or stopping treatment with other medicines.
  - Medicines which may increase ciclosporin blood levels: antibiotics (such as erythromycin or azithromycin), anti-fungal medicines (voriconazole, itraconazole), medicines used for heart problems or high blood pressure (such as: diltiazem, nifedipine, verapamil, amiodarone), metoclopramide (used to stop nausea), oral contraceptives, danazol (used to treat menstrual disorders), medicines used to treat gout (allopurinol), cholic acid and its derivatives (used to treat gallstones), protease inhibitors used to treat AIDS, imatinib (used to treat leukemia or tumors), colchicine, telaprevir (used to treat hepatitis C), cannabidiol (uses amongst others include treatment of seizures).
  - Medicines which may decrease ciclosporin blood levels: barbiturates (medicines used to induce sleep), certain anti-convulsants (such as carbamazepine or phenytoin), octreotide (used to treat acromegaly or neuroendocrine tumors in the gut), anti-bacterial medicines used to treat tuberculosis, orlistat (helps weight loss), herbal medicines containing St. John's wort, ticlopidine (used after a stroke), certain medicines which lower blood pressure (bosentan), and terbinafine (an anti-fungal medicine used to treat infections of the toes and nails).
- Other medicines which may affect the kidneys such as: anti-bacterial medicines (gentamycin, tobramycin, ciprofloxacin), anti-fungal medicines which contain amphotericin B, medicines used for urinary tract infections which contain trimethoprim, medicines used to treat cancer which contain melphalan, medicines used to lower the amount of acid in the stomach (acid secretion inhibitors of the H<sub>2</sub>-receptor antagonist type), tacrolimus, pain killers (non-steroid anti-inflammatory medicines such as diclofenac), fibric acid (used to lower fat in the blood).
- Nifedipine, used to treat high blood pressure and angina. Gum swelling that might spread toward the teeth may occur when taking nifedipine during the course of treatment with ciclosporin.
- Digoxin (used to treat heart problems), medicines which lower cholesterol (HMG-CoA reductase inhibitors also called statins), prednisolone, etoposide (used to treat cancer), repaglinide (oral anti-diabetic preparation), immunosuppressants (everolimus, sirolimus), ambrisentan and specific anti-cancer medicines called anthracyclines (such as doxorubicin).

If these cases apply to you (or you are unsure), refer to the doctor before taking **Deximune**.

### **Use of the medicine and food**

Do not take **Deximune** with grapefruit or grapefruit juice, since this may affect the activity of the medicine.

**Deximune** can be taken with or without food.

### **Pregnancy and breastfeeding**

Consult the doctor or pharmacist before taking the medicine. The doctor will discuss with you the potential risk of taking **Deximune** during pregnancy.

**Inform the doctor if you are pregnant or intend to become pregnant.** Experience with **Deximune** in pregnancy is limited. In general, **Deximune** should not be taken during pregnancy. If you must take this medicine, the doctor will discuss with you the benefits and potential risks associated with taking the medicine during pregnancy.

**Inform your doctor if you are breastfeeding.** Breastfeeding is not recommended during treatment with **Deximune** as ciclosporin, the active ingredient in **Deximune**, passes into breast milk, and may affect your baby.

### **Hepatitis C**

Tell your doctor if you have hepatitis C. Your liver functions may change during hepatitis C treatment, and this may affect the ciclosporin levels in your blood. Your doctor may need to closely monitor your ciclosporin blood levels and adjust the dosage after you start hepatitis C treatment.

### **Driving and using machines**

**Deximune** contains ethyl lactate, which is hydrolyzed to ethanol (alcohol) and lactic acid in the gastrointestinal tract. This may affect your ability to drive or use machines. As for children, they should be warned about riding a bicycle or playing near roads etc.

### **Important information about some of the ingredients of the medicine**

**Deximune** contains ethyl lactate that changes into ethanol (alcohol) and lactic acid in the gastrointestinal tract. Each **Deximune** 25 mg, 50 mg and 100 mg capsule contains 32 mg, 65 mg and 129 mg alcohol, respectively, which is equivalent to 14.2% v/v.

A 500 mg dose of **Deximune** contains a quantity of alcohol that is equivalent to approximately 17 ml beer or 7 ml wine. Such a small quantity of alcohol has no noticeable effect.

**Deximune** contains lecithin (soya). If you are allergic to peanut or soya, do not use this medicine.

**Deximune** contains macrogolglycerol hydroxystearate, which may cause stomach upset and diarrhea.

## **3. How to use the medicine?**

Always use the medicine according to the doctor's instructions. Check with your doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

### **Do not exceed the recommended dose.**

The dosage of the medicine will be adjusted for you by the doctor only, according to your specific needs. A too high dosage may affect your kidneys. Blood tests and hospital visits should be performed regularly, especially after a transplant. This will enable you to discuss the treatment with the doctor and indicate the problems you experience.

### **The dosage and frequency of administration**

The doctor will adjust the right dosage of **Deximune** for you, depending on your body weight and the reason for taking the medicine. The doctor will also tell you how often to take the medicine.

Follow your doctor's instructions exactly, and never change the dosage yourself, even if you feel well.

### **If you were previously taking a different dosage form of oral ciclosporin**

The doctor will monitor the ciclosporin levels in your blood very closely for a short time following the switch from one oral dosage form to another.

When you switch from one oral dosage form of ciclosporin to another, you may experience side effects. If this happens, please tell the doctor or pharmacist, as the dosage you are taking may need to be adjusted. **Never change** the dosage yourself unless instructed to do so by the doctor.

## **Instructions for use**

### **When to take Deximune**

It is important to take the medicine at the same time every day, especially if you have undergone a transplant.

### **How to take Deximune**

The daily dosage should always be taken in two separate doses.

Remove the capsule from the blister. Swallow the capsule whole with water. Do not chew/divide/crush.

### **Duration of treatment**

The doctor will tell you how long you need to take **Deximune**. This depends on whether the reason for the treatment is after a transplant or for the treatment of a severe skin disease, rheumatoid arthritis, uveitis or nephrotic syndrome. Treatment of severe rash usually lasts for 8 weeks.

Keep taking **Deximune** for as long as your doctor tells you.

If you have questions about how long to take **Deximune**, talk to the doctor or pharmacist.

### **If you have accidentally taken a higher dosage**

If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you. You may need medical treatment.

### **If you forgot to take the medicine**

If you forgot to take this medicine at the designated time, take a dose as soon as you remember, unless it is almost time for your next dose. Continue taking the medicine as usual. Never take two doses at the same time!

### **If you stop taking the medicine**

Continue with the treatment as recommended by the doctor.

Do not stop treatment with **Deximune** without instruction from the doctor. Continue treatment even if you feel well. Stopping treatment with **Deximune** may increase the risk of rejection of the transplanted organ.

**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 on the use of this medicine, consult the doctor or pharmacist.**

## **4. Side effects**

Like any medicine, the use of **Deximune** 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.

**Some side effects may be serious:**

**Refer to a doctor immediately if you notice the following serious side effects:**

- Like other medicines that suppress the immune system, ciclosporin may influence your body's ability to fight against infections and may cause tumors or other cancers, particularly of the skin. Signs of infection might be fever or sore throat.
- If you experience changes in your vision, loss of coordination, clumsiness, memory loss, difficulty speaking or understanding what other people say, and muscle weakness, these might be symptoms of an infection of the brain called progressive multifocal leukoencephalopathy (PML).
- Brain disorders with signs such as: seizures, confusion, disorientation, reduced responsiveness, personality changes, agitation, sleeplessness, vision disorders, blindness, coma, paralysis of part or all of the body, stiff neck, loss of coordination with or without abnormal speech or eye movements.
- Swelling at the back of the eye which may be associated with blurred vision and may cause a vision disorder because of the increased pressure inside the head (benign intracranial hypertension).
- Liver problems and damage with or without yellowing of the skin and eyes, nausea, loss of appetite and dark urine.
- Kidney disorders which may greatly reduce the urine output.

- Low level of red blood cells or platelets. The signs include pale skin, tiredness, breathlessness, dark urine (a sign of the breakdown of red blood cells), bruising or bleeding for no obvious reasons, confusion, disorientation, reduced alertness and kidney problems.

### **Additional side effects**

**Very common side effects** (effects that occur in more than 1 in 10 users):

Kidney disorders, high blood pressure, headache, involuntary shaking of the body, excessive growth of body and facial hair, high level of lipids in the blood.

If any of these side effects affects you severely, **refer to the doctor**.

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

Seizures, liver disorders, high level of sugar in the blood, tiredness, loss of appetite, nausea, vomiting, abdominal discomfort or abdominal pain, diarrhea, excessive hair growth, acne, hot flushes, fever, low level of white blood cells, numbness or tingling, muscle pain, muscle spasm, stomach ulcer, overgrowth (swelling) of the gums until they cover the teeth, high level of uric acid or potassium in the blood, low level of magnesium in the blood.

If any of these side effects affects you severely, **refer to the doctor**.

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

Symptoms of brain disorders including sudden fits, mental confusion, insomnia, disorientation, vision disorders, unconsciousness, weakness in the limbs, impaired movements.

Additionally, rash, general swelling, weight gain, low level of red blood cells, low level of platelets in the blood which may increase the risk of bleeding.

If any of these side effects affects you severely, **refer to the doctor**.

**Rare side effects** (effects that occur in 1-10 out of 10,000 users):

Nerve disorder with feeling of numbness or tingling in the fingers and toes, inflammation of the pancreas with severe upper stomach pain, muscle weakness, loss of muscle strength, pain in muscles of the legs, hands or anywhere in the body, destruction of red blood cells involving kidney problems with symptoms such as swelling of the face, stomach, hands and/or feet, decreased urination, breathing difficulties, chest pain, fits (seizures), loss of consciousness, abnormal changes in menstrual cycle, breast enlargement in men.

If any of these side effects affects you severely, **refer to the doctor**.

**Very rare side effects** (effects that occur in less than 1 in 10,000 users):

Swelling at the back of the eye which may be associated with an increase in pressure inside the head and vision disorders.

If this side effect affects you severely, **refer to the doctor**.

**Side effects with unknown frequency** (effects for which a frequency has not yet been determined):

Serious liver problems with and without yellowing of the eyes or skin, nausea, loss of appetite, dark colored urine, swelling of the face, stomach, feet, hands or the whole body, bleeding underneath the skin or purple skin patches, sudden bleeding with no apparent cause, migraine or severe headache often with nausea, vomiting and sensitivity to light, pain in legs and feet.

If any of these side effects affects you severely, **refer to the doctor**.

**If a side effect occurs, if one of the side effects worsens or if you suffer from a side effect which is not mentioned in this leaflet, consult the doctor.**

### **Additional side effects in children and adolescents:**

There are no additional side effects expected in children and adolescents when compared with adults.

### **Reporting side effects:**

Side effects can be reported to the Ministry of Health by clicking the link

"דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website ([www.health.gov.il](http://www.health.gov.il)) directing to the online form for reporting side effects or via the link:

<https://sideeffects.health.gov.il>

## **5. How to store the medicine?**

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants 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 (תאריך תפוגה) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 25°C. Do not refrigerate and/or freeze.
- Leave the capsules in the original blister until use. When a blister is opened, a characteristic smell of the medicine can be noticed which does not indicate anything wrong with the capsules.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

## **6. Additional information**

### **In addition to the active ingredient, the medicine also contains:**

Ethyl lactate, gelatin, macrogolglycerol hydroxystearate, polysorbate 20, sorbitan oleate, triglyceride, purified water, glycerol, lecithin, titanium dioxide (E171), iron oxide black (E172).

### **What the medicine looks like and what the package contains:**

A grey, soft gelatin capsule with a "DX 25 mg" imprint (in **Deximune 25**), "DX 50 mg" (in **Deximune 50**) and "DX 100 mg" (in **Deximune 100**).

Approved package sizes: 10, 20, 30, 50 capsules. Not all package sizes may be marketed.

Revised in November 2022 according to MOH guidelines.

### **Drug registration number at the national drug registry of the Ministry of Health:**

**Deximune 25:** 124-49-30359-11

**Deximune 50:** 126-73-30601-11

**Deximune 100:** 124-48-30358-11

**Manufacturer and registration holder:** Dexcel Ltd., 1 Dexcel St., Or Akiva 3060000, Israel