

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986

This medicine is dispensed with a doctor's prescription only

Vesanoid® Capsules

Active ingredient and its quantity:

Each capsule contains:
tretinoin 10 mg

Inactive ingredients and allergens: See section 6 'Additional information' and section 2 'Important information about some of this medicine's ingredients'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

Special warnings for women

- Before starting to use **Vesanoid**, tell your doctor if you are pregnant, think you are pregnant or are planning to become pregnant.
- You should not become pregnant during and within one month after stopping treatment with Vesanoid. If you do become pregnant while taking Vesanoid, it is very likely that your baby will be born seriously deformed.
- Women of childbearing age **should use** effective birth control throughout treatment and for one month after treatment is stopped. Your doctor will advise you on what methods of contraception are the most appropriate for you.
- If you are taking oral contraceptives with a low dose of progestogen (also called "mini-pill"), your doctor will tell you to stop using this contraceptive and will prescribe a different contraceptive for the time you are being treated with Vesanoid.
- During the treatment period, women should take a pregnancy test every month.
- Tell your doctor immediately if you become pregnant while taking this medicine.
- Do not breastfeed during treatment with Vesanoid. Vesanoid enters the breast milk and could therefore harm your baby.

1. What is this medicine intended for?

Vesanoid is intended for the treatment of patients with acute promyelocytic leukaemia (APL), a type of blood cancer.

Therapeutic group: Vesanoid contains the active ingredient of tretinoin, which belongs to a group of medicines called 'retinoids'. These medicines are similar to vitamin A.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient (tretinoin) or to any of the other ingredients in this medicine (see section 6 'Additional information').
- you are sensitive (allergic) to other 'retinoid' medicines (including isotretinoin, acitretin and tazarotene).

- you are sensitive (allergic) to peanuts or soya. This is because Vesanoid contains soya-bean oil.
- you are pregnant, planning to become pregnant or breast-feeding (see section 2 'Pregnancy, breast-feeding and fertility').
- you are taking tetracycline (a type of antibiotic).
- you are taking vitamin A or another medicine that belongs to the 'retinoid' group.

Special warnings about using this medicine

Before treatment with Vesanoid, tell your doctor if:

- you have any other illness
- you have ever had any mental health problems including depression, aggressive tendencies or mood changes. This is because using Vesanoid may affect your mood.
- you have allergies.
- you have been told by your doctor that you have an intolerance to certain sugars. This is because Vesanoid contains sorbitol (a type of sugar).

If any of the above conditions applies to you (or you are not sure), consult your doctor or pharmacist before taking Vesanoid.

Mental health problems:

You may not notice some changes in your mood and behaviour and so it is very important that you tell your friends and family that this medicine could affect your mood and behaviour. They may notice these changes and help you identify any problems that you need to talk to your doctor about.

- You should inform your doctor immediately, if any of the following appear:
 - a severe headache with nausea or vomiting
 - difficulty in breathing
 - fever
 - feeling dizzy
 - chest or back pain

You will need to look out for these effects while taking Vesanoid. See section 4 'Side effects' for more details. Your doctor may decide to change the dose of your medicine or to prescribe an additional medicine.

Children

There is limited safety and efficacy information on the use of tretinoin in children.

Tests and follow-up

Women taking Vesanoid should take a pregnancy test every month during treatment with the medicine.

Drug interactions

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including nonprescription medications and dietary supplements.

This is extremely important, as using more than one medicine at the same time can strengthen or weaken the effect of the medicines. Therefore, you should not take Vesanoid with any other medicine unless you have told your doctor and they have agreed.

Particularly if you are taking:

- rifampicin and erythromycin (antibiotics)
- glucocorticoids (for treatment of allergies and inflammation)

- phenobarbital (for treatment of epilepsy)
- pentobarbital (for treatment of insomnia)
- azole antifungals (e.g. ketoconazole, fluconazole, itraconazole, posaconazole)
- protease inhibitors or macrolides (e.g. clarithromycin)
- cimetidine (for treatment of stomach ulcers)
- verapamil and diltiazem (for treatment of heart conditions or high blood pressure)
- ciclosporin (used following organ or bone marrow transplants)
- tranexamic acid, aminocaproic acid and aprotinin (used to reduce bleeding)

Do not take the following medicines while taking Vesanoïd:

- tetracycline antibiotics
- vitamin A
- low-dose progestogens for birth control (also called 'mini-pill'). If you are taking low-dose progestogens for birth control, your doctor will tell you to stop and will prescribe a different contraceptive.

Using this medicine and food

Take the medicine during or shortly after a meal.

Pregnancy, breast-feeding and fertility

Before starting treatment with Vesanoïd

Tell your doctor immediately if:

- you are pregnant
- you think you are pregnant
- you intend to become pregnant.

You should not become pregnant during and within one month (four weeks) after stopping treatment with Vesanoïd. **If you do become pregnant while taking Vesanoïd, it is very likely that your baby will be born deformed.**

During treatment with Vesanoïd

- **During treatment with Vesanoïd and for four weeks after stopping treatment, you and your partner should use effective and continued contraception (birth control).** Your doctor will tell you what methods of contraception you can use. If you are taking low-dose progestogens (mini-pill) for birth control, your doctor will tell you to stop taking them and will prescribe a different oral contraceptive for you.
- Women taking Vesanoïd should take a pregnancy test every month during treatment with Vesanoïd.
- **Tell your doctor immediately if you become pregnant while taking Vesanoïd.** You and your doctor will discuss the right treatment for you if you are pregnant and have acute promyelocytic leukaemia.

Do not breast-feed your baby while taking Vesanoïd.

Vesanoïd enters the breast milk and could therefore harm your baby.

Driving and using machines

Use of this medicine might impair your alertness, especially if you experience dizziness or severe headaches. Therefore, take caution when driving a car, operating dangerous machines and in any activity for which you must be alert.

Important information about some of this medicine's ingredients

This medicine contains soya-bean oil. If you are allergic to peanut or soya, do not use this medicine.

This medicine contains 1.93 - 2.94 mg sorbitol (a type of sugar) in each capsule. If you have been told by your doctor that you have an intolerance to some sugars, inform your doctor before taking this medicine.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, meaning it is actually 'sodium-free'.

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine, and it depends on the nature of your illness, your reaction to the medicine, your weight and height.

The recommended dosage is usually:

Adults: The daily dose is 45 mg/m², about 8 capsules a day, divided into two equal doses.

Children: The daily dose is 45 mg/m², divided into two equal doses. Children who suffer from severe headaches during treatment may receive a lower dose.

Adults with kidney or liver diseases: The daily dose is 25 mg/m², divided into two equal doses.

The maximum number of days for treatment with Vesanoïd is 90 days. During the treatment with Vesanoïd or immediately afterwards, your doctor will begin treatment with other medicines.

Do not exceed the recommended dose.

Method of administration

- Swallow the capsules whole with a glass of water, preferably with a meal or shortly thereafter.
- Do not chew the capsule.
- Do not open the capsule, and do not take a capsule that appears defective.
- Take your medicine at the same time each day. Making sure to take it at a set time will improve the effectiveness of the medicine and will help you remember to take the medicine.

If you have accidentally taken a higher dose, tell your doctor immediately.

If you have taken an overdose or if a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take this medicine at the required time, take a dose as soon as you remember and tell your doctor immediately. Do not take a double dose to make up for the one you forgot.

Adhere to the treatment as recommended by the doctor.

If you feel that the effect of this medicine is too strong or too weak, consult your doctor or pharmacist.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Vesanoid may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Tell your doctor immediately if you suffer from:

- fever, especially with breathing difficulties, coughing, feeling dizzy, chest pain and abdominal pain.
- a severe headache with nausea or vomiting, difficulty in breathing, fever, feeling dizzy, or chest or back pain. Your doctor may decide to change the dose of your medicine or to prescribe an additional medicine.
- severe stomach pain which spreads to your back (possible sign of inflammation of the pancreas (pancreatitis)).
- fever with dark lumpy markings on your skin, generally on your face and neck (possible sign of “Sweet’s syndrome” or acute febrile neutrophilic dermatosis).
- a painful swelling of the legs, sudden chest pain or difficulty breathing (possible sign of a blood clot).
- a pain in your chest that spreads to your arm or neck (possible sign of a heart attack).
- double vision and feeling dizzy, especially with nausea or vomiting, ringing in your ears and headache (possible sign of increased pressure in your head).
- an unexplained headache or migraine, which can include disturbed vision (possible sign of a stroke).

Tell your doctor immediately if you experience signs of any of the side effects listed above.

Additional side effects:

Very common side effects (may affect more than 1 in 10 users):

- hair loss
- an irregular heartbeat
- changes to your eyesight or hearing
- bone or joint pain, chest pain or abdominal pain
- skin rash, itching, redness, peeling or inflammation
- dry skin, mouth or nose; swollen, dry or cracked lips
- breathing difficulties such as asthma, which may get worse (respiratory failure)
- conjunctivitis or dry eyes, which may be a problem if you wear contact lenses
- difficulty sleeping
- Increased sweating
- headaches or feeling dizzy
- feeling tired, cold or generally unwell
- feeling confused, worried or depressed
- pins and needles (tingling sensation) or numbness of your hands or feet
- loss of appetite, nausea or vomiting, stomach upset, stomach ache, inflammation of the pancreas (pancreatitis), inflammation of the lips, diarrhoea or constipation

- changes in blood test values such as higher levels of transaminases, blood creatinine or blood fats (triglycerides and cholesterol).

Side effects of unknown frequency (frequency cannot be estimated from the existing data):

- genital ulcers
- serious bacterial infections (necrotising fasciitis)
- kidney problems (renal infarct)
- swollen muscles or swollen blood vessels (vasculitis)
- red painful lumps under the skin, generally on your legs (erythema nodosum)
- loss of appetite, nausea or vomiting, with a headache, feeling drowsy or weak (possible sign of too much calcium in your blood)
- other changes to your blood (shown in blood tests) such as too many platelets (thrombocytosis), a change in the number of white blood cells (basophilia) or increased histamine levels
- inflammation of the myocardial muscle (myocarditis) or inflammation of the pericardium outside the heart (pericarditis) which can lead to breathlessness, palpitation, or chest pain.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Reporting side effects

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or you can also use this link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
- Store below 30°C in a tightly closed bottle and protect from light.
- Do not throw away any medicine via wastewater or household waste. Ask the pharmacist how to destroy medicines that you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, this medicine also contains:

Capsule content:

Soya-bean oil, partially hydrogenated soya-bean oil, yellow beeswax, hydrogenated soya-bean oil.

Capsule shell:

Gelatin, glycerol, karion 83 (containing hydrogenated hydrolyzed starch, sorbitol and mannitol), iron oxide yellow, iron oxide red, titanium dioxide.

Each capsule contains 1.93 - 2.94 mg sorbitol.

What the medicine looks like and contents of the pack:

The package contains an amber-coloured glass bottle containing 100 capsules.
Half of each capsule is orange-yellow and the other half is reddish-brown.

Registration holder's name and address:

Tzamal Bio-Pharma Ltd., 20 Hamagshimim St., Kiryat Matalon, Petah-Tikva.

Manufacturer's name and address:

CHEPLAPHARM Arzneimittel GmbH, Greifswald, 17489, Germany.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 101-07-28446

This leaflet was revised in October 2023 according to Ministry of Health guidelines.

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