

PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS

(PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

ZOKINVY 50 mg hard gelatin capsules

ZOKINVY 75 mg hard gelatin capsules

The active ingredient and its quantity in a dosage unit:

Each ZOKINVY capsule contains lonafarnib 50 mg or 75 mg.

For a list of inactive ingredients and allergens in the preparation: see section 6 "Additional information" in this leaflet.

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor 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?

ZOKINVY is intended for the treatment of adults and children 12 months of age and older, who have a certain body surface area:

- To lower the mortality risk in patients with Hutchinson-Gilford progeria syndrome (HGPS).
- For treatment of patients with certain types of processing-deficient progeroid laminopathies.

ZOKINVY is not intended for patients with non-Hutchinson-Gilford progeria syndromes or for treatment of progeroid laminopathies that are not of the processing-deficient types, since ZOKINVY would not be expected to be effective in these patients

Therapeutic class: ZOKINVY belongs to a group of preparations that are basic substances for body metabolism.

ZOKINVY contains the active ingredient lonafarnib, which inhibits the enzyme farnesyltransferase, thus preventing the accumulation of progerin or progerin-like proteins in the inner membrane of the cell nucleus.

2. Before using the medicine

Do not use the medicine if:

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| <ul style="list-style-type: none">• You are sensitive (allergic) to the active ingredient or to any of the other ingredients the medicine contains (see section 6).• You are taking:<ul style="list-style-type: none">- Medicines that are strong or moderate CYP3A inhibitors or inducers- Midazolam- Lovastatin or simvastatin or atorvastatin <p>Ask your healthcare team if you are not sure whether your medicine is one of those listed above.</p> |
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Special warnings regarding the use of the medicine

Before treatment with ZOKINVY, tell the doctor if:

- You have kidney problems
- You have eye problems
- You are pregnant or planning to become pregnant. ZOKINVY may harm the fetus. Women who are able to become pregnant should use effective contraception during treatment with ZOKINVY.
- You are breastfeeding or planning to breastfeed. It is unknown whether ZOKINVY can pass into breastmilk. Talk to your doctor about the best way to feed your baby during treatment with ZOKINVY.

Children and adolescents

Treatment with ZOKINVY is intended for children aged 12 months and above. It is not known whether ZOKINVY is safe and effective for children under 12 months 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 the pharmacist. Especially if you are taking:

- Certain statins: lovastatin, simvastatin, atorvastatin – DO NOT use these specific statins concomitantly with ZOKINVY. ZOKINVY may increase the side effects of those medicines, which include: myopathy, rhabdomyolysis.
- Midazolam – DO NOT use this medicine concomitantly with ZOKINVY. ZOKINVY may increase the side effects of midazolam, which include: significant sedation or respiratory depression.
- Loperamide – concomitant use with ZOKINVY may increase the risk of loperamide's side effects.
- Digoxin and dabigatran – concomitant use with ZOKINVY may increase the risk of those medicines' side effects.
- Medicines of the strong CYP3A enzyme inhibitors type, e.g., ketoconazole – concomitant use with ZOKINVY may increase the risk of ZOKINVY's side effects.
- Medicines of the strong CYP3A enzyme inducers type, e.g., rifampin – concomitant use with ZOKINVY may impair the efficacy of the treatment with ZOKINVY.
- Medicines that are metabolized by the CYP2C19 enzyme, e.g., omeprazole – concomitant use with ZOKINVY may increase the risk of those medicines' side effects.

Use of the medicine and food

ZOKINVY should be taken with food.

Grapefruit and sour/bitter oranges ("Seville oranges") – avoid consumption of grapefruit or "Seville oranges" while using ZOKINVY, as they may increase the risk of ZOKINVY's side effects.

Pregnancy, breastfeeding and fertility:

Pregnancy

ZOKINVY may harm the fetus when administered to a pregnant woman.

Women who are able to become pregnant should use effective contraception during treatment with ZOKINVY.

Breastfeeding

It is unknown whether lonafarnib passes into breastmilk.

Talk to your doctor about the best way to feed your baby during treatment with ZOKINVY.

Driving and operating machinery:

ZOKINVY is not expected to affect the ability to drive or operate machinery.

Important information about some of the ingredients of the medicine:

This medicine contains less than 1 mmol (23 mg) of sodium per capsule, and is therefore considered sodium-free.

3. How should you use the medicine?

Always use the preparation according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the preparation.

The dosage and treatment regimen will be determined only by the doctor.

The generally accepted dosage for ZOKINVY is: twice a day with the morning and evening meals.

Do not exceed the recommended dose.

Do not stop taking the medicine without consulting with your doctor. Your doctor may change the dosage of ZOKINVY if needed.

Your doctor will prescribe the dose required for you. The dose is based on your height and weight.

The capsules should be swallowed whole with an adequate amount of water. **Do not chew** the capsules.

If you or your child cannot swallow the capsules whole, see the "Instructions for use" for details on how to prepare and give/take a dose of ZOKINVY after mixing the contents of the capsules with either orange juice or applesauce.

All ZOKINVY doses must be freshly prepared and taken within about 10 minutes of preparation.

Do not take ZOKINVY with a juice that contains grapefruit or sour/bitter oranges ("Seville oranges").

Duration of treatment: the duration of treatment will be determined by the treating doctor in accordance with your medical condition, the efficacy of the treatment and the side effects.

If you accidentally took a higher dosage: if you took an overdose or if a child swallowed this medicine by mistake, go to the doctor or to a hospital emergency room immediately and take the package of the medicine with you.

If you forgot to take the medicine, take the dose of the medicine as soon as possible with food up to 8 hours before taking the next dose. If less than 8 hours remain before the next dose, skip the forgotten dose and take the next dose of ZOKINVY at the scheduled time.

Follow the treatment as recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

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

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

4. Side effects

As with any medicine, using ZOKINVY 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.

ZOKINVY may cause serious side effects, including:

Severe kidney problems. ZOKINVY may cause severe kidney problems. Your doctor will monitor your kidney function regularly during treatment with ZOKINVY.

Eye problems. ZOKINVY may cause problems with night vision. Contact your doctor right away if any changes occur in your vision.

The most common side effects of ZOKINVY include:

- Vomiting
- Diarrhea
- Infection
- Nausea
- Decreased appetite
- Tiredness
- Upper respiratory tract infection
- Abdominal pain
- Joint and muscle pain
- Changes in electrolyte balance
- Weight loss
- Headache
- Bone marrow suppression
- Elevated liver enzymes in blood tests
- Decreased blood bicarbonate
- Cough
- Hypertension

Contact your doctor if you continue to experience nausea, vomiting or diarrhea that leads to loss of appetite and weight loss during treatment with ZOKINVY.

ZOKINVY may cause an increase in blood pressure (hypertension). The doctor will check your blood pressure during treatment with ZOKINVY. Contact your doctor right away if you experience symptoms of high blood pressure, which include: headaches, shortness of breath, nosebleeds, flushing, tiredness, dizziness, vision problems, irregular heartbeat, or chest pain.

ZOKINVY may cause fertility problems in women and men, which may affect your ability to have children. Talk to your doctor if you have concerns about fertility.

These are not all the possible side effects of ZOKINVY. For more information, ask your doctor.

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 your doctor.

Reporting side effects

Side effects may be reported to the Ministry of Health by clicking on the link “Report side effects due to medicinal treatment” found on the Ministry of Health website homepage (www.health.gov.il), which will direct you to the online form for reporting side effects, or by clicking on the following link:

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

In addition, you can report by emailing the marketing authorization holder’s Patient Safety Unit at: drugsafety@neopharmgroup.com

5. How to store the medicine?

Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.

Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

Storage conditions:

Store at a temperature below 25°C. Do not store in the refrigerator.

After opening the bottle – use within 30 days, store at a temperature below 25°C.

After mixing with liquid – (orange juice or applesauce, see section 3 and the section “Instructions for use”) – use immediately.

6. Additional information

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

Povidone, hard gelatin capsule, poloxamer 188, croscarmellose sodium, silicon dioxide, magnesium stearate.

What does the medicine look like and what are the contents of the package?

50 mg: yellow, hard, two-piece capsules with black imprinting of “50” on the body of the capsule and “LNF” on the cap of the capsule. The capsules contain white to off-white powder.

75 mg: light orange, hard, two-piece capsules with black imprinting of “75” on the body of the capsule and “LNF” on the cap of the capsule. The capsule contains white to off-white powder.

Both types of capsules are marketed in an HDPE bottle. Each bottle contains 30 capsules. Each bottle also contains a desiccant.

Name and address of the marketing authorization holder:

Neopharm Ltd., 6 Hashiloach St., P.O.B. 3340, Petach Tikva 4917001.

Name and address of the manufacturer:

Sentynl Therapeutics, Inc., 420 Stevens Avenue, Suite 200, Solana Beach, California (CA), 92075, USA.

Registration number of the medicine in the national drug registry of the Ministry of Health:

ZOKINVY 50 mg: 169-67-36861-99

ZOKINVY 75 mg: 169-68-36862-99

Zokinvy cap. PIL vr. 02A





Instructions for use

These instructions for use contain information on how to mix and give/take a dose of ZOKINVY if the capsules cannot be swallowed whole.

Read the instructions for use before you start giving/taking ZOKINVY and each time you get a new package, as it may contain new information. This information does not replace the need to consult with your doctor regarding your or your child's medical condition or treatment.

Supplies needed for preparing and giving or taking a dose of ZOKINVY

Before mixing a dose of ZOKINVY, gather the following supplies:

- The prescribed amount of ZOKINVY capsules for you or your child. Place the capsule or capsules on a clean, flat surface.
- Either orange juice or applesauce. **Do not mix with juice that contains grapefruit or bitter/sour oranges (“Seville oranges”).**
- If mixing with orange juice: a clean measuring cup with 5 milliliter (mL) and 10 mL markings,  
OR if mixing with applesauce: a clean teaspoon.
- A clean cup for each ZOKINVY capsule.  
- A clean teaspoon for stirring.

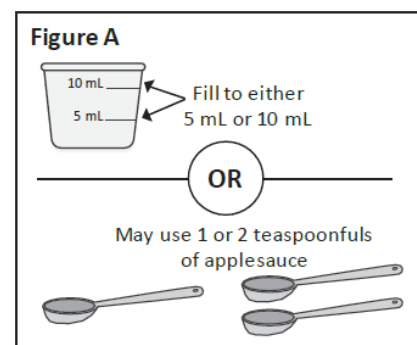
How to open ZOKINVY capsules and mix their contents

Step 1:

If mixing with orange juice: use a measuring cup to measure either 5 mL or 10 mL of orange juice.

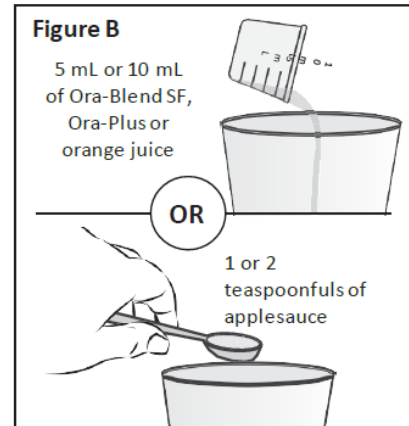
If mixing with applesauce: measure with either 1 or 2 teaspoons of applesauce.

You can choose to use 5 mL or 10 mL of liquid (orange juice) or one or two teaspoons of applesauce (**see Figure A**).



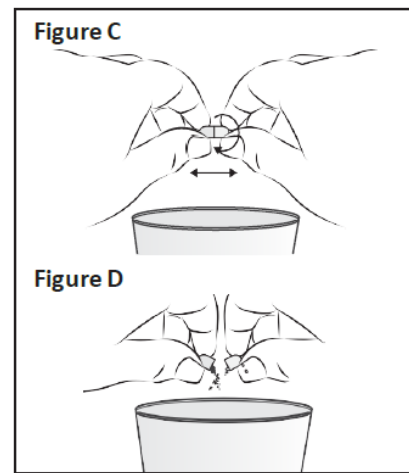
Step 2:

Transfer the orange juice **or** applesauce measured in Step 1 into a clean cup (**see Figure B**).



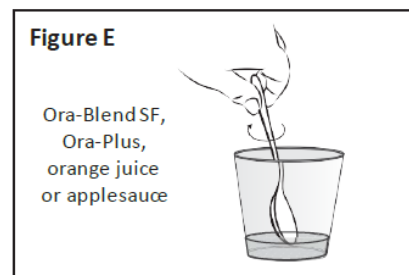
Step 3:

Hold one ZOKINVY capsule above the clean cup containing the liquid (orange juice) or applesauce. Hold both ends of the ZOKINVY capsule between your thumb and forefinger. Gently twist and pull apart the two parts of the capsule (**see Figure C**). Empty the contents of the capsule directly into the clean cup (**See Figure D**).



Step 4:

Using a clean teaspoon, stir the contents of the capsule well (**see Figure E**). If you are only required to take one capsule, skip to Step 6. If you are required to take 2 capsules, go to Step 5.



Step 5:

If you are required to take 2 capsules, repeat **Steps 1 through 4** for the second capsule. After completing the process of preparing the second capsule, give/take the 2 servings together in one cup or as 2 servings in two separate cups, in order for you or your child to take an entire dose of ZOKINVY. After you finish, go to **Step 6**.

Step 6:

Give/take the ZOKINVY dose with the morning and evening meals, within about 10 minutes of its preparation.

