

Package leaflet: Information for the patient

Zokinvy 50 mg hard capsules Zokinvy 75 mg hard capsules lonafarnib

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side-effects you may get. See the end of section 4 for how to report side-effects.

Read this entire leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Zokinvy is and what it is used for
2. What you need to know before you take Zokinvy
3. How to take Zokinvy
4. Possible side effects
5. How to store Zokinvy
6. Contents of the pack and other information

1. What Zokinvy is and what it is used for

What Zokinvy is

Zokinvy contains the active substance lonafarnib.

What Zokinvy is used for

This medicine is used to treat patients aged 12 months and older with the following rare disorders:

- Hutchinson-Gilford progeria syndrome
- processing-deficient progeroid laminopathies

These illnesses are caused by changes in genes needed to make certain proteins. Normal versions of these proteins help to keep cells strong and stable. However, the altered genes cause a build-up of harmful forms of the proteins called progerin or progerin-like proteins. These harmful proteins lead to cell damage that resembles the effects of aging.

How Zokinvy works

Zokinvy works by helping to reduce the build-up of the harmful progerin or progerin-like proteins.

2. What you need to know before you take Zokinvy

Do not take Zokinvy

- if you are allergic to lonafarnib or any of the other ingredients in this medicine (listed in section 6).

- with medicines known as strong CYP3A inhibitors (these can reduce the breakdown of Zokinvy in the body, leading to more side effects, see Other medicines and Zokinvy, below).
- with the medicine midazolam
- with the medicines atorvastatin, lovastatin, simvastatin
- if you have severe hepatic (liver) impairment

Warnings and precautions

Talk to your doctor, pharmacist or nurse before taking Zokinvy.

Please tell your doctor immediately if you:

- are over 10 years of age. Treatment results can vary depending on the age when you start taking Zokinvy.
- have persistent vomiting or diarrhoea and prolonged loss of appetite or weight (see section 4).
- start to take the anti-diarrhoeal medicine loperamide. Because of the interaction between Zokinvy and loperamide, it will be important for your doctor to provide dosing guidance and monitor your use of this medicine.
- are having surgery. You must not use midazolam, a medicine commonly used during surgery, with Zokinvy. Your doctor can provide instructions for this situation.
- experience increased levels of liver enzymes shown by blood tests. Your doctor should monitor your liver function while taking this medicine.
- develop any symptoms of kidney problems. Your doctor should monitor your kidney function while taking this medicine.
- experience any new visual changes. Your doctor should monitor your vision and eye health while taking this medicine.
- are taking a medicine that is a moderate or strong CYP3A inducer. These types of medicines should be avoided (see Other medicines and Zokinvy, below).
- are taking a medicine that is a moderate CYP3A inhibitor. These types of medicines should be avoided (see Other medicines and Zokinvy, below).
- have a known dysfunctional polymorphism in CYP3A4.
- have a progeroid syndrome caused by a mutation in a gene other than *LMNA* or *ZMPSTE24* and do not cause a build-up of the harmful proteins called progerin or progerin-like proteins. Zokinvy is not expected to be effective for these types of progeroid syndromes. Examples of progeroid syndromes that Zokinvy is not expected to provide benefit include, Werner syndrome, Bloom syndrome, Rothmund–Thomson syndrome, Cockayne syndrome, xeroderma pigmentosum, trichothiodystrophy and ataxia-telangiectasia.

Children

Do not give this medicine to children under 12 months of age because it has not been studied in this age group.

Other medicines and Zokinvy

Tell your doctor or pharmacist if you are taking or might take any other medicines.

Some medicines may interact with Zokinvy when taken together. The following medicines must not be combined with Zokinvy:

- medicines that are strong CYP3A inhibitors (they can reduce the breakdown of Zokinvy in the body, leading to more side effects; ask your pharmacist or doctor if any of your other medicines are of this kind)
- medicines that are weak or moderate CYP3A inhibitors (they can reduce the breakdown of Zokinvy in the body, leading to more side effects; ask your pharmacist or doctor if any of your other medicines are of this kind). Your doctor may temporarily reduce your dose of Zokinvy while taking a weak or moderate CYP3A inhibitor

- midazolam (used to treat seizures and for surgical procedures - tell your doctor you are taking Zokinvy if you are planning to have surgery)
- atorvastatin, lovastatin or simvastatin (used to lower blood cholesterol)
- medicines that are strong, moderate or weak CYP3A inducers (these can increase the breakdown of Zokinvy in the body, making the medicine less effective; ask your pharmacist or doctor if any of your other medicines are of this kind)
- loperamide (used to treat diarrhoea). The dose of loperamide should not exceed 1 mg daily. Children less than 2 years of age should not take loperamide.
- metformin (used to treat type 2 diabetes)
- medicines that are CYP2C19 substrates (ask your pharmacist or doctor if any of your other medicines are of this kind). If you must take a CYP2C19 substrate, your doctor may need to adjust your dose of the CYP2C19 substrate and monitor your side effects more closely.
- St. John's wort or St. John's wort-containing products (a herbal medicine used to treat mild depression)
- medicines that are P-glycoprotein substrates (ask your pharmacist or doctor if any of your other medicines are this kind). If you must take a P-glycoprotein substrate, your doctor may need to adjust your dose of the P-glycoprotein substrate and monitor your side effects more closely.
- medicines that are OCT1 substrates (ask your pharmacist or doctor if any of your other medicines are this kind)
- oral contraceptives

Zokinvy with food and drink

Do not take Zokinvy with foods or drinks that contain grapefruit, cranberries, pomegranates or Seville (bitter) orange (such as orange marmalade). Foods or drinks containing these fruits may increase the side effects of Zokinvy.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Zokinvy has not been tested in pregnant women.

Zokinvy is not recommended during pregnancy.

Females of childbearing potential must use effective contraception while taking Zokinvy and for at least 1 week after the final dose. Males with female partners of childbearing potential must use effective contraception while taking Zokinvy and for at least 3 months after the final dose. Add a barrier method of contraception if systemic steroids are used for contraception.

It is not known if Zokinvy passes into breast milk and could affect a breast-fed baby. If you wish to breast feed, discuss the benefits and possible risks of doing so or of stopping Zokinvy with your doctor first.

It is not yet known if this medicine affects fertility in men or women.

Driving and using tools or machines

Zokinvy has a minor influence on the ability to drive and use machines. Fatigue may occur following administration of Zokinvy.

Zokinvy contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to take Zokinvy

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

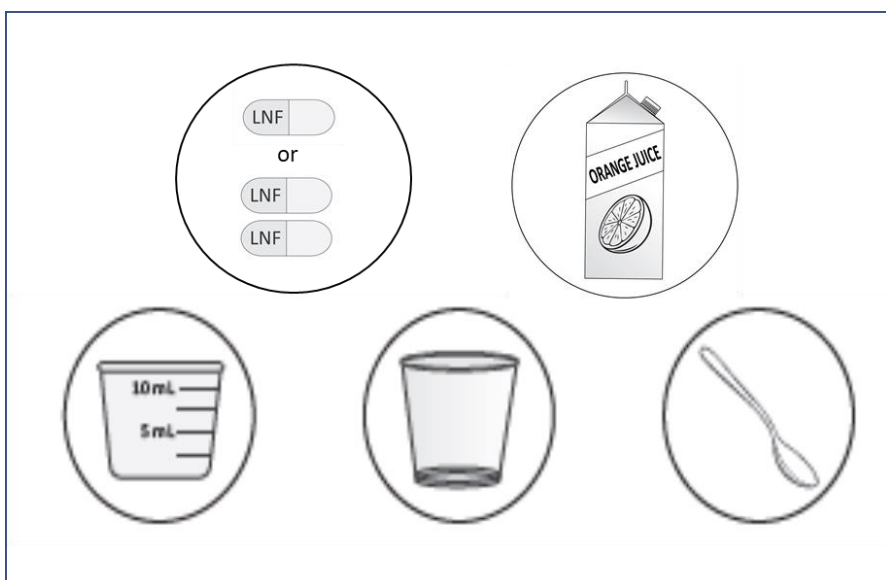
- Zokinvy is taken as 1 or 2 capsules twice a day, about 12 hours apart (morning and evening) with food. The dose of Zokinvy is based on your height and weight.
- Your doctor will work out the right starting dose of Zokinvy for you. This may mean taking capsules of different strengths to make up the right amount. After 4 months of treatment with Zokinvy, your doctor may increase your dose.
- Make sure you know how many capsules you need to take at every dose and the strength of each capsule you need. Ask your doctor, pharmacist or nurse to write it down (including the colour of the capsule(s) to be taken for each dose).
- Take the capsules with food, washing them down with enough water to help you swallow them. Taking Zokinvy with food may help to reduce side effects.

If you cannot swallow a Zokinvy capsule whole

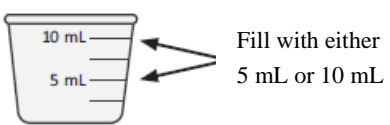
- If you cannot swallow a Zokinvy capsule whole, use the following directions for mixing the capsule content with orange juice.






What you need to mix Zokinvy with orange juice

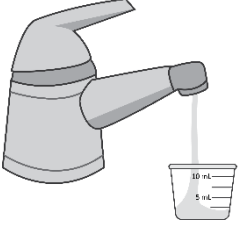

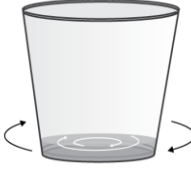
- Mix a fresh dose of Zokinvy for each use.
- Set aside the right number of Zokinvy capsules for your dose. Place the capsule or capsules on a clean flat surface.
- Use orange juice only. Do not use other drinks to mix Zokinvy.
- A clean medicine cup with 5 mL and 10 mL measurement levels.
- A clean cup for each Zokinvy capsule to be mixed.
- A clean spoon for stirring the mixture.



How to mix Zokinvy with orange juice

<p>Step 1:</p> <ul style="list-style-type: none">• Using a clean medicine cup, measure either 5 mL or 10 mL of orange juice.• You can choose to use 5 mL or 10 mL of orange juice.	 <p>Fill with either 5 mL or 10 mL</p>
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<p>Step 2:</p> <p>Pour the orange juice measured in Step 1 into a clean cup.</p>	
<p>Step 3:</p> <ul style="list-style-type: none"> • Hold a Zokinvy capsule above the cup containing the orange juice. • Hold the capsule between your thumb and forefinger on both sides. • Gently twist and pull apart the capsule. 	
<p>Step 4:</p> <p>Empty all the contents of the capsule into the cup containing the orange juice.</p>	
<p>Step 5:</p> <ul style="list-style-type: none"> • Using a clean spoon, mix the capsule contents and orange juice well. • If only 1 capsule is to be taken, skip to Step 7. • If 2 capsules are to be taken, proceed to Step 6. 	
<p>Step 6:</p> <ul style="list-style-type: none"> • If 2 capsules will be taken, repeat Steps 1 through 5 for the second capsule. • Once the second capsule is mixed - the 2 servings can either be combined in a single cup or remain in 2 serving cups. • After you finish, go to Steps 7, 8 and 9. 	
<p>Step 7:</p> <p>Take all of the Zokinvy mixture:</p> <ul style="list-style-type: none"> • with food. • within about 10 minutes of preparing. <p>Each dose must be mixed and consumed within 10 minutes. The mixture should only be prepared at the time it is to be consumed.</p>	<p>TAKE WITHIN</p> 

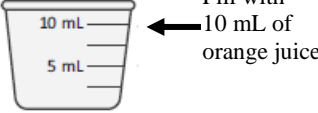
<p>Step 8:</p> <p>Rinse the medicine cup used to measure the orange juice and fill it with 5 mL of water for each capsule mixed with orange juice.</p>	
<p>Step 9:</p> <ul style="list-style-type: none"> • Pour the water measured in Step 8 into the cup used to mix the Zokinvy and orange juice (a). • Gently swirl the water around the cup (b). Consume the water. 	<div style="display: flex; flex-direction: column; align-items: center;"> <div style="margin-bottom: 20px;"> <p>(a)</p>  </div> <div> <p>(b)</p>  </div> </div>

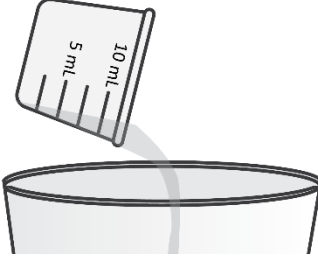
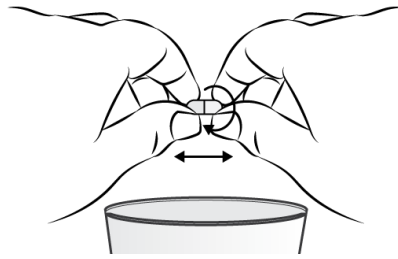


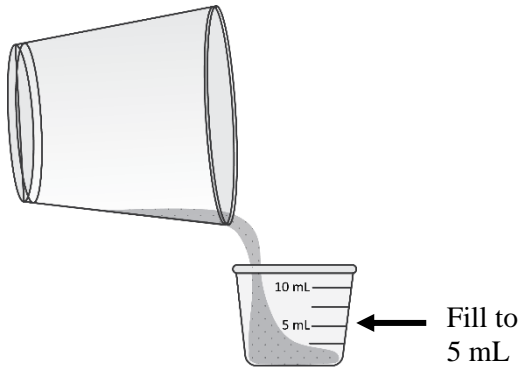
Patients starting Zokinvy with a body surface area between 0.30 m² and 0.38 m², patients taking a weak CYP3A inhibitor concomitantly with Zokinvy and experiencing persistent side-effects and patients with a dysfunctional CYP3A4 polymorphism requiring a reduced daily dose less than or equal to 50 mg


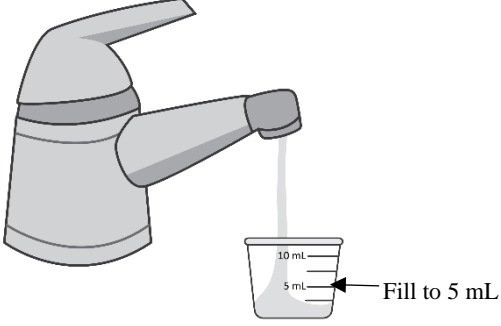
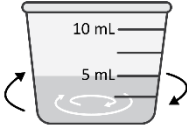
Before beginning to mix Zokinvy with orange juice, read What you need to mix Zokinvy with orange juice.

For patients with a body surface area between 0.30 m² and 0.38 m², the daily starting dose of Zokinvy is 75 mg (37.5 mg twice daily with food). Each dose is prepared fresh using a 75 mg capsule and mixed with 10 mL of orange juice. Half of the 10-mL mixture will be consumed.

For patients taking Zokinvy and a weak CYP3A inhibitor and experiencing persistent side-effects or with a dysfunctional CYP3A4 polymorphism, your doctor may reduce your daily dose of Zokinvy by 50%. Prepare each dose fresh. If your reduced daily dose is 50 mg (25 mg twice daily), mix the contents of a 50 mg capsule in 10 mL of orange juice. Half of the 10-mL mixture will be consumed. Generally, 14 days after ending treatment with the weak CYP3A inhibitor or upon your side-effects ending, your doctor will increase your dose to its previous level. Your doctor will provide you with specific guidance.

<p>Step 1:</p> <p>Use a clean medicine cup and fill it with 10 mL of orange juice.</p>	
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<p>Step 2:</p> <p>Pour the orange juice measured in Step 1 into a clean cup for mixing.</p>	
<p>Step 3:</p> <ul style="list-style-type: none"> Depending on your doctor's direction, hold either a Zokinvy 75 mg or 50 mg capsule above the cup containing the orange juice. Hold the capsule between your thumb and forefinger on both sides. Gently twist and pull apart the capsule. 	
<p>Step 4:</p> <ul style="list-style-type: none"> Empty all the contents of the capsule into the cup containing the orange juice. 	
<p>Step 5:</p> <p>Using a clean spoon, mix the capsule contents and orange juice well.</p>	
<p>Step 6:</p> <p>Pour 5 mL of the orange juice and Zokinvy mixture from the mixing cup into a clean medicine cup.</p>	

<p>Step 7:</p> <p>Take the 5-mL Zokinvy and orange juice mixture from the medicine cup:</p> <ul style="list-style-type: none"> • with food • within about 10 minutes of preparing <p>Each dose must be mixed and consumed within 10 minutes. The mixture should only be prepared at the time it is to be consumed.</p>	<p>TAKE WITHIN</p> 
<p>Step 8:</p> <p>Fill the medicine cup used to consume the Zokinvy and orange juice mixture with 5 mL of water.</p>	
<p>Step 9:</p> <p>Gently swirl the water around the medicine cup. Consume the water.</p>	

Drink lots of water while taking Zokinvy

It is important to drink lots of water and other liquids while taking Zokinvy. This may help to reduce problems linked to diarrhoea or vomiting.

Ask your doctor about the amount of water or other liquids that you should drink each day.

Your doctor will discuss with you which liquids you can drink to make sure that you are getting the correct amount of fluids each day.

Do not eat foods or drink juices that contain grapefruit, cranberries, pomegranates or Seville oranges (known as sour or bitter oranges).

If you take more Zokinvy than you should

If you take more capsules than you should, stop taking the medicine and contact your doctor.

If you forget to take Zokinvy

If you forget to take a dose, and 8 hours or more remain until your next planned dose, take the missed dose as soon as possible with some food. If less than 8 hours remains before the next scheduled dose, skip the missed dose and resume taking Zokinvy at the next scheduled dose.

If you stop taking Zokinvy

Do not stop taking Zokinvy without talking to your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects. Tell your doctor immediately if you:

- have persistent nausea, vomiting or diarrhoea that leads to loss of appetite, weight loss or dehydration. Vomiting or diarrhoea are very common (may affect more than 1 in 10 people) and may lead to electrolyte deficiencies requiring supportive care. Your doctor may monitor your weight, appetite and how much you eat and drink to help detect any of these possible electrolyte conditions.

Tell your doctor immediately if you notice any of the serious side effects above.

Very common (may affect more than 1 in 10 people)

- increased liver enzymes shown by blood tests, which indicate stress on the liver
- stomach pain
- fatigue (tiredness)
- constipation
- sinus infections or other upper respiratory tract infections
- decreased haemoglobin shown by blood tests
- decreased bicarbonate shown by blood tests

Common (may affect up to 1 in 10 people)

- body aches and body pain, including back pain and pain in extremity
- fever
- decrease in levels of sodium, potassium, albumin, creatinine shown by blood tests
- increase in levels of magnesium shown by blood tests
- cough
- flatulence
- rash
- pruritus (itchy skin)
- cerebral ischaemia (stroke)
- headache
- runny nose
- nasal congestion (blocked nose)
- nosebleed
- sore throat
- depression
- oral pustule (mouth sores)
- painful boil-like swelling near the anus (perirectal abscess)
- pneumonia
- influenza
- decrease in blood cell counts (such as white blood cell count) shown by blood tests
- tingling in hands and feet
- dizziness
- irritation, inflammation or ulcers of the large intestine (colitis)
- indigestion (may include feelings of bloating, discomfort, feeling too full or gas)
- inflammation of the stomach lining (gastritis)
- bleeding of the large intestine, rectum or anus

- dry skin
- skin darkening (hyperpigmentation)
- chest pain
- chills
- tooth fracture

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you help provide more information on the safety of this medicine.

5. How to store Zokinvy

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and on the bottle after “EXP”. The expiry date refers to the last day of that month.

Store in the original package. Keep the bottle tightly closed in order to protect from moisture. This medicinal product does not require any special temperature storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Zokinvy contains

- The active substance is lonafarnib
Zokinvy 50 mg hard capsules: each capsule contains 50 mg lonafarnib.
Zokinvy 75 mg hard capsules: each capsule contains 75 mg lonafarnib.
- The other ingredients are:
Capsule contents: croscarmellose sodium (see section 2 “Zokinvy contains sodium”), magnesium stearate, poloxamer, povidone and silica, colloidal anhydrous
Capsule shell:
Zokinvy 50 mg hard capsules: gelatin, titanium dioxide, yellow iron oxide and sunflower lecithin
Zokinvy 75 mg hard capsules: gelatin, titanium dioxide, yellow iron oxide, red iron oxide and sunflower lecithin
Printing ink: shellac, iron oxide black

What Zokinvy looks like and contents of the pack

Zokinvy 50 mg hard capsules are opaque yellow hard capsules, marked with “LNF” and “50” in black ink.

Zokinvy 75 mg hard capsules are opaque light orange hard capsules, marked with “LNF” and “75” in black ink.

The bottle pack contains 30 hard capsules and a desiccant. The desiccant is in a cannister and that cannister is included in the bottle, containing the capsules.

Marketing Authorisation Holder

EigerBio Europe Ltd.
1 Castlewood Avenue
Rathmines, D06 H685, Ireland

Manufacturer

Patheon, part of Thermo Fisher Scientific Inc.
2100 Syntex Court
Mississauga, Ontario
L5N 7K9
Canada

This leaflet was last revised in MONTH YEAR

This medicine has been authorised under ‘exceptional circumstances’.

This means that because of the rarity of this disease it has been impossible to get complete information on this medicine.

The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:

<http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.

This leaflet is available in all EU/EEA languages on the European Medicines Agency website.