PACKAGE LEAFLET

Package leaflet: Information for the user

Nintedanib Hexal 150 mg, zachte capsules

nintedanib

Read all of this 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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What [Nationally completed name] is and what it is used for

[Nationally completed name] contains the active substance nintedanib, a medicine belonging to the class of so-called tyrosine kinase inhibitors, and it is used for the treatment of the following diseases:

Idiopathic pulmonary fibrosis (IPF) in adults
IPF is a condition in which the tissue in your lungs becomes thickened, stiff and scarred over time. As a result, scarring reduces the ability to transfer oxygen from the lungs into the bloodstream and it becomes difficult to breathe deeply. This medicine helps to reduce further scarring and stiffening of the lungs.

Other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype in adults
Besides IPF, there are other conditions in which the tissue in your lungs becomes thickened, stiff, and scarred over time (lung fibrosis) and keeps worsening (progressive phenotype). Examples of these conditions are hypersensitivity pneumonitis, autoimmune ILDs (such as rheumatoid arthritis associated ILD), idiopathic nonspecific interstitial pneumonia, unclassifiable idiopathic interstitial pneumonia, and other ILDs. This medicine helps to reduce further scarring and stiffening of the lungs.

Clinically significant, progressive fibrosing interstitial lung diseases (ILDs) in children and adolescents from 6 to 17 years old
Lung fibrosis may occur in patients with Childhood Interstitial Lung Disease (chILD). When this is the case, the tissue in the lungs of children and adolescents becomes thickened, stiff, and scarred over time. [Nationally completed name] helps to reduce further scarring and stiffening of the lungs.

Systemic sclerosis associated interstitial lung disease (SSc-ILD) in adults, adolescents and children aged 6 years and older
Systemic sclerosis (SSc), also known as scleroderma (and juvenile systemic sclerosis in children and adolescents), is a rare chronic autoimmune disease that affects connective tissue in many parts of the body. SSc causes fibrosis (scarring and stiffening) of the skin and other internal organs such as the lungs. When the lungs are affected by fibrosis, it is called interstitial lung disease (ILD), and so the condition is called SSc-ILD. Fibrosis in the lungs reduces the ability to transfer oxygen into the bloodstream, and breathing capacity is reduced. This medicine helps to reduce further scarring and stiffening of the lungs.

2. What you need to know before you take [Nationally completed name]

Do not take [Nationally completed name]
- if you are allergic to nintedanib or any of the other ingredients of this medicine (listed in section 6),
- if you are pregnant.

Warnings and precautions
Talk to your doctor or pharmacist before taking [Nationally completed name] if you:
- have or have had liver problems,
- have or have had problems with your kidneys, or if an increased amount of protein has been detected in your urine,
- have or have had bleeding problems,
- take blood-thinning medicines (such as warfarin, phenprocoumon or heparin) to prevent blood clotting,
- take pirfenidone as this may increase the risk of having diarrhoea, nausea, vomiting and liver problems,
- have or have had problems with your heart (for example a heart attack),
- have recently had surgery. Nintedanib may affect the way your wounds heal. Therefore, your treatment with this medicine will usually be stopped for a while if you are having a surgery. Your doctor will decide when to resume your treatment with this medicine.
- have high blood pressure,
- have abnormally high blood pressure in the blood vessels of the lungs (pulmonary hypertension),
- have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall.

Based on this information your doctor may do some blood tests, for example to check your liver function. Your doctor will discuss the results of these tests with you and decide whether you may receive [Nationally completed name].

Inform your doctor immediately while taking this medicine if you:
- get diarrhoea. Treating diarrhoea early is important (see section 4);
- vomit or feel sick (nausea);
- have unexplained symptoms such as yellowing of your skin or the white part of your eyes (jaundice), dark or brown (tea coloured) urine, pain on the upper right side of your stomach area (abdomen), bleeding or bruising more easily than normal, or feeling tired. This could be symptoms of serious liver problems;
- have severe pain in your stomach, fever, chills, sickness, vomiting, or abdominal rigidity or bloating, as these could be symptoms of a hole in the wall of your gut (‘gastrointestinal perforation’). Also, tell your doctor if you had peptic ulcers or diverticular disease in the past, or

are concomitantly treated with anti-inflammatory drugs (NSAIDs) (used to treat pain relief and swelling) or steroids (used for inflammation and allergies), as this may increase this risk;
- have a combination of severe pain or cramping in your stomach, red blood in your stool or diarrhea as these could be symptoms of a bowel inflammation from inadequate blood supply; -
- have pain, swelling, reddening, warmth of a limb as this could be symptoms of a blood clot in one of your veins (a type of blood vessel);
- have chest pressure or pain, typically on the left side of the body, pain in the neck, jaw, shoulder or arm, a fast heartbeat, shortness of breath, nausea, vomiting, as this could be symptoms of a heart attack;
- have any major bleeding;
- experience bruising, bleeding, fever, fatigue and confusion. This may be a sign of damage to blood vessels known as thrombotic microangiopathy (TMA);
- experience symptoms such as headache, vision changes, confusion, seizure or other neurologic disturbances such as weakness in an arm or a leg, with or without high blood pressure. This could be symptoms of a brain condition called posterior reversible encephalopathy syndrome (PRES).

Children and adolescents
[Nationally completed name] should not be taken by children under 6 years of age.
Your doctor may perform regular dental examinations at least every 6 months until development of teeth is completed, and monitor your growth annually (bone imaging) while you take this medicine.

Other medicines and [Nationally completed name]
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including herbal medicines and medicines obtained without a prescription.

[Nationally completed name] can interact with certain other medicines. The following medicines are examples that may increase the levels of nintedanib in your blood, and hence may increase the risk for side effects (see section 4):
- a medicine used to treat fungal infections (ketoconazole)
- a medicine used to treat bacterial infections (erythromycin)
- a medicine that affects your immune system (cyclosporine)

The following medicines are examples that may lower the levels of nintedanib in your blood and thus may reduce the effectiveness of [Nationally completed name]:
- an antibiotic used to treat tuberculosis (rifampicin)
- medicines to treat seizures (carbamazepine, phenytoin)
- a herbal medicine to treat depression (St. John's Wort)

Pregnancy and breast-feeding
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.

Pregnancy
Do not take this medicine during pregnancy, as it can harm your unborn baby and cause birth defects.

You must have a pregnancy test done to ensure you are not pregnant before starting treatment with this medicine. Please talk to your doctor.

Contraception
- Women who can become pregnant must use a highly effective method of birth control to prevent pregnancy when they start taking [Nationally completed name], while they are taking [Nationally completed name] and for at least 3 months after stopping treatment.

- You should discuss the most appropriate methods of contraception for you with your doctor.
- Vomiting and/or diarrhoea or other gastrointestinal conditions can affect the absorption of oral hormonal contraceptives, such as birth control pills, and may reduce their effectiveness. Therefore, if experiencing these, talk to your doctor to discuss an alternative more appropriate method of contraception.
- Tell your doctor or pharmacist immediately if you become pregnant or think you may be pregnant during treatment with this medicine.

Breast-feeding
Do not breast-feed during the treatment with this medicine since there may be a risk of harm to the breast-fed child.

Driving and using machines
This medicine may have a minor influence on your ability to drive and use machines. You should not drive or use machines if you feel sick.

3. How to take [Nationally completed name]

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

Take the capsules twice daily approximately 12 hours apart at about the same time every day, for example one capsule in the morning and one capsule in the evening. This ensures that a steady amount of nintedanib is maintained in your blood stream. Swallow the whole capsules with water and do not chew the capsules. It is recommended that you take the capsules with food, i.e. during or immediately before or after a meal. Do not open or crush the capsule, to avoid unintended exposure to the capsule contents (see section 5). For the ease of swallowing, you can take the capsules with a small amount (one teaspoonful) of cold or room temperature soft food, such as apple sauce or chocolate pudding. Swallow immediately and do not chew the capsule, to ensure it stays intact.

Adults
The recommended dose is one capsule of 150 mg twice daily (a total of 300 mg per day).
Do not take more than the recommended dose of two [Nationally completed name] 150 mg capsules per day.

If you do not tolerate the recommended dose of two [Nationally completed name] 150 mg capsules per day (see possible side effects in section 4) your doctor may reduce the daily dose of [Nationally completed name]. Do not reduce the dose or stop the treatment by yourself without consulting your doctor first.

Your doctor may reduce your recommended dose to two times 100 mg per day (a total of 200 mg per day). In this case your doctor will prescribe [Nationally completed name] 100 mg capsules for your treatment. Do not take more than the recommended dose of two [Nationally completed name] 100 mg capsules per day if your daily dose was reduced to 200 mg per day.

Use in children and adolescents
The recommended dose depends on the weight of the patient.
Tell your doctor if any time during the treatment the weight of the patient is below 13.5 kg.
Tell your doctor if you have liver problems.
Your doctor will determine the correct dose. Your doctor may adjust the dose as treatment progresses.
If you do not tolerate the recommended dose of [Nationally completed name] per day (see possible side effects in section 4) your doctor may reduce the daily dose of [Nationally completed name].

Do not reduce the dose or stop the treatment by yourself without consulting your doctor first.

Weight-Based dosing for [Nationally completed name] capsules in children and adolescents:

Weight range in kilograms (kg)	Nintedanib dose in milligrams (mg)
13.5 - 22.9 kg	50 mg (two 25 mg capsules*) twice daily
23.0 - 33.4 kg	75 mg (three 25 mg capsules*) twice daily
33.5 - 57.4 kg	100 mg (one 100 mg capsule or four 25 mg capsules*) twice daily
57.5 kg and above	150 mg (one 150 mg capsule or six 25 mg Capsules*) twice daily

* 25 mg capsule strength is not available for [nationally completed name], please consider the alternative product available in market.

If you take more [Nationally completed name] than you should
Contact your doctor or pharmacist immediately.

If you forget to take [Nationally completed name]
Do not take two capsules together if you have forgotten to take your earlier dose. You should take your next dose of [Nationally completed name] as planned at the next scheduled time recommended by your doctor or pharmacist.

If you stop taking [Nationally completed name]
Do not stop taking [Nationally completed name] without consulting your doctor first. It is important to take this medicine every day, as long as your doctor prescribes it for you.

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

4. Possible side effects

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

You need to pay special attention if you get the following side effects during treatment with [Nationally completed name]:

Diarrhoea (**very common**, may affect more than 1 in 10 people):
Diarrhoea may lead to dehydration: a loss of fluid and important salts (electrolytes, such as sodium or potassium) from your body. At the first signs of diarrhoea drink plenty of fluids and contact your doctor immediately. Start appropriate anti-diarrhoeal treatment, e.g. with loperamide, as soon as possible.

The following other side effects were observed during treatment with nintedanib (the active ingredient in this medicine).
Talk to your doctor if you get any side effects.

Idiopathic pulmonary fibrosis (IPF)
Very common side effects (may affect more than 1 in 10 people)
- Feeling sick (nausea)
- Pain in the lower body (abdomen)
- Abnormal liver test results

Common side effects (may affect up to 1 in 10 people)
- Vomiting
- Loss of appetite
- Weight loss
- Bleeding
- Rash
- Headache

Uncommon side effects (may affect up to 1 in 100 people)
- Pancreatitis
- Inflammation of the large bowel
- Serious liver problems
- Low platelet count (thrombocytopenia)
- High blood pressure (hypertension)
- Jaundice, that is a yellow colour to the skin and whites of the eyes due to high levels of bilirubin
- Itching
- Heart attack
- Hair loss (alopecia)
- Increased amount of protein in your urine (proteinuria)

Not known (cannot be estimated from the available data)
- Renal failure
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)
- A brain condition with symptoms such as headache, vision changes, confusion, seizure or other neurologic disturbances such as weakness in an arm or a leg, with or without high blood pressure (posterior reversible encephalopathy syndrome)

<u>Other chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype</u>
Very common side effects (may affect more than 1 in 10 people)
- Feeling sick (nausea)
- Vomiting
- Loss of appetite
- Pain in the lower body (abdomen)
- Abnormal liver test results

Common side effects (may affect up to 1 in 10 people)
- Weight loss
- High blood pressure (hypertension)
- Bleeding
- Serious liver problems
- Rash
- Headache

Uncommon side effects (may affect up to 1 in 100 people)
- Pancreatitis
- Inflammation of the large bowel
- Low platelet count (thrombocytopenia)
- Jaundice, that is a yellow colour to the skin and whites of the eyes due to high levels of bilirubin
- Itching
- Heart attack
- Hair loss (alopecia)
- Increased amount of protein in your urine (proteinuria)

Not known (cannot be estimated from the available data)
- Renal failure
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)
- A brain condition with symptoms such as headache, vision changes, confusion, seizure or other neurologic disturbances such as weakness in an arm or a leg, with or without high blood pressure (posterior reversible encephalopathy syndrome)

Systemic sclerosis associated interstitial lung disease (SSc-ILD)
Very common side effects (may affect more than 1 in 10 people)
- Feeling sick (nausea)
- Vomiting
- Pain in the lower body (abdomen)
- Abnormal liver test results

Common side effects (may affect up to 1 in 10 people)
- Bleeding
- High blood pressure (hypertension)
- Loss of appetite
- Weight loss
- Headache

Uncommon side effects (may affect up to 1 in 100 people)
- Inflammation of the large bowel
- Serious liver problems
- Renal failure
- Low platelet count (thrombocytopenia)
- Rash
- Itching

Not known (cannot be estimated from the available data)
- Heart attack
- Pancreatitis
- Jaundice, that is a yellow colour to the skin and whites of the eyes due to high levels of bilirubin
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)
- Hair loss (alopecia)
- Increased amount of protein in your urine (proteinuria)
- A brain condition with symptoms such as headache, vision changes, confusion, seizure or other neurologic disturbances such as weakness in an arm or a leg, with or without high blood pressure (posterior reversible encephalopathy syndrome)

Fibrosing interstitial lung diseases (ILDs) in children and adolescents

Side effects in children and adolescents were similar to side effects in adult patients.
Talk to your doctor if you get any side effects.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 can help provide more information on the safety of this medicine.

5. How to store [Nationally completed name]

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 the blister. The expiry date refers to the last day of that month.

Store in the original blister packaging in order to protect from moisture.

Do not use this medicine if you notice that the blister containing the capsules is opened or a capsule is broken.
If you are in contact with the content of the capsule, wash off your hands immediately with plenty of water (see section 3).

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 [Nationally completed name] contains
- The active substance is nintedanib. Each capsule contains nintedanib esilate equivalent to 150 mg nintedanib.-
- The other ingredients are:
  - Capsule fill: triglycerides, medium-chain, hard fat and polyglyceryl-3 dioleate (E 475)
  - Capsule shell: gelatin (E 441), glycerol (85%) (E 422), titanium dioxide (E 171), iron oxide red (E 172) and iron oxide yellow (E 172)
  - Printing ink: shellac (E 904), black iron oxide (E 172) and propylene glycol (E 1520).

What [Nationally completed name] looks like and contents of the pack
[Nationally completed name] <150 mg> <soft capsules> (capsules) are brown-coloured, opaque, oblong soft-gelatin capsules, measuring 15 to 19 mm in length, containing yellow viscous suspension and are imprinted in black ink with “NT 150”.

[Nationally completed name] <150 mg> <soft capsules> are available in a carton box containing

30 x 1 and 60 x 1 soft capsules in OPA/Al/PVC-Aluminium unit dose perforated blisters.

120 x 1 soft capsules in OPA/Al/PVC-Aluminum unit dose perforated blisters.

Not all pack sizes may be marketed.

Houder van de vergunning voor het in de handel brengen en fabrikant

Vergunninghouder:
Hexal AG
Industriestrasse 25
83607 Holzkirchen
Duitsland

Fabrikant:

Pharmadox Healthcare Limited
KW20A Kordin Industrial Park
Paola PLA 3000
Malta

Adalvo Limited
Malta Life Scienes Park Building 1, Level 4
Sir Temi Zammit Buildings
San Ġwann Industrial Estate, SGN 3000
Malta

Qualimetrix S.A.
Mesogeion Avenue 579
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Athene
15343
Griekenland

Lek Pharmaceuticals d.d.
Verovškova ulica 57
1526 Ljubljana
Slovenië

In het register ingeschreven onder:
Nintedanib Hexal 150 mg, zachte capsules – RVG 130897

Dit medicijn is geregistreerd in lidstaten van de Europese Economische Ruimte onder de volgende namen:

Nederland	Nintedanib Hexal 150 mg, zachte capsules
Duitsland	Nintedanib HEXAL 150 mg Weichkapseln

Deze bijsluiter is voor het laatst goedgekeurd in oktober 2026