

## Package leaflet: Information for the patient

### Nintedanib Clonmel 100 mg soft 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 Nintedanib Clonmel is and what it is used for
2. What you need to know before you take Nintedanib Clonmel
3. How to take Nintedanib Clonmel
4. Possible side effects
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#### 1. What Nintedanib Clonmel is and what it is used for

Nintedanib Clonmel capsules contain the active substance nintedanib. Nintedanib blocks the activity of a group of proteins which are involved in the development of new blood vessels that cancer cells need to supply them with food and oxygen. By blocking the activity of these proteins, nintedanib can help stop the growth and spread of the cancer.

This medicine is used in combination with another cancer medicine (docetaxel) to treat a cancer of the lung called non-small cell lung cancer (NSCLC). It is for adult patients whose NSCLC is of a certain type (“*adenocarcinoma*”) and who had already received one treatment with another medicine to treat this cancer but whose tumour started to grow again.

#### 2. What you need to know before you take Nintedanib Clonmel

##### Do not take Nintedanib Clonmel

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

##### Warnings and precautions

Talk to your doctor or pharmacist before taking Nintedanib Clonmel if you:

- have or had liver problems, if you have or had bleeding problems, particularly recent bleeding in the lung
- have or have had problems with your kidneys or if an increased amount of protein has been detected in your urine
- take blood-thinning medicines (such as warfarin, phenprocoumon, heparin or acetylsalicylic acid) to prevent blood clotting. Treatment with Nintedanib Clonmel may lead to a higher risk of bleeding
- have recently had a surgery or plan to have a surgery. Nintedanib may affect the way your wounds heal. Therefore treatment with Nintedanib Clonmel will usually be interrupted if you are having surgery. Your doctor will decide when to resume your treatment with this medicine
- have cancer that has spread to the brain
- have high blood pressure
- 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 carry out some blood tests, for example to check your liver function and to determine how fast your blood can clot. Your doctor will discuss the results of these tests with you and decide whether you can be given this medicine.

Inform your doctor immediately while taking this medicine if:

- you get diarrhoea. Treatment of diarrhoea at the first signs is important (see section 4)
- you vomit or feel sick (nausea)
- you 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
- you develop fever, chills, fast breathing or a fast heartbeat. These could be signs of infection or infection of the blood (sepsis) (see section 4)
- you experience severe pain in your stomach area, 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')
- you experience a combination of some or all of the symptoms thereafter: sudden severe abdominal pain or cramping, red blood in your stool, diarrhea or constipation, nausea and vomiting as these could be symptoms of a bowel inflammation from reduced blood flow ('ischaemic colitis')
- you experience pain, swelling, reddening, warmth of a limb or if you experience chest pain and difficulty to breathe as these could be symptoms of a blood clot in one of your veins
- you have any major bleeding
- you experience 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
- any side effect(s) you may get (see section 4) becomes serious

### **Children and adolescents**

This medicine has not been studied in children or adolescents to treat a cancer of the lung (NSCLC) and is therefore not to be taken by children and adolescents below the age of 18 years.

### **Other medicines and Nintedanib Clonmel**

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.

This medicine can interact with certain other medicines. The following medicines may increase the blood levels of nintedanib, the active substance of Nintedanib Clonmel, and hence may increase the risk for side effects (see section 4):

- Ketoconazole (used to treat fungal infections)
- Erythromycin (used to treat bacterial infections)

The following medicines may decrease the blood levels of nintedanib and thus may lead to reduction of the effectiveness of Nintedanib Clonmel:

- Rifampicin (an antibiotic used to treat tuberculosis)
- Carbamazepine, phenytoin (used to treat seizures)
- St. John's Wort (a herbal medicine to treat depression)

### **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.

### Contraception

- Women who can become pregnant must use a highly effective method of birth control to prevent pregnancy, when they start taking Nintedanib Clonmel, while they are taking Nintedanib Clonmel 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

It is not known if the medicine passes into breast milk and could cause harm to a breast-fed child. Therefore, women should not breast-feed during treatment with this medicine.

### Fertility

The effect of this medicine on human fertility has not been investigated.

### **Driving and using machines**

This medicine may have 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 Nintedanib Clonmel**

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

Do not take Nintedanib Clonmel on the same day as your chemotherapy treatment with docetaxel.

Swallow the capsules whole with water and do not chew them. It is recommended to take the capsules with food, that is during or immediately before or after a meal.

Do not open or crush the capsule (see section 5).

The recommended dose is four capsules per day (this is a total of 400 mg nintedanib per day). Do not take more than this dose.

This daily dose should be split into two doses of two capsules about 12 hours apart, for example two capsules in the morning and two capsules in the evening. These two doses should be taken at around the same time each day. Taking the medicine this way ensures that a steady amount of nintedanib is maintained in the body.

### **Dose reduction**

If you cannot tolerate the recommended dose of 400 mg per day because of side effects (see section 4), your doctor may reduce the daily dose of this medicine. Do not reduce the dose or stop the treatment yourself without consulting your doctor first.

Your doctor may reduce your recommended dose to 300 mg per day (two capsules of 150 mg). In this case your doctor will prescribe nintedanib 150 mg soft capsules for your treatment.

If necessary, your doctor may further reduce your daily dose to 200 mg per day (two capsules of 100 mg). You will be prescribed the appropriate capsule strength by your doctor if this happens. In both cases, you should take one capsule of the appropriate strength twice daily approximately 12 hours apart with food (for example in the morning and in the evening) at about the same time of the day.

In case your doctor has stopped your chemotherapy with docetaxel you should continue to take Nintedanib Clonmel twice daily.

**If you take more Nintedanib Clonmel than you should**

Contact your doctor or pharmacist immediately.

**If you forget to take Nintedanib Clonmel**

Do not take a double dose to make up for a forgotten dose. Take your next dose of this medicine as planned at the next scheduled time and at the dose recommended by your doctor or pharmacist.

**If you stop taking Nintedanib Clonmel**

Do not stop taking this medicine 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 do not take this medicine as prescribed by your doctor, this cancer treatment may not work properly.

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 Nintedanib Clonmel:

- ***Diarrhoea (very common, may affect more than 1 in 10 people)***

Diarrhoea may lead to a loss of fluid and important salts (electrolytes, such as sodium or potassium) in your body. At the first signs of diarrhoea drink plenty of fluids and contact your doctor immediately. Start appropriate anti-diarrhoeal treatment, such as with loperamide, as soon as possible after having contacted your doctor.

- ***Febrile neutropenia and sepsis (common, may affect up to 1 in 10 people)***

Treatment with this medicine may lead to a reduced number of a type of your white blood cells (neutropenia) which are important for the body's reaction against bacterial or fungal infections. As a consequence of neutropenia, fever (febrile neutropenia) and blood infection (sepsis) may occur. Tell your doctor immediately if you develop fever, chills, fast breathing or a fast heartbeat. During treatment with Nintedanib Clonmel your doctor will regularly monitor your blood cells and examine you for signs of infection, such as inflammation, fever or tiredness.

The following side effects were observed under treatment with nintedanib (the active ingredient in this medicine):

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

- Diarrhoea – please see above
- Painful, numb and/or tingling feeling in fingers and toes (peripheral neuropathy)
- Feeling sick (nausea)
- Throwing up (vomiting)
- Pain in the stomach (abdomen)
- Bleeding
- Decrease in the number of white blood cells (neutropenia)
- Inflammation of the mucous membranes lining the digestive tract including sores and ulcers in the mouth (mucositis, including stomatitis)
- Rash
- Decreased appetite
- Electrolyte imbalance
- Increased liver enzyme values (alanine aminotransferase, aspartate aminotransferase, blood alkaline phosphatase) in the blood as seen from blood tests
- Hair loss (alopecia)

**Common side effects (may affect up to 1 in 10 people)**

- Blood poisoning (sepsis) - please see above
- Decrease in the number of white blood cells accompanied by fever (febrile neutropenia)

- Blood clots in the veins (venous thromboembolism), especially in the legs (symptoms include pain, redness, swelling, and warmth of a limb), which may travel through blood vessels to the lungs causing chest pain and difficulty in breathing (if you notice any of these symptoms, seek medical advice immediately)
- High blood pressure (hypertension)
- Fluid loss (dehydration)
- Abscesses
- Low platelet count (thrombocytopenia)
- Jaundice (hyperbilirubinaemia)
- Increased liver enzyme values (gamma-glutamyltransferase) in the blood as seen from blood tests
- Weight loss
- Itching
- Headache
- Increased amount of protein in your urine (proteinuria)

**Uncommon side effects** (may affect up to 1 in 100 people)

- Occurrence of holes in the wall of your gut (gastrointestinal perforation)
- Serious liver problems
- Inflammation of the pancreas (pancreatitis)
- Myocardial infarction
- Renal failure

**Not known** (frequency cannot be estimated from the available data)

- Inflammation of the large bowel
- An enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)

**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:

Ireland:

HPRA Pharmacovigilance

Website: [www.hpra.ie](http://www.hpra.ie)

Malta:

ADR Reporting

Website: [www.medicinesauthority.gov.mt/adrportal](http://www.medicinesauthority.gov.mt/adrportal)

By reporting side effects you can help provide more information on the safety of this medicine.

**5. How to store Nintedanib Clonmel**

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

This medicine does not require any special storage conditions.

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 Nintedanib Clonmel contains

- The active substance is nintedanib. Each capsule contains 100 mg nintedanib (as esilate).
- The other ingredients are:
  - Capsule fill: triglycerides, medium-chain, hard fat and polyglyceryl-3 dioleate
  - Capsule shell: gelatin, glycerol, titanium dioxide (E 171), iron oxide red (E 172) and iron oxide yellow (E 172), water purified.
  - Printing ink: shellac, carmine (E 120), propylene glycol (E 1520) and simeticone.

### What Nintedanib Clonmel looks like and contents of the pack

Nintedanib Clonmel 100 mg are peach-coloured, opaque, oblong soft capsules containing yellow viscous suspension, imprinted with “NT 100” in red ink and approximately 16 mm in length.

Nintedanib Clonmel 100 mg soft capsules are available in carton box with perforated unit dose blisters.

Pack size:

30 x 1 soft capsules

60 x 1 soft capsules

Multipacks of 120 (2 packs with 60 x 1) soft capsules

Not all pack sizes may be marketed.

### Marketing Authorisation Holder

Clonmel Healthcare Ltd, Waterford Road, Clonmel, Co. Tipperary, Ireland

### Manufacturer

Pharmadox Healthcare Limited, KW20A Kordin Industrial Park, Paola PLA 3000, Malta

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

Qualimetrix S.A., 579 Mesogeion Avenue Agia Paraskevi, Athens, 15343, Greece

STADA Arzneimittel AG, Stadastrasse 2 - 18, Dortelweil, Bad Vilbel, Hassia, 61118, Germany

Clonmel Healthcare Ltd, Waterford Road, Clonmel, Co. Tipperary, Ireland

**This medicine is authorised in the Member States of the European Economic Area under the following names:**

Iceland	Nintedanib STADA Nordic 100 mg mjúk hylki
Belgium	Nintedanib Eurogenerics 100 mg zachte capsules
Germany	Nintedanib AL 100 mg Weichkapsen
Ireland	Nintedanib Clonmel 100 mg soft capsules
Luxembourg	Nintedanib Eurogenerics 100 mg capsules molles
Malta	Nintedanib Clonmel 100 mg soft capsules

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