

**Ofev<sup>®</sup> Soft Capsules 100mg****Ofev<sup>®</sup> Soft Capsules 150mg**

Nintedanib (as esilate)

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

**1. What OFEV is and what it is used for**

OFEV contains the active substance nintedanib, a medicine belonging to the class of so-called tyrosine kinase inhibitors. OFEV is used for the treatment of non-small cell lung cancer (NSCLC), idiopathic pulmonary fibrosis (IPF), chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype and systemic sclerosis associated interstitial lung disease (SSc-ILD) in adults.

**Idiopathic pulmonary fibrosis (IPF)**

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. OFEV helps to reduce scarring and stiffening of the lungs.

**Chronic fibrosing interstitial lung diseases (ILDs) with a progressive phenotype**

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 (e.g. rheumatoid arthritis associated ILD), idiopathic nonspecific interstitial pneumonia, unclassifiable idiopathic interstitial pneumonia, and other ILDs. Ofev helps to reduce further scarring and stiffening of the lungs.

**Systemic sclerosis associated interstitial lung disease (SSc-ILD)**

Systemic sclerosis (SSc), also known as scleroderma, 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. OFEV helps to slow the rate of decline in pulmonary function.

### **Non-small cell lung cancer (NSCLC)**

OFEV 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 OFEV**

### **Do not take OFEV**

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

### **Warnings and precautions**

Talk to your doctor or pharmacist before taking OFEV:

- if you have or have had liver problems
- if you have or have had problems with your kidneys, or if an increased amount of protein has been detected in your urine.
- if you have or have had bleeding problems
- if you take blood-thinning medicines (such as warfarin, or heparin or acetylsalicylic acid) to prevent blood clotting
- if you have or have had problems with your heart (for example a heart attack),
- if you have recently had surgery or plan to have a surgery. Nintedanib may affect the way your wounds heal. Therefore, your treatment with OFEV will usually be stopped or be interrupted for a while if you are having a surgery. Your doctor will decide when to resume your treatment with this medicine.
- if you have high blood pressure
- if you have abnormally high blood pressure in the blood vessels of the lungs (pulmonary hypertension),
- if you have or have had an aneurysm (enlargement and weakening of a blood vessel wall) or a tear in a blood vessel wall
- if you have cancer that has spread to the brain (*for NSCLC*)

Based on this information your doctor may do 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 may receive OFEV.

Inform your doctor immediately while taking this medicine:

- if you get diarrhoea. Treating diarrhoea early is important (see section 4)
- if you vomit or feel sick (nausea)
- if 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

- if you 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
- if you have pain, swelling, reddening, warmth of a limb or if you experience chest pain and difficulty to breathe as this could be symptoms of a blood clot in one of your veins (a type of blood vessel)
- if you 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.
- if you have any major bleeding.
- if you develop fever as this could be a symptom of febrile neutropenia or sepsis (*for NSCLC*).
- if you have a combination of severe pain or cramping in your stomach, red blood in your stool or diarrhea as these could be symptoms of bowel inflammation from inadequate blood supply.

### **Children and adolescents**

OFEV should not be taken by children and adolescents under 18 years of age.

### **Other medicines and OFEV**

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.

OFEV 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 OFEV:

- 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 OFEV. Please talk to your doctor.

#### Contraception

- Women who can become pregnant must use a highly effective method of birth control to prevent pregnancy while they are taking OFEV 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 OFEV.

#### Breast-feeding

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

#### **Driving and using machines**

OFEV may have minor influence on your ability to drive and use machines. You should not drive or use machines if you feel sick.

#### **OFEV contains soya lecithin**

The capsules contain soya lecithin. If you are allergic to soya or peanut, do not take this medicine.

### **3. How to take OFEV**

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

#### **For idiopathic pulmonary fibrosis (IPF):**

#### **For systemic sclerosis associated interstitial lung disease (SSc-ILD):**

#### **For chronic fibrosing ILDs with a progressive phenotype:**

The recommended dose is one capsule of 150 mg twice daily (a total of 300 mg per day). Take the capsules twice daily approximately 12 hours apart at about the same time every day (for example in the morning and 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 (see section 5).

OFEV capsules may be taken with a small amount (teaspoonful) of cold or room temperature soft food, such as apple sauce or chocolate pudding, and must be swallowed unchewed immediately, to ensure the capsule stays intact.

Do not take more than the recommended maximum daily dose of two OFEV 150 mg capsules per day.

If you do not tolerate the recommended dose of two OFEV 150 mg capsules per day, your doctor may reduce the daily dose of OFEV. 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 OFEV 100 mg capsules for your treatment. Do not take more than the recommended dose of two OFEV 100 mg capsules per day if your daily dose was reduced to 200 mg per day.

**For non-small cell lung cancer (NSCLC):**

Treatment with OFEV should be initiated and supervised by a physician experienced in the use of anticancer therapies.

The recommended dose of OFEV is 200 mg twice daily administered approximately 12 hours apart, on days 2 to 21 of a standard 21-day docetaxel treatment cycle. The recommended maximum daily dose of 400 mg should not be exceeded.

Do not take OFEV on the same day as your chemotherapy treatment with docetaxel (= day 1).

For posology, method of administration, and dose modifications of docetaxel, please refer to the corresponding product information for docetaxel.

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 OFEV. 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 OFEV 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 at about the same time of the day (for example in the morning and in the evening).

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

Swallow the capsules whole with water and do not chew them. It is recommended to take the capsules with food, i.e. during or immediately before or after a meal. Do not open or crush the capsule (see section 5)

**If you take more OFEV than you should**

Contact your doctor or pharmacist immediately.

**If you forget to take OFEV**

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

**If you stop taking OFEV**

Do not stop taking OFEV 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 OFEV:

Evaluation of the side effects is based on the following frequencies:

Very common: may affect more than 1 in 10 people

Common: may affect up to 1 in 10 people

Uncommon: may affect up to 1 in 100 people

**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 this medicine.**

Talk to your doctor if you get any side effects.

<i>Side effects</i>	<i>Frequency</i>
	<b>Non-small cell lung cancer (NSCLC)</b>
Blood poisoning (sepsis)	common
Decrease in the number of white blood cells (neutropenia)	Very common
Decrease in the number of white blood cells accompanied by fever (febrile neutropenia)	common
Abscesses	common
Loss of appetite	Very common
Electrolyte imbalance	Very common
Low platelet count (Thrombocytopenia)	Common
Fluid loss (dehydration)	Common
Weight loss	Common
Painful, numb and/or tingling feeling in fingers and toes (Peripheral neuropathy)	Very common
Headache	Common
Bleeding	Very common
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)	Common
High blood pressure (hypertension)	Common
Feeling sick (nausea)	Very common
Pain in the lower body (abdomen)	Very common
Vomiting	Very common
Pancreatitis	Uncommon
Gastrointestinal Perforation	Uncommon

Serious liver problems	Uncommon
Increased liver enzyme values in the blood as seen from blood tests:	
Alanine aminotransferase increased	Very common
Aspartate aminotransferase increased	Very common
Blood alkaline Phosphatase increased	Very common
Gamma-Glutamyltransferase increased	Common
Jaundice (hyperbilirubinaemia)	Common
Inflammation of the mucous membranes lining the digestive tract including sores and ulcers in the mouth (Mucositis, including stomatitis)	Very common
Rash	Very common
Hair loss (alopecia)	Very common
Itching (pruritus)	Common
Increased amount of protein in your urine (proteinuria)	Common

<i>Side effects</i>	<i>Frequency</i>		
	<i>Idiopathic pulmonary fibrosis (IPF)</i>	<i>Other chronic fibrosing ILDs with a progressive phenotype</i>	<i>Systemic sclerosis associated interstitial lung disease (SSc-ILD)</i>
Low platelet count (thrombocytopenia)	Uncommon	Uncommon	Uncommon
Loss of appetite	Common	Very common	Common
Weight loss	Common	Common	Common
High blood pressure (hypertension)	Uncommon	Common	Common
Bleeding	Common	Common	Common
Feeling sick (nausea)	Very common	Very common	Very common
Pain in the lower body (abdomen)	Very common	Very common	Very common
Vomiting	Common	Very common	Very common
Pancreatitis	Uncommon	Uncommon	-
Serious liver problems	Uncommon	Common	Uncommon
Increased liver enzyme values in the blood as seen from blood tests	Very common	Very common	Very common
Blood alkaline Phosphatase increased	Uncommon	Common	Common

Jaundice, a yellow colour to the skin and whites of the eyes due to high levels of bilirubin (hyperbilirubinaemia)	Uncommon	Uncommon	-
Rash	Common	Common	Uncommon
Itching (pruritus)	Uncommon	Uncommon	Uncommon
Hair loss (alopecia)	Uncommon	Uncommon	-
Headache	Common	Common	Common
Renal Failure	-	-	Uncommon
Increased amount of protein in your urine (proteinuria)	Uncommon	Uncommon	-

#### Reporting of side effects

If any of the side effects gets serious or, if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. By reporting side effects, you can help provide more information on the safety of this medicine.

#### **5. How to store OFEV**

Do not store OFEV above 25°C.

Store in the original package in order to protect from moisture.

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

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 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.

#### **6. Contents of the pack and other information**

##### **What OFEV contains**

- The active substance is nintedanib. Each capsule contains 100 mg or 150mg nintedanib (as esilate).
- The other ingredients are:  
*Capsule fill:* Medium-chain triglycerides, hard fat, soya lecithin (E322)  
*Capsule shell:* Gelatin (porcine), glycerol (85%), titanium dioxide (E171), iron oxide red (E172), iron oxide yellow (E172)  
*Printing ink:* Shellac glaze, iron oxide black (E172), propylene glycol (E1520)

##### **What OFEV looks like and contents of the pack**



OFEV 100 mg capsules are peach-coloured, opaque, oblong soft-gelatin capsules imprinted on one side in black with the Boehringer Ingelheim company symbol and the figure “100”, and containing a bright yellow viscous suspension.

OFEV 150 mg capsules are brown-coloured, opaque, oblong soft-gelatin capsules imprinted on one side in black with the Boehringer Ingelheim company symbol and the figure “150”, and containing a bright yellow viscous suspension.

Two pack-sizes of OFEV capsules are available:

- 6 strips of 10 soft capsules in aluminium/aluminium blisters
- 12 strips of 10 soft capsules in aluminium/aluminium blisters

Not all pack-sizes may be marketed.

### **Marketing Authorisation Holder and Manufacturer**

The marketing authorization holder for OFEV is:

Boehringer Ingelheim Singapore Pte Ltd  
300 Beach Road #37-00  
The Concourse  
Singapore 199555

The manufacturer for OFEV is:

Catalent Germany Eberbach GmbH  
Gammelsbacher Str. 2  
69412 Eberbach  
Germany  
for

Boehringer Ingelheim International GmbH  
Ingelheim am Rhein  
Germany

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