

Ofev	Proposed Patient Information
100 mg, 150 mg	August 2020

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

The dispensing of this medicine requires a physician's prescription

Ofev®

100 mg

Soft capsules

Nintedanib

Each capsule of Ofev 100 mg contains nintedanib 100 mg (as esilate)

Ofev®

150 mg

Soft capsules

Nintedanib

Each capsule of Ofev 150 mg contains nintedanib 150 mg (as esilate)

For the list of inactive ingredients - see Section 6.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, refer to your physician or pharmacist. This medicine has been prescribed to treat your medical condition. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

Important information for women of childbearing age:

Ofev can cause birth defects or even death of unborn babies. Do not get pregnant during treatment with Ofev. Women capable of getting pregnant must have a pregnancy test before starting treatment with Ofev. Women capable of getting pregnant must use highly effective contraception during treatment and for at least 3 months after the last dose of Ofev. Women using hormonal contraceptive methods must also use an additional contraceptive method (such as male condoms or spermicides). If you become pregnant or plan to become pregnant while taking Ofev, tell your physician right away.

1. What is this medicine intended for?

- The medicine is intended to treat a lung disease called idiopathic pulmonary fibrosis (IPF) in adults.
- The medicine is intended to treat adults with chronic (long lasting) fibrosing interstitial lung disease (ILD) with a progressive phenotype.
- The medicine is intended to slow the rate of decline in pulmonary function in patients with systemic sclerosis associated with interstitial lung disease.

Therapeutic group: Kinase inhibitor.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) or have previously experienced severe sensitivity (allergy) to the active ingredient nintedanib, or to any of the other ingredients that this medicine contains (for a list of inactive ingredients, see Section 6 – 'Additional information').
- you are pregnant or breastfeeding. See the box above.

Special warnings regarding use of this medicine

Before treatment with Ofev tell your physician about all your medical conditions, including if:

- You have liver problems.
- You have problems with your heart.

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- You have a history of blood clots.
- You have bleeding disorders or have a family history of bleeding disorders.
- You have recently undergone surgery in the abdominal area.
- You are a smoker.
- You have high blood pressure.
- 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 experience unexplained symptoms such as: yellowing of the skin or of the white part of the eyes (jaundice) caused by a rise in bilirubin, dark or brown urine (color of tea), pain in the right upper abdomen, bleeding or bruising more easily than usual, feeling tired, anorexia, lethargy (a state of inactivity and absence of reaction), loss of appetite, stop the treatment and contact a physician immediately.

If you have diarrhea, inform the physician immediately upon appearance of the first sign, or if you have persistent diarrhea, nausea or vomiting. During treatment with Ofev, the physician will recommend that you drink a lot of fluids or take medicines to treat these side effects. Tell the physician if you are taking non-prescription laxatives, stool softeners, other medicines or other nutritional supplements which can cause diarrhea.

If you experience symptoms of a heart attack, contact a physician immediately. These symptoms include: chest tightness or pain, pain in the arm, back, neck or jaw, or shortness of breath.

If you experience symptoms of stroke, contact a physician immediately. These symptoms include: numbness or weakness on one side of the body, difficulty speaking, headache or dizziness.

If you have abnormal bleeding, bruising or a non-healing wound, tell the physician. Ofev may increase your chance of bleeding problems. Tell the physician if you are taking anticoagulants or over the counter aspirin.

If you have abdominal pain or swelling, tell the physician. Ofev may increase your chance of gastric wall or intestinal perforation.

Smoking

If you are a smoker, it is recommended that you stop smoking before starting treatment with Ofev and during the course of treatment. Smoking may reduce the effectiveness of the treatment.

Children and adolescents

Ofev is not intended for children and adolescents under the age of 18, because there is insufficient information about treatment with Ofev in this age group.

Tests and follow-up

Your physician may order some blood tests before starting treatment with Ofev.

You must have a pregnancy test before starting treatment with Ofev.

Before starting treatment and during treatment with Ofev, your physician will order blood tests to monitor your liver function.

Other medicines and Ofev

If you are taking or have recently taken other medicines, including non-prescription medications and nutritional supplements, tell your physician or pharmacist. Particularly if you are taking:

- Ketoconazole (to treat fungal infections), erythromycin (an antibiotic) may increase the blood level of Ofev.
- Hypericum (St. John's Wort, a herbal medicine to treat depression), rifampicin (an antibiotic), carbamazepine and phenytoin (to treat epilepsy) may reduce the effectiveness of Ofev.
- Anticoagulants may increase your risk of bleeding when taken together with Ofev.

When receiving a new medicine, make sure to show your physician and pharmacist a list of the medicines that you are taking regularly.

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Using the medicine and food

Take Ofev capsules with a meal. See Section 3: 'How to use this medicine'.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, consult a physician or a pharmacist before taking this medicine. **Please see "Important information for women of childbearing age" above. Ofev may cause birth defects or even death of unborn babies.**

Do not breastfeed during treatment with Ofev because there may be a risk of harm to your baby.

3. How to use this medicine?

Always use according to the physician's instructions. Check with your physician or pharmacist if you are not sure about your dose or about how to take this medicine. Your physician will determine your dose and how you should take the medicine. **Do not exceed the recommended dose.**

The recommended dosage of Ofev is 150 mg twice daily administered 12 hours apart.

Based on your blood tests, your physician may decide to change your dose.

Do not take more than 300 mg Ofev a day. Take the medicine with a meal and swallow it whole with some water. **Do not chew or crush the capsule because the medicine tastes bitter.**

If you have accidentally taken a higher dose, the side effects described in Section 4 may be more severe. Contact your physician immediately or go to a hospital emergency room and bring the medicine package with you.

If you have taken an overdose, or if a child has accidentally swallowed some medicine, go immediately to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine

If you forget to take the medicine at the scheduled time, do not take a double dose. Skip the forgotten dose and take the next dose of Ofev as planned at the next scheduled time; take the dose recommended by your physician. Persist with the treatment as recommended by the physician. Even if your health improves, do not stop treatment with this medicine without consulting your physician.

If you stop taking the medicine

Do not stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and dose each time you take the medicine. Wear glasses if you need them. If you have any further questions about using this medicine, consult your physician or the pharmacist.

4. Side effects

Like all medicines, Ofev may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Ofev may cause severe side effects, such as:

- **If used to treat pregnant women, Ofev can cause birth defects or even death of unborn babies (see the box at the top of this leaflet).**
- **Liver problems.** Contact a physician immediately if you experience unexplained side effects such as: yellowing of the skin or of the white part of the eyes (jaundice), dark or brown urine (color of tea), pain in the right upper abdomen, bleeding or bruising more easily than usual, feeling tired, or decreased appetite. Your physician will order blood tests regularly to check your liver function while you are taking Ofev.
- **Diarrhea, nausea and vomiting.** Your physician may recommend drinking fluids or taking medicines to treat these side effects. Tell the physician if you have diarrhea,

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nausea or vomiting, or if these symptoms worsen or do not go away. Tell your physician if you are taking over the counter laxatives, stool softeners, and other medicines or nutritional supplements which may cause diarrhea.

- **Heart attack.** Contact a physician immediately if you experience symptoms of a heart problem. These symptoms include: chest pain or tightness, pain in your arm, back, neck or jaw, or shortness of breath.
- **Stroke.** Contact a physician immediately if you experience symptoms of stroke. These symptoms include: numbness or weakness on one side of the body, difficulty speaking, headache or dizziness.
- **Bleeding problems.** Ofev may increase the risk of bleeding. Tell the physician if you have abnormal bleeding, bruising or a non-healing wound.
- **Perforation of the stomach or intestinal wall perforation.** Ofev may increase the risk of a perforation of your stomach or your intestinal wall. Tell the physician if you have abdominal pain or swelling.
See additional information about these effects in Section 2 'Special warnings regarding use of this medicine'.

The following additional side effects are classified according to their incidence:

- **Very common side effects (affect more than 1 in 10 users):**
Diarrhea, nausea, abdominal pain, vomiting, elevated liver enzymes, loss of appetite, weight loss, skin ulcers, tiredness
- **Common side effects (affect 1-10 users in 100):**
Headache, hypertension, back pain, dizziness, fever
- **Uncommon side effects (affect 1-10 users in 1,000):**
Alopecia

Side effects reported post-marketing, so their frequency cannot be estimated:

- Liver function injury (DILI)
- Serious bleeding events (some of them life threatening) and non-serious bleeding events
- Pancreatitis
- Reduced number of platelets (thrombocytopenia)
- Rash
- Itch
- Enlargement and weakening of a blood vessel wall or a tear in a blood vessel wall (aneurysms and artery dissections)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your physician.

Reporting side effects

You can report side effects to the Ministry of Health by clicking on the link "Reporting side effects of medication" on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link:
<https://sideeffects.health.gov.il/>

5. How to store the medicine?

Store below 25°C. Store in the original package in order to protect from moisture.

Avoid poisoning! To prevent poisoning, store this medicine and all other medicines in a closed place out of reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a physician.

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

Do not use the medicine if the package is damaged.

Do not discard medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

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6. Additional information

- In addition to the active ingredient this medicine also contains:
Capsule fill: Triglycerides, hard fat, lecithin (E322)
Capsule coating: Gelatin, glycerol, titanium dioxide, iron oxide red, iron oxide yellow, black ink (Opacode®)

- What the medicine looks like and what are the contents of the package:
Ofev 100 mg: opaque, oblong, peach-colored capsules imprinted in black with the Boehringer Ingelheim company symbol and the number "100".

Ofev 150 mg: opaque, oblong, brown capsules imprinted in black with the Boehringer Ingelheim company symbol and the number "150".

The capsules are packed in blisters. There are 10 capsules per blister tray. A total of 30 or 60 capsules per pack. Not all pack sizes may be marketed.

- Registration holder and importer: Boehringer Ingelheim Israel Ltd., 89 Medinat Ha-Yehudim, P.O.B. 4124, Hertzliya-Pituach 4676672.
- Manufacturer: Boehringer Ingelheim Pharma, Ingelheim am Rhein, Germany.
- This leaflet was revised in August 2020.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Ofev 100 mg: 154-74-34335-00
Ofev 150 mg: 154-75-34339-00