

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 a 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 further questions, refer to the 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 may 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 at the start of treatment, during treatment with Ofev and for at least 3 months after the last dose. Contraceptive medicines may not work as well in women having vomiting, diarrhea, or other problems reducing the medicine's absorption. If you have any of these problems, talk with your physician about which highly effective birth control method is right for you. If you become pregnant or plan to become pregnant while taking Ofev, contact your physician right away.

1. What is this medicine intended for?

- The medicine is intended to treat lung disease called idiopathic pulmonary fibrosis (IPF) in adults.
- The medicine is intended to treat adults with chronic (long lasting) fibrosing interstitial lung diseases (ILDs) 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 the list of inactive ingredients, see Section 6 - 'Additional information').
- you are pregnant or breastfeeding. See information in the box above.

Special warnings regarding use of this medicine

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

- You have liver problems.
- You have heart problems.
- 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 stomach 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.
- You have an increased amount of protein in your urine (proteinuria).
- You have bruising, bleeding, fever, fatigue, and confusion. This may be a sign of damage to blood vessels called thrombotic microangiopathy (TMA).

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 upper right side of your stomach area, 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 may 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 your 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 non-prescription aspirin.

If you have pain or swelling in your stomach area, tell the physician. Ofev may increase your chance of a tear in your stomach or intestinal wall, or ischemic colitis.

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 in this age group.

Tests and follow-up

Your physician should order certain 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, the physician will perform blood tests to monitor your liver function.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medications and nutritional supplements, tell the 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 the physician and pharmacist a list of the medicines that you are taking regularly.

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 starting 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 as the risk of injury to your baby can not be ruled out.

3. How to use this medicine?

Always use according to the physician's instructions. Check with the physician or pharmacist if you are not sure about the dose or about how to take this medicine.

Only your physician will determine your dose and how you should take this medicine.

Do not exceed the recommended dose.

The recommended dosage of Ofev is 150 mg twice daily administered orally 12 hours apart. Based on your blood tests, your physician may decide to change your dosage.

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

Do not crush or open Ofev capsules. If you or your caregiver accidentally comes in contact with the content of the capsule, wash hands well right away.

If you have accidentally taken a higher dosage, the side effects described in Section 4 may be more severe. Contact the 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 this 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 at the dosage recommended by the physician. Persist with the treatment as recommended by the physician. Even if your health improves, do not stop treatment with this medicine without consulting the physician.

If you stop taking the medicine

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

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

4. Side effects

As with any medicine, use of 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 upper right side of your stomach area, bleeding or bruising more easily than usual, feeling tired, or decreased appetite. The physician will perform blood tests regularly to check the 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, nausea or vomiting, or if these symptoms worsen or do not go away. Tell the physician if you are taking non-prescription 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 the 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 your 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.
- Tear in the stomach or intestinal wall (perforation).** Ofev may increase your chance of a tear in your stomach or intestinal wall. Tell the physician if you have pain or swelling in your stomach area.
- Increased protein in your urine (proteinuria).** Ofev may increase your chances of having protein in the urine. Tell your physician if you have signs and symptoms of protein in the urine such as foamy urine, swelling, including in your hands, arms, legs, or feet, or sudden weight gain.

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, stomach 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, and whose frequency cannot be estimated:

- Liver function injury (DILI)
- Serious bleeding events (some of them life threatening) and non-serious bleeding events
- Ischemic colitis
- Increased protein in the urine (proteinuria)
- Pancreatitis
- Reduced number of platelets (thrombocytopenia) in your blood
- 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 the physician.

Reporting side effects

You can report side effects to the Ministry of Health by clicking on the link "Reporting side effects of drug treatment" 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 this 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.

6. Additional information

- In addition to the active ingredient this medicine also contains:
Capsule fill: Triglycerides, hard fat, lecithin (E322)
Capsule coating: Gelatin, glycerol, yellow iron oxide, red iron oxide, titanium dioxide, black ink (Opacode®)
- What the medicine looks like and what the contents of the package are:
Ofev 100 mg: opaque, oblong, peach-colored, soft gelatin capsules imprinted on one side in black with the Boehringer Ingelheim company symbol and the number "100".
Ofev 150 mg: opaque, oblong, brown, soft gelatin capsules imprinted on one side 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 St., P.O. Box 4124, Herzliya Pituach 4676672.
- Manufacturer's name and address: Boehringer Ingelheim Pharma GmbH & CO.KG, Ingelheim am Rhein, Germany.
- This leaflet was revised in February 2022 according to MOH guidelines.
- 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