Simple Dosing and **Clear** Monitoring in IPF[1]

PI
Prescribing information

Dosing

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Contraindications

OFEV® (nintedanib) is indicated for the treatment of idiopathic pulmonary fibrosis (IPF) in adults.[1]
This material is for use in Ireland only.

Boehringer Ingelheim

Adverse events should be reported to the Health Products Regulatory Authority at www.hpra.ie or by email to medsafety@hpra.ie. Adverse events should also be reported to Boehringer Ingelheim Pharmacovigilance on 01 291 3960 or by email to PV_local_uk_ireland@boehringer-ingelheim.com

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OFEV® nintedanib

Dosing

The recommended dose of OFEV® is 150 mg twice daily. A 100 mg capsule is available if 150 mg is not tolerated[1]

1x capsule (taken with food and water)*

Twice daily (approximately 12 hours apart)

No titration on initiation

*The capsule should be taken with food, swallowed whole with water, and should not be chewed or crushed.[1]

OFEV® nintedanib

Monitoring

Monitoring is recommended with OFEV®[1]

Pulmonary hypertension

Patients with mild to moderate pulmonary hypertension require close monitoring*

Renal impairment or renal failure

Patients should be monitored during treatment, particularly those with risk factors for renal impairment/failure. In case of renal impairment/failure, therapy adjustment should be considered

Pregnancy

Pregnancy testing must be conducted prior to, and during treatment with OFEV®, and additional contraception is advised†

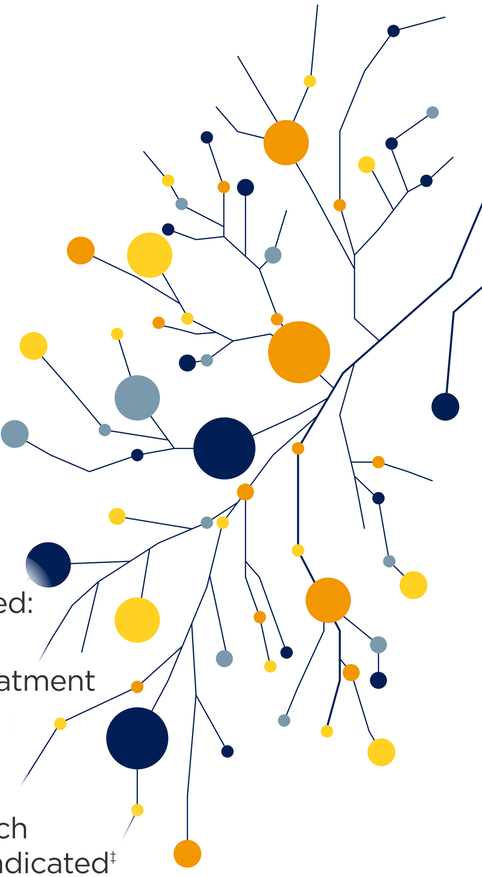
Patient characteristics

Those with low body weight (<65 kg), Asian, female patients, and the elderly require close monitoring

Hepatic transaminase and bilirubin levels

These levels must be monitored:

- before initiation
- during the first month of treatment
- at regular intervals during the subsequent two months of treatment
- periodically thereafter, at each patient visit or as clinically indicated‡



If co-administered with OFEV®, potent P-gp inhibitors (e.g. ketoconazole, erythromycin or cyclosporine) may increase exposure to OFEV®. In such cases, patients should be monitored closely for tolerability of OFEV®.[1]

Treatment interruption should be considered in patients who develop signs or symptoms of nephrotic syndrome.[1]

Treatment with OFEV® should be discontinued in patients who develop laboratory or clinical findings associated with thrombotic microangiopathy (TMA) and a thorough evaluation for TMA should be completed.[1]

Please refer to the Summary of Product Characteristics for a complete list of special warnings and precautions.[1]

***OFEV® should not be used in patients with severe pulmonary hypertension.[1]**

†Women of childbearing potential should be advised to avoid becoming pregnant while receiving treatment with OFEV® and to use highly effective contraceptive methods at initiation of, during and at least 3 months after the last dose of OFEV®. If the patient becomes pregnant, OFEV® must be discontinued.[1]

‡In patients with mild hepatic impairment, a reduced dose of 100 mg twice daily is recommended. OFEV® is not recommended in patients with moderate or severe hepatic impairment.[1]

Monitoring

Hepatic transaminase and bilirubin levels[1]

These levels must be monitored before initiation and during the first month of treatment, as well as during the following two months and beyond, at each patient visit or as clinically indicated:

Transaminase (AST or ALT) level	Recommendation
>3x ULN	Reduce dose, or interrupt OFEV® therapy and closely monitor patients
On return to baseline	Treatment may be reintroduced at the full dose or at a reduced dose
Levels are associated with clinical indications of liver injury	Permanently discontinue therapy

Exposure to OFEV® increased linearly with patient age which may result in higher risk of developing liver enzyme elevations. Drug interactions: If co-administered with OFEV®, potent P-gp inhibitors (e.g. ketoconazole, erythromycin or cyclosporine) may increase exposure to OFEV®. In such cases, patients should be monitored closely for tolerability of OFEV®.

AST: aspartate aminotransferase; **ALT:** alanine aminotransferase; **ULN:** upper limit of normal.

‡In patients with mild hepatic impairment, a reduced dose of 100 mg twice daily is recommended. OFEV® is not recommended in patients with moderate or severe hepatic impairment.[1]

OFEV® nintedanib

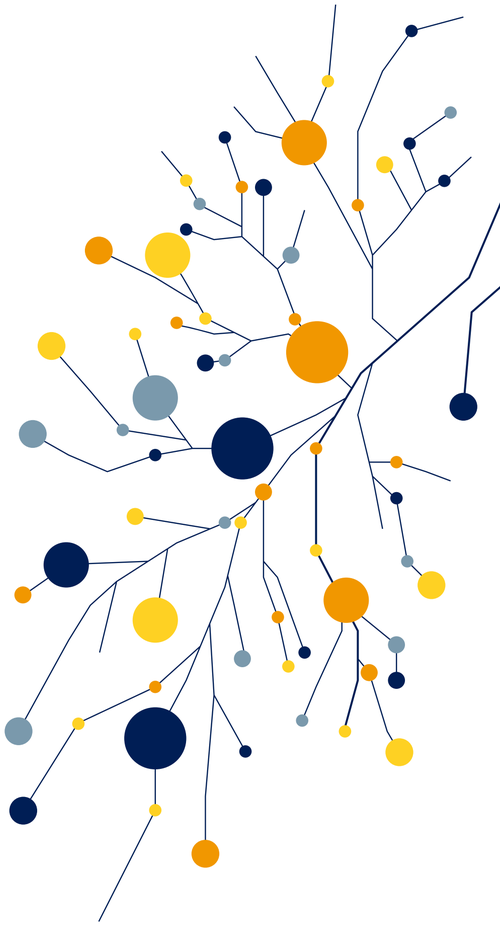
Management of diarrhoea

Diarrhoea is the most frequently reported adverse event with OFEV® but is manageable in most patients:[1,2]

The most common adverse events in INPULSIS® were gastrointestinal, which were mainly mild-to-moderate in intensity[1–3]

In patients who experienced diarrhoeal events, **3.3%** were severe in intensity[1]

In INPULSIS-1 and INPULSIS-2, discontinuation rates due to diarrhoea were less than **5%** in patients treated with OFEV®2*†



Other adverse events

Along with diarrhoea, the most frequently reported adverse events associated with the use of OFEV® included nausea and vomiting, abdominal pain, decreased appetite, decreased weight and elevated levels of hepatic enzymes.[1] Please refer to the Summary of Product Characteristics for a complete list of adverse events[1]

*10% of patients who initiated OFEV® in the INPULSIS®-ON trial discontinued due to diarrhoeal events.[3]

†INPULSIS-1 and INPULSIS-2 were Phase 3, randomised, double-blind, placebo-controlled trials studying the efficacy of OFEV® in patients with IPF. A total of 1066 patients were randomised to receive OFEV® or placebo. The primary endpoint was the annual rate of decline in forced vital capacity.[2]

OFEV® real-world evidence

In a global pharmacovigilance database study in patients with IPF, data were collected over 4 years from 2014–2018, with an estimated cumulative exposure to OFEV® of 60,107 patient-years:

97% of diarrhoeal events were non-serious[4]*

Only **34%** of patients with diarrhoea reported more than one episode[4]

The safety profile of OFEV® is consistent with that observed in clinical trials with no new safety concerns observed

*Serious cases of diarrhoea leading to dehydration and electrolyte disturbances have been reported in post-marketing surveillance.[1]

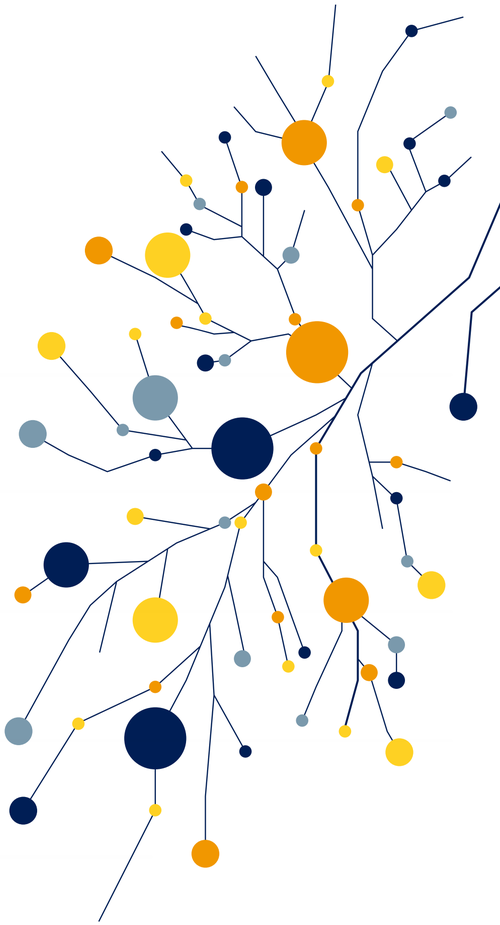
A total of 1066 patients were randomised to receive OFEV® or placebo. The primary endpoint was the annual rate of decline in forced vital capacity.[2]

OFEV® nintedanib

Management of diarrhoea

Diarrhoea is the most frequently reported adverse event with OFEV®* but is manageable in most patients:[1,2]

Diarrhoea management	Recommendation
Dietary advice[5]	Avoid high-fibre foods and alcohol. Advise eating low-fibre foods[5]
First signs of diarrhoea[1]	Hydrate, initiate anti-diarrhoeals[1]
If intervention is insufficient[1]	Interrupt or reduce OFEV®†, and discontinue if severe diarrhoea persists[1]



*Along with diarrhoea, the most frequently reported adverse reactions associated with the use of OFEV® included nausea and vomiting, abdominal pain, decreased appetite, decreased weight and elevated levels of hepatic enzyme.[1] Please refer to the Summary of Product Characteristics for a complete list of adverse events.[1]

†The treatment may be resumed at a reduced dose (100 mg twice daily) or at the full dose (150 mg twice daily).[1]

OFEV® nintedanib

Contraindications

OFEV® is contraindicated in:[1]

Patients who are:

Pregnant*

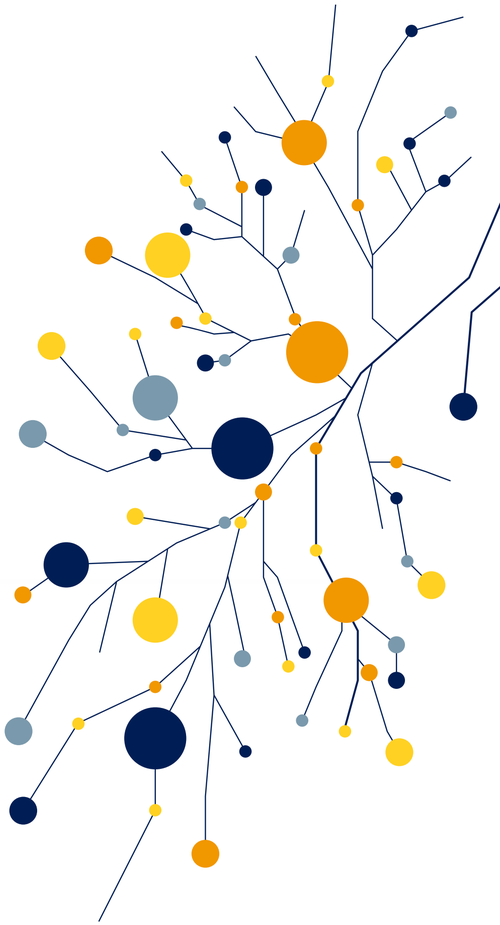
Patients who have a hypersensitivity to:

Nintedanib

Peanut

Soya

Any of the excipients†



*If the patient becomes pregnant, OFEV® must be discontinued.[1]

†Please refer to the Summary of Product Characteristics for a complete list of excipients, and special warnings and precautions.[1]

Checklist

Before prescribing OFEV®, consider:[1]

- ☐ **Contraindications**
- ☐ **Hepatic function, including**
  - ☐ Current hepatic impairment
  - ☐ Liver function tests
- ☐ **Patient weight**
- ☐ **Patient race**
- ☐ **Patient gender**
- ☐ **Patient age**
- ☐ **Renal impairment/failure risk**
- ☐ **Bleeding risk**
- ☐ **Cardiovascular risk, including**
  - ☐ Current conditions
  - ☐ Blood pressure
- ☐ **Gastrointestinal perforation risk**
- ☐ **Ischaemic colitis risk**
- ☐ **Wound healing risk**
- ☐ **Nephrotic range proteinuria risk**
- ☐ **Thrombotic microangiopathy**
- ☐ **Severe pulmonary hypertension**
- ☐ **Pregnancy**
  - ☐ Current pregnancy
  - ☐ Use of highly effective contraception

Please click here to view section 4.4 of the SmPC for more detailed information on Special Warnings and Precautions for Use

References

1. OFEV® 100 mg and 150 mg soft capsules Summary of Product Characteristics. Boehringer Ingelheim Ltd.
2. Richeldi L, du Bois RM, Raghu G, *et al.* Efficacy and safety of nintedanib in idiopathic pulmonary fibrosis. *N Engl J Med.* 2014;370:2071–2082.
3. Crestani B, Huggins JT, Costabel U, *et al*. Long-term safety and tolerability of nintedanib in patients with idiopathic pulmonary fibrosis: results from the open-label extension study, INPULSIS-ON. *Lancet Resp Med.* 2018; http://dx.doi.org/10.1016/S2213-2600(18)30339-4.
4. Lasky J, Criner G, Lazarus H. Safety of Nintedanib in Patients with Idiopathic Pulmonary Fibrosis: Global Pharmacovigilance Data. *Adv Ther* 2020;37:4209–4219.
5. International Foundation for Gastrointestinal Disorders, (2019). Diet Strategies for Managing Chronic Diarrhea. Available at: https://www.iffgd.org/gi-disorders/diarrhea/nutrition-strategies/. Date Accessed: September 2021.