PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

The medicine is dispensed with a doctor's prescription only

ESBRIET®
801 mg
Film-coated tablets

Composition:

Each tablet contains:
pirfenidone 801 mg

ESBRIET®
267 mg
Film-coated tablets

Each tablet contains:
pirfenidone 267 mg

Inactive ingredients: see section 6 "Further Information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist. Keep this leaflet; you may need to read it again.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Esbriet contains the active ingredient *pirfenidone* and is used for the treatment of mild to moderate Idiopathic Pulmonary Fibrosis (IPF) in adults.

Therapeutic group:

Esbriet is an immunosuppressant.

Idiopathic pulmonary fibrosis is a condition in which the lung tissues become swollen and scarred over time and as a result, it is difficult to breathe deeply. This makes it hard for the lungs to function properly. **Esbriet** helps to reduce scarring and swelling in the lungs, and helps you breathe better.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are allergic (sensitive) to the active ingredient pirfenidone, or any of the additional ingredients contained in the medicine which are mentioned in section 6 "Further Information"
- you have previously experienced angioedema with pirfenidone, including symptoms such as swelling of the face, lips and/or tongue which may be associated with breathing difficulties or wheezing
- you are taking a medicine called fluvoxamine (used to treat depression and obsessive compulsive disorder)
- you have a severe or end-stage liver disease
- you have a severe or end-stage kidney disease requiring dialysis

If any of the aforementioned conditions apply to you, do not use **Esbriet**. If you are unsure, consult the attending doctor or pharmacist.

Special warnings regarding use of the medicine:

Consult the doctor before taking **Esbriet**.

- You may become more sensitive to sunlight (photosensitivity reaction) when taking **Esbriet**. Avoid exposure to the sun (including sunlamps) while taking **Esbriet**. Use a sunscreen daily and cover your arms, legs and head to reduce exposure to sunlight (see section 4 "Side Effects").
- Do not take other medicines such as tetracycline antibiotics (e.g., doxycycline), which may make you more sensitive to sunlight.
- Inform your doctor if you suffer from kidney problems.
- Inform your doctor if you suffer from mild to moderate liver problems.
- You should stop smoking before and during treatment with **Esbriet**. Smoking cigarettes may reduce the effect of the medicine.
- **Esbriet** may cause dizziness and tiredness. Exercise caution when performing activities for which you have to be alert and functioning.
- **Esbriet** can cause weight loss. Your doctor will monitor your weight while you are taking the medicine.
- Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with **Esbriet** treatment. Stop using **Esbriet** and seek medical attention immediately if you notice any of the symptoms related to the serious skin reactions described in section 4.

Smoking

You should stop smoking before and during the treatment with **Esbriet**. Smoking cigarettes may reduce the effect of the medicine.

Children and adolescents

This medicine is not intended for children and adolescents below the age of 18.

Tests and follow-up

Esbriet may cause severe liver problems and some cases have been fatal. You will need to undergo a blood test before you start taking the medicine, once a month for the first six months of treatment and once every three months thereafter while taking this medicine, in order to check that your liver is functioning properly. It is important that you undergo these routine blood tests for as long as you are taking **Esbriet**.

If you are taking, have recently taken, or may take other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

In particular, inform the doctor or pharmacist if you are taking the following medicines, since they may alter the effect of **Esbriet**:

- Medicines that may increase the side effects of **Esbriet**:
  - enoxacin (a certain type of antibiotic)
  - ciprofloxacin (a certain type of antibiotic)
  - amiodarone (used to treat certain types of heart disease)
  - propafenone (used to treat certain types of heart disease)
  - fluvoxamine (used to treat depression and obsessive compulsive disorder)
- Medicines that may reduce the effectiveness of **Esbriet**:
  - omeprazole (for the treatment of conditions such as indigestion and gastroesophageal reflux)
  - rifampicin (a certain type of antibiotic)

Use of Esbriet – food and drink

Swallow the tablets whole with water, during or after a meal, to reduce side effects such as nausea and dizziness (see section 4 "Side Effects").

Do not drink grapefruit juice during treatment with **Esbriet**. Grapefruit juice may prevent **Esbriet** from working properly.

Pregnancy and breast-feeding

As a precautionary measure, it is preferable to avoid using **Esbriet** if you are pregnant, planning a pregnancy or think you may be pregnant, since the potential risks to the fetus are unknown.

If you are breast-feeding, or plan to breast-feed, inform the doctor or pharmacist before taking **Esbriet**. It is not known whether the medicine passes into breast milk.

In case you decide to breast-feed, the doctor will discuss with you the risks and benefits of taking the medicine while breast-feeding.

Driving and operating machinery

Do not drive or operate machinery if you feel dizzy or tired after taking **Esbriet**.

Important information about some of this medicine's ingredients

Esbriet contains sodium.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, therefore it is essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use this preparation according to the doctor's instructions. You should check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.

A specialist physician experienced in the diagnosis and treatment of idiopathic pulmonary fibrosis will decide on the commencement of treatment with **Esbriet** preparation and will monitor the treatment.

The dosage and treatment regimen will be determined by the doctor only. The usual dosage is generally:

The medicine will usually be given to you in increasing dosages as follows:

- for the first 7 days of treatment: take a dose of 267 mg, 3 times a day with a meal (a total of 801 mg/day)
- from day 8 to day 14: take a dose of 534 mg (two **Esbriet 267 mg** units), 3 times a day with a meal (a total of 1602 mg/day)
- from day 15 onwards (maintenance dosage): take 801 mg 3 times a day with a meal (a total of 2403 mg/day)

The usual daily maintenance dosage of **Esbriet** is 801 mg (one **Esbriet 801 mg** tablet), 3 times a day with a meal, a total of 2403 mg/day.

Swallow the tablets whole with water, during or after a meal, to reduce the risk of side effects such as nausea and dizziness. Refer to your doctor if symptoms continue.

Do not exceed the recommended dose.

Dosage reduction due to side effects:

The doctor may reduce the dosage if you suffer from side effects such as abdominal problems, skin reactions to sunlight or sunlamps, or significant changes in liver enzymes.

If you accidentally took a higher dosage

If you took an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor, a pharmacist or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you forgot to take the medicine at the required time, take it as soon as you remember, but separate each dose by at least 3 hours.

Do not take a double dose to compensate for the forgotten one.

Adhere to the treatment as recommended by the doctor.

If you stop taking the medicine

In certain situations, the doctor will advise you to stop taking **Esbriet**.

If for any reason you have to stop taking **Esbriet** for more than 14 consecutive days, the doctor will restart treatment with **Esbriet 267 mg** and will instruct you to first take 1 unit 3 times a day, and will then gradually increase the dosage to 801 mg, 3 times a day.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of **Esbriet** may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Stop taking Esbriet and inform the doctor immediately if you suffer from the following effects:

- swelling of the face, lips and/or tongue, itching, urticaria, breathing difficulties or wheezing, or fainting sensation, which are signs of angioedema, a severe allergic reaction or anaphylaxis.
- yellowing of the eyes or skin, dark urine, which may also be accompanied by itching of the skin, pain in the upper right side of the abdomen, loss of appetite, bleeding or bruising more easily than in the past, or feeling tired. These may be signs of impaired liver function and can indicate liver injury, which is an uncommon side effect.
- reddish non-elevated, or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms. These signs and symptoms may indicate Stevens-Johnson syndrome or toxic epidermal necrolysis.

Additional side effects:

Inform the doctor if you experience any side effect.

Very common side effects (may affect more than 1 in 10 patients):

- infections of the throat or the airways going into the lungs and/or sinusitis
- feeling sick (nausea)
- stomach problems such as acid reflux, vomiting, and feeling constipated
- diarrhea
- indigestion or abdominal pain
- weight loss
- decreased appetite
- difficulty sleeping
- tiredness
- dizziness
- headache
- shortness of breath
- cough
- aching joints/joint pains

Common side effects (may affect up to 1 in 10 patients):

- bladder infections
- feeling sleepy
- changes in sense of taste
- hot flushes
- stomach problems, such as feeling bloated, abdominal pain and discomfort, heartburn, and passing wind
- blood tests that may show increased levels of liver enzymes
- skin reactions after going out in the sun or using sunlamps
- skin problems, such as itching, skin redness, red skin, dry skin and skin rash
- muscle pain
- feeling weak or feeling low in energy
- chest pain
- sunburns

Uncommon side effects (may affect up to 1 in 100 patients):

- low blood sodium level which may cause headache, dizziness, confusion, weakness, muscle cramps or nausea and vomiting.
- blood tests which may show a decrease in white blood cells

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the bottle and carton. The expiry date refers to the last day of that month.
- Do not store above 30°C.
- Do not dispose of medicines into the wastewater or into a household waste bin. Consult a pharmacist regarding ways to dispose of medicines no longer required. These measures will help protect the environment.

6. FURTHER INFORMATION

Esbriet contains the active ingredient pirfenidone.

Esbriet 267 mg: Each tablet contains 267 mg active ingredient.

In addition to the active ingredient, the medicine also contains:

Microcrystalline cellulose, povidone K30, silica colloidal anhydrous, croscarmellose sodium, polyvinyl alcohol, titanium dioxide (E 171), macrogol 3350, talc, magnesium stearate, iron oxide yellow (E 172).

Esbriet 801 mg: Each tablet contains 801 mg active ingredient.

In addition to the active ingredient, the medicine also contains:

Microcrystalline cellulose, povidone K30, silica colloidal anhydrous, croscarmellose sodium, polyvinyl alcohol, titanium dioxide (E 171), macrogol 3350, talc, magnesium stearate, iron oxide red (E 172), iron oxide black (E 172).

What the medicine looks like and the contents of the package:

Esbriet 267 mg film-coated tablets are yellow, oval, biconvex, debossed with "*PFD*".

Esbriet 801 mg film-coated tablets are brown, oval, biconvex, debossed with "*PFD*".

Esbriet 267 mg and Esbriet 801 mg tablets: The medicine is available in bottle packaging containing 90 tablets.

License holder and address: Roche Pharmaceuticals (Israel) Ltd., P.O.B. 6391, Hod Hasharon 4524079.

Manufacturer's name and address: F. Hoffmann-La Roche Ltd., Basel, Switzerland.

This leaflet was revised in December 2021 according to MOH guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Esbriet 267 mg: 162-66-35826-00

Esbriet 801 mg: 160-86-35231-00