*To be sold by retail on the prescription of a Pulmonologist only.*

**PRESCRIBING INFORMATION**

**The use of Pirfenidone has shown to cause an abnormal chromosomal structure on exposure to light in genotoxicity tests; therefore it is important to explain to the patient about the potential of the drug to cause carcinogenesis of the skin on exposure to light.**

**Pirfenidone should only be prescribed under the supervision of a physician familiar with the treatment of Idiopathic Pulmonary Fibrosis.**

**1. GENERIC NAME**

Pirfenidone Tablets IP 267mg

Pirfenidone Tablets IP 801mg

**Pulmofib 267** पल्मोफिब २६७

**Pulmofib 801** पल्मोफिब ८०१

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Pirfenidone Tablets IP 267mg Each Film Coated Tablet Contains
Pirfenidone IP-------267 mg
Colour: Titanium Dioxide IP

Pirfenidone Tablets IP 801mg
Each Film Coated Tablet Contains
Pirfenidone IP-------801 mg
Colour: Titanium Dioxide IP

**3. DOSAGE FORM AND STRENGTH**

Pirfenidone is available as film coated tablets 267 mg and 801 mg.

**4. CLINICAL PARTICULARS**

**4.1 Indications**

Pirfenidone is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

**4.2 Posology and Method of Administration**

***Testing Prior to Pirfenidone Administration***

Conduct liver function tests prior to initiating treatment with Pirfenidone.

***Recommended Dosing***

The recommended daily maintenance dosage of Pirfenidone is 801 mg three times daily for a total of 2403 mg/day. Doses should be taken with food at the same time each day. Upon initiation of treatment, titrate to the full dosage of 2403 mg/day over a 14-day period as follows:

| Treatment days | Dosage |
|---|---|
| Days 1 through 7 | 267 mg three times daily (801 mg/day) |
| Days 8 through 14 | 534 (267x2) mg three times daily (1602 mg/day) |
| Days 15 onward | 801 mg three times daily (2403 mg/day) |

Dosages above 2403 mg/day are not recommended for any patient. Patients should not take 2 doses at the same time to make up for a missed dose. Patients should not take more than 3 doses per day.

***Dosage Modifications due to Adverse Reactions***

Patients who miss 14 or more days of Pirfenidone should re-initiate treatment by undergoing the initial 2-week titration regimen up to the full maintenance dosage. For treatment interruption of less than 14 days, the dosage prior to the interruption can be resumed.

If patients experience significant adverse reactions (i.e., gastrointestinal, photosensitivity reaction or rash), consider temporary dosage reductions or interruptions of Pirfenidone to allow for resolution of symptoms.

*Gastrointestinal events*: In patients who experience intolerance to therapy due to gastrointestinal undesirable effects, patients should be reminded to take the medicinal product with food. If symptoms persist, the dose of pirfenidone may be reduced to 267 mg – 534(267x2)mg, two to three times a day with food with re-escalation to the recommended daily dose as tolerated. If symptoms continue, patients may be instructed to interrupt treatment for one to two weeks to allow symptoms to resolve.

*Photosensitivity reaction or rash*: Patients who experience a mild to moderate photosensitivity reaction or rash should be reminded to use a sunblock daily and avoid exposure to the sun. The dose of pirfenidone may be reduced to 801 mg each day (267 mg three times a day). If the rash persists after 7 days, Pirfenidone should be discontinued for 15 days, with re-escalation to the recommended daily dose in the same manner as the dose escalation period.

Patients who experience severe photosensitivity reaction or rash should be instructed to interrupt the dose and to seek medical advice. Once the rash has resolved, Pirfenidone may be re-introduced and re-escalated up to the recommended daily dose at the discretion of the physician.

Dosage Modification due to Elevated Liver Enzymes

Dosage modifications or interruptions may also be necessary when liver enzyme and bilirubin elevations are exhibited. For liver enzyme elevations, modify the dosage as follows:

If a patient exhibits >3 but ≤5 × the upper limit of normal (ULN) ALT and/or AST without symptoms or hyperbilirubinemia after starting Pirfenidone therapy:

- ✓ Discontinue confounding medications, exclude other causes, and monitor the patient closely.
- ✓ Repeat liver chemistry tests as clinically indicated.
- ✓ The full daily dosage may be maintained, if clinically appropriate, or reduced or inter rupted (e.g., until liver chemistry tests are within normal limits) with subsequent re-ti tration to the full dosage as tolerated.

If a patient exhibits >3 but ≤5 × ULN ALT and/or AST accompanied by symptoms or hyperbilirubinemia:

- ✓ Permanently discontinue Pirfenidone.
- ✓ Do not rechallenge patient with Pirfenidone.

If a patient exhibits >5 × ULN ALT and/or AST:

- ✓ Permanently discontinue Pirfenidone.
- ✓ Do not rechallenge patient with Pirfenidone

Dosage Modification due to Drug Interactions

*Strong CYP1A2 Inhibitors (e.g., fluvoxamine, enoxacin)*

Reduce Pirfenidone to 267 mg three times a day (801 mg/day).

*Moderate CYP1A2 Inhibitors (e.g., ciprofloxacin)*

With use of ciprofloxacin at a dosage of 750 mg twice daily, reduce Pirfenidone to 534 (267x2) mg three times a day (1602 mg/day).

***Method of administration***

Pirfenidone is for oral use. The tablets are to be swallowed whole with water and taken with food to reduce the possibility of nausea and dizziness

**4.3 Contraindications**

- Hypersensitivity to the active substance or to any of the excipients used in the for mulation.
- History of angioedema with pirfenidone.
- Concomitant use of fluvoxamine.
- Severe hepatic impairment or end stage liver disease.
- Severe renal impairment (CrCl <30 ml/min) or end stage renal disease requiring di alysis.

**4.4 Special Warnings and Precautions for Use**

Elevated Liver Enzymes

Increases in ALT and AST >3 × ULN have been reported in patients treated with Pirfenidone. In some cases these have been associated with concomitant elevations in bilirubin. Increases in ALT and AST ≥3 × ULN were reversible with dose modification or treatment discontinuation. No cases of liver transplant or death due to liver failure that were related to Pirfenidone have been reported. However, the combination of transaminase elevations and elevated bilirubin without evidence of obstruction is generally recognized as an important predictor of severe liver injury that could lead to death or the need for liver transplants in some patients. Conduct liver function tests (ALT, AST, and bilirubin) prior to the initiation of therapy with Pirfenidone in all patients, then monthly for the first 6 months and every 3 months thereafter. Dosage modifications or interruption may be necessary for liver enzyme elevations.

Photosensitivity Reaction or Rash

The majority of the photosensitivity reactions occurred during the initial 6 months.1Instruct patients to avoid or minimize exposure to sunlight (including sunlamps), to use a sunblock (SPF 50 or higher), and to wear clothing that protects against sun exposure. Additionally, instruct patients to avoid concomitant medications known to cause photosensitivity. Dosage reduction or discontinuation may be necessary in some cases of photosensitivity reaction or rash.

Gastrointestinal Disorders

The most common (>2%) gastrointestinal events that led to dosage reduction or interruption were nausea, diarrhea, vomiting, and dyspepsia. The incidence of gastrointestinal events was highest early in the course of treatment (with highest incidence occurring during the initial 3 months) and decreased over time. Dosage modifications may be necessary in some cases of gastrointestinal adverse reactions.

Angioedema

Reports of angioedema (some serious) such as swelling of the face, lips and/or tongue which may be associated with difficulty breathing or wheezing have been received in association with use of Pirfenidone in the post-marketing setting. Therefore, patients who develop signs or symptoms of angioedema following administration of Pirfenidone should immediately discontinue treatment. Patients with angioedema should be managed according to standard of care. Pirfenidone must not be used in patients with a history of angioedema due to Pirfenidone.

Dizziness

Dizziness has been reported in patients taking Pirfenidone. Therefore, patients should know how they react to this medicinal product before they engage in activities requiring mental alertness or coordination. If dizziness does not improve or if it worsens in severity, dose adjustment or even discontinuation of Pirfenidone may be warranted.

Fatigue

Fatigue has been reported in patients taking Pirfenidone. Therefore, patients should know how they react to this medicinal product before they engage in activities requiring mental alertness or coordination.

Weight loss

Weight loss has been reported in patients treated with Pirfenidone. Physicians should monitor patient's weight, and when appropriate encourage increased caloric intake if weight loss is considered to be of clinical significance.

Hyponatraemia

Hyponatraemia has been reported in patients treated with Pirfenidone. As the symptoms of hyponatraemia may be subtle and masked by the presence of concomitant morbidities, regular monitoring of the relevant laboratory parameters is recommended, especially in the presence of evocative signs and symptoms such as nausea, headache or dizziness.

**4.5 Drug Interactions**

Approximately 70–80% of pirfenidone is metabolised via CYP1A2 with minor contributions from other CYP isoenzymes including CYP2C9, 2C19, 2D6, and 2E1.

Consumption of grapefruit juice is associated with inhibition of CYP1A2 and should be avoided during treatment with pirfenidone.

Fluvoxamine and inhibitors of CYP1A2

Pirfenidone is contraindicated in patients with concomitant use of fluvoxamine. Fluvoxamine should be discontinued prior to the initiation of pirfenidone therapy and avoided during pirfenidone therapy due to the reduced clearance of pirfenidone. Other therapies that are inhibitors of both CYP1A2 and one or more other CYP isoenzymes involved in the metabolism of pirfenidone (e.g. CYP2C9, 2C19, and 2D6) should be avoided during pirfenidone treatment.

In vitro and in vivo extrapolations indicate that strong and selective inhibitors of CYP1A2 (e.g. enoxacin) have the potential to increase the exposure to pirfenidone by approximately 2 to 4-fold. If concomitant use of pirfenidone with a strong and selective inhibitor of CYP1A2 cannot be avoided, the dose of pirfenidone should be reduced to 801 mg daily (267 mg, three times a day). Patients should be closely monitored for emergence of adverse reactions associated with pirfenidone therapy. Discontinue pirfenidone if necessary.

Moderate CYP1A2 Inhibitors

Concomitant administration of pirfenidone and ciprofloxacin (a moderate inhibitor of CYP1A2) moderately increases exposure to pirfenidone. If ciprofloxacin at the dosage of 750 mg twice daily cannot be avoided, dosage reductions are recommended. Monitor patients closely when ciprofloxacin is used at a dosage of 250 mg or 500 mg once daily.

Pirfenidone should be used with caution in patients treated with other moderate inhibitors of CYP1A2 (e.g. amiodarone, propafenone).

Concomitant CYP1A2 and other CYP Inhibitors

Agents or combinations of agents that are moderate or strong inhibitors of both CYP1A2 and one or more other CYP isoenzymes involved in the metabolism of pirfenidone (i.e., CYP2C9,

2C19, 2D6, and 2E1) should be discontinued prior to and avoided during pirfenidone treatment.

Cigarette smoking and inducers of CYP1A2

Smoking has the potential to induce hepatic enzyme production and thus increase medicinal product clearance and decrease exposure. Concomitant use of strong inducers of CYP1A2 including smoking should be avoided during pirfenidone therapy based on the observed relationship between cigarette smoking and its potential to induce CYP1A2. Patients should be encouraged to discontinue use of strong inducers of CYP1A2 and to stop smoking before and during treatment with pirfenidone.

In the case of moderate inducers of CYP1A2 (e.g. omeprazole), concomitant use may theoretically result in a lowering of pirfenidone plasma levels.

Co-administration of medicinal products that act as potent inducers of both CYP1A2 and the other CYP isoenzymes involved in the metabolism of pirfenidone (e.g. rifampicin) may result in significant lowering of pirfenidone plasma levels. These medicinal products should be avoided whenever possible.

**4.6 Use in Special Populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)**

***Pregnancy***

There are no data from the use of Pirfenidone in pregnant women.

In animals placental transfer of pirfenidone and/or its metabolites occurs with the potential for accumulation of pirfenidone and/or its metabolites in amniotic fluid. At high doses (≥1,000 mg/kg/day) rats exhibited prolongation of gestation and reduction in foetal viability. As a precautionary measure, it is preferable to avoid the use of Pirfenidone during pregnancy.

***Breast-feeding:***

It is unknown whether pirfenidone or its metabolites are excreted in human milk. Available pharmacokinetic data in animals have shown excretion of pirfenidone and/or its metabolites in milk with the potential for accumulation of pirfenidone and/or its metabolites in milk.

A decision must be made whether to discontinue breast-feeding or to discontinue from Pirfenidone therapy, taking into account the benefit of breast-feeding for the child and the benefit of Pirfenidone therapy for the mother.

***Fertility:***

No adverse effects on fertility were observed in preclinical studies.

***Elderly***

No overall differences in safety or effectiveness were observed between older and younger patients. No dose adjustment is necessary in patients 65 years and older.

***Paediatric population***

Safety and effectiveness of Pirfenidone in pediatric patients have not been established.

***Renal impairment***

No dose adjustment is necessary in patients with mild renal impairment. Pirfenidone should be used with caution in patients with moderate ($CL_{cr}$ 30–50 mL/min) renal impairment. Monitor for adverse reactions and consider dosage modification or discontinuation of Pirfenidone as needed.

Pirfenidone therapy should not be used in patients with severe renal impairment (CrCl <30 ml/min) or end stage renal disease requiring dialysis.

***Hepatic impairment***

No dose adjustment is necessary in patients with mild to moderate hepatic impairment (i.e. Child-Pugh Class A and B). However, since plasma levels of pirfenidone may be increased in some individuals with mild to moderate hepatic impairment, caution should be used with Pirfenidone treatment in this population. Pirfenidone therapy should not be used in patients with severe hepatic impairment or end stage liver disease.

***Smoking***

Smoking causes decreased exposure to Pirfenidone, which may alter the efficacy profile of Pirfenidone. Instruct patients to stop smoking prior to treatment with Pirfenidone and to avoid smoking when using Pirfenidone

**4.7 Effects on Ability to Drive and Use Machines**

Pirfenidone may cause dizziness and fatigue, which could have a moderate influence on the ability to drive or use machines, therefore patients should exercise caution when driving or operating machinery if they experience these symptoms.

**4.8 Undesirable Effects**

Adverse reactions are listed by System Organ Class (SOC) and within each frequency grouping [Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000)] the adverse reactions are presented in order of decreasing seriousness.

| System organ class | ADRs with frequency |
|---|---|
| **Infections and infestations** | Common: Upper respiratory tract infection; urinary tract infection |
| **Blood and lymphatic system disorders** | Rare: Agranulocytosis |
| **Immune system disorders** | Uncommon: Angioedema |
| **Metabolism and nutrition disorders** | Very common: Anorexia<br>Common: Weight decreased; decreased appetite<br>Uncommon: Hyponatraemia |
| **Psychiatric disorders** | Common: Insomnia |
| **Nervous system disorders** | Very common: Headache<br>Common: Dizziness, somnolence, dysgeusia, lethargy |
| **Vascular disorders** | Common: Hot flush |
| **Respiratory, thoracic and mediastinal disorders** | Common: Dyspnoea, Cough, Productive cough |
| **Gastrointestinal disorders** | Very common: Dyspepsia, Nausea, Diarrhoea<br>Common: Gastroesophageal reflux disease; vomiting; abdominal distension; abdominal discomfort; abdominal pain; abdominal pain upper; stomach discomfort; gastritis; constipation; flatulence |
| **Hepatobiliary disorders** | Common: ALT increased, AST increased, gamma glutamyl transferase increased<br>Rare: Total serum bilirubin increased in combination with increases of ALT and AST |
| **Skin and subcutaneous tissue disorders** | Very common: Photosensitivity reaction, Rash<br>Common: Pruritus, erythema, dry skin, rash erythematous, rash macular, rash pruritic |
| **Musculoskeletal and connective tissue disorders** | Common: Myalgia, arthralgia |
| **General disorders and administration site conditions** | Very common: Fatigue<br>Common: Asthenia, non-cardiac chest pain |
| **Injury, poisoning and procedural complications** | Common: Sunburn |

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. To report Suspected Adverse Reactions, contact MSN Laboratories Private Limited at pharmacovigilance@msnlabs.com or through company website www.msnlabs.com->Contact us->Medical Enquiry/ to report a side effect.

**4.9 Overdose**

There is limited clinical experience with over dosage. In the event of a suspected overdosage, appropriate supportive medical care should be provided, including monitoring of vital signs and observation of the clinical status of the patient.

**5. PHARMACOLOGICAL PROPERTIES**

**5.1 Mechanism of action**

The mechanism of action of pirfenidone has not been fully established. However, existing data suggest that pirfenidone exerts both antifibrotic and anti-inflammatory properties in a variety of in vitro systems and animal models of pulmonary fibrosis (bleomycin- and transplant-induced fibrosis).

IPF is a chronic fibrotic and inflammatory pulmonary disease affected by the synthesis and release of pro-inflammatory cytokines including tumors necrosis factor-alpha (TNF-α) and interleukin-1-beta (IL-1β) and pirfenidone has been shown to reduce the accumulation of inflammatory cells in response to various stimuli.

Pirfenidone attenuates fibroblast proliferation, production of fibrosis-associated proteins and cytokines, and the increased biosynthesis and accumulation of extracellular matrix in response to cytokine growth factors such as, transforming growth factor-beta (TGF-β) and platelet-derived growth factor (PDGF).

**5.2 Pharmacodynamic Properties**

Pharmacotherapeutic group: Immunosuppressants, other immunosuppressants

ATC code: L04AX05

*Cardiac Electrophysiology:*

Relative to placebo, the maximum mean change from baseline in study-specific QT interval was 3.2 milliseconds (ms) and 2.2ms for pirfenidone 2403 mg/day and 4005 mg/day, respectively. No volunteer had a QTc interval greater than 480ms or change from baseline greater than 60ms. Although there was no evidence that pirfenidone prolonged the QTc interval in this study, a definitive conclusion may not be drawn as the positive control (moxifloxacin) did not perform as expected in this study, and pirfenidone at 4005 mg/day (1.7 times the maximum recommended dose) did not cover the maximum pirfenidone exposure increase with co-administration of fluvoxamine, a strong CYP1A2 inhibitor.

**5.3 PHARMACOKINETIC PROPERTIES**

Absorption

Following oral administration of a single dose of 801 mg to healthy older adult volunteers (50-66 years of age) in the fed state, the rate of pirfenidone absorption slowed, while the AUC in the fed state was approximately 80-85% of the AUC observed in the fasted state. Bioequivalence was demonstrated in the fasted state when comparing the 801 mg tablet to three 267 mg capsules. In the fed state, the 801 mg tablet met bioequivalence criteria based on the AUC measurements compared to the capsules, while the 90% confidence intervals for Cmax (108.26% - 125.60%) slightly exceeded the upper bound of standard bioequivalence limit (90% CI: 80.00% - 125.00%).

A reduced incidence of adverse events (nausea and dizziness) was observed in fed subjects when compared to the fasted group. Therefore, it is recommended that pirfenidone be administered with food to reduce the incidence of nausea and dizziness.

Distribution

Pirfenidone binds to human plasma proteins, primarily to serum albumin. The overall mean binding ranged from 50% to 58% at concentrations observed in clinical studies (1 to 100µg/ml). Mean apparent oral steady-state volume of distribution is approximately 70 l, indicating that pirfenidone distribution to tissues is modest.

Metabolism

Approximately 70–80% of pirfenidone is metabolised via CYP1A2 with minor contributions from other CYP isoenzymes including CYP2C9, 2C19, 2D6, and 2E1. *In vitro* data indicate some pharmacologically relevant activity of the major metabolite (5-carboxy-pirfenidone) at concentrations in excess of peak plasma concentrations in IPF patients. This may become clinically relevant in patients with moderate renal impairment where plasma exposure to 5-carboxy-pirfenidone is increased.

Elimination

Pirfenidone is excreted predominantly as metabolite 5-carboxy-pirfenidone, mainly in the urine (approximately 80% of the dose). The majority of pirfenidone was excreted as the 5-carboxy metabolite (>95% of that recovered), with less than 1% of pirfenidone excreted unchanged in urine.

***Special populations***

*Hepatic impairment*

The pharmacokinetics of pirfenidone and the 5-carboxy-pirfenidone metabolite were compared in subjects with moderate hepatic impairment (Child-Pugh Class B) and in subjects with normal hepatic function. Results showed that there was a mean increase of 60% in pirfenidone exposure after a single dose of 801 mg pirfenidone (3 x 267 mg capsule) in patients with moderate hepatic impairment. Pirfenidone should be used with caution in patients with mild to moderate hepatic impairment and patients should be monitored closely for signs of toxicity especially if they are concomitantly taking a known CYP1A2 inhibitor. Pirfenidone is contraindicated in severe hepatic impairment and end stage liver disease.

*Weight*

No clinically relevant differences in the pharmacokinetics of pirfenidone were observed in subjects with mild to severe renal impairment compared with subjects with normal renal function. The parent substance is predominantly metabolised to 5-carboxy-pirfenidone. Exposure to 5-carboxy-pirfenidone increases 3.5 fold or more in patients with moderate renal impairment. Clinically relevant pharmacodynamic activity of the metabolite in patients with moderate renal impairment cannot be excluded. No dose adjustment is required in patients with mild renal impairment who are receiving pirfenidone. Pirfenidone should be used with caution in patients with moderate renal impairment. The use of pirfenidone is contraindicated in patients with severe renal impairment (CrCl <30ml/min) or end stage renal disease requiring dialysis

*Geriatric population*

Results of population pharmacokinetic analysis suggest that no dosage adjustment is needed in geriatric patients.

*Gender*

Results of population pharmacokinetic analysis of pirfenidone showed no significant differences in pharmacokinetics between males and females.

*Obesity*

Results of population pharmacokinetic analysis showed that obesity (Body Mass Index [BMI] greater than or equal to 30 $kg/m^2$) has no significant effect on the pharmacokinetics of pirfenidone.

*Race*

Population pharmacokinetic analysis showed that race has no significant effect on the pharmacokinetics of pirfenidone.

**6. NONCLINICAL PROPERTIES**

**6.1 Animal Toxicology or Pharmacology**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

In repeated dose toxicity studies increases in liver weight were observed in mice, rats and dogs; this was often accompanied by hepatic centrilobular hypertrophy. Reversibility was observed after cessation of treatment. An increased incidence of liver tumours was observed in carcinogenicity studies conducted in rats and mice. These hepatic findings are consistent with an induction of hepatic microsomal enzymes, an effect which has not been observed in patients receiving Pirfenidone. These findings are not considered relevant to humans.

A statistically significant increase in uterine tumours was observed in female rats administered 1,500 mg/kg/day, 37 times the human dose of 2,403 mg/day. The results of mechanistic studies indicate that the occurrence of uterine tumours is probably related to a chronic dopamine-mediated sex hormone imbalance involving a species specific endocrine mechanism in the rat which is not present in humans.

Reproductive toxicology studies demonstrated no adverse effects on male and female fertility or postnatal development of offspring in rats and there was no evidence of teratogenicity in rats (1,000 mg/kg/day) or rabbits (300 mg/kg/day). In animals placental transfer of pirfenidone and/or its metabolites occurs with the potential for accumulation of pirfenidone and/or its metabolites in amniotic fluid. At high doses (≥450 mg/kg/day) rats exhibited a prolongation of oestrous cycle and a high incidence of irregular cycles. At high doses (≥1,000 mg/kg/day) rats exhibited a prolongation of gestation and reduction in fetal viability. Studies in lactating rats indicate that pirfenidone and/or its metabolites are excreted in milk with the potential for accumulation of pirfenidone and/or its metabolites in milk.

Pirfenidone showed no indication of mutagenic or genotoxic activity in a standard battery of tests and when tested under UV exposure was not mutagenic. When tested under UV exposure pirfenidone was positive in a photo-clastogenic assay in Chinese hamster lung cells.

Phototoxicity and irritation were noted in guinea pigs after oral administration of pirfenidone and with exposure to UVA/UVB light. The severity of phototoxic lesions was minimised by application of sunscreen.

**7. PHARMACEUTICAL PARTICULARS**

**7.1 Incompatibilities**

None

**7.2 Packing Information**

10's PVC/PVDC Blister pack

**7.3 Storage and Handling Instructions**

**Store at a temperature not exceeding 30°C.**

Keep out of reach of children.

**8. PATIENT COUNSELLING INFORMATION**

Advise the patient to read package insert.

Liver Enzyme Elevations

Advise patients that they may be required to undergo liver function testing periodically. Instruct patients to immediately report any symptoms of a liver problem (e.g., skin or the white of eyes turn yellow, urine turns dark or brown [tea colored], pain on the right side of stomach, bleed or bruise more easily than normal, lethargy)

Photosensitivity Reaction or Rash

Advise patients to avoid or minimize exposure to sunlight (including sunlamps) during use of PIRFENIDONE because of concern for photosensitivity reactions or rash. Instruct patients to use a sunblock and to wear clothing that protects against sun exposure. Instruct patients to report symptoms of photosensitivity reaction or rash to their physician. Temporary dosage reductions or discontinuations may be required.

Gastrointestinal Events

Instruct patients to report symptoms of persistent gastrointestinal effects including nausea, diarrhea, dyspepsia, vomiting, gastro-esophageal reflux disease, and abdominal pain. Temporary dosage reductions or discontinuations may be required.

Smokers

Encourage patients to stop smoking prior to treatment with Pirfenidone and to avoid smoking when using Pirfenidone.

Take with Food

Instruct patients to take Pirfenidone with food to help decrease nausea and dizziness.

**9. DETAILS OF MANUFACTURER**

Manufactured by:
**MSN Laboratories Private Limited**
Formulation Division, Unit-II,
Sy.No. 1277, 1319 to 1324,
Nandigama (Village & Mandal),
Rangareddy (District),
Telangana - 509 228, India.

**10. DETAILS OF MANUFACTURING LICENCE NUMBER**

M.L.No.: 5/MN/TS/2014/F/G, 26/08/2019

**11. DATE OF REVISION**

March 2021.

D032436-00