NHS
Cambridgeshire and Peterborough
Clinical Commissioning Group

Shared Care Guideline

Pirfenidone for idiopathic pulmonary fibrosis (MONITORING IN PRIMARY CARE ONLY)

Executive Summary

- Pirfenidone is recommended as an option for treating idiopathic pulmonary fibrosis only if the person has a forced vital capacity (FVC) between 50% and 80% predicted
- It should be discontinued if there is evidence of disease progression (a decline in per cent predicted FVC of 10% or more within any 12-month period)
- Patients liver function should be monitored as below
- Patients should be educated on how to take Pirfenidone and potential side effects
- Pirfenidone has a number of potential drug interactions that prescribers should be aware of.
- Hospital specialist teams will be responsible for pirfenidone prescribing and supply.
- The responsibilities of the hospital specialist, GP and patient for this Shared Care Guideline can be found within this document here

Sharing of care depends on communication between the specialist, GP and the patient or their parent/carer. The intention to share care should be explained to the patient and accepted by them. Patients are under regular follow-up and this provides an opportunity to discuss drug therapy. The doctor/healthcare professional who prescribes the medication has the clinical responsibility for the drug and the consequences of its use. Further information about the general responsibilities of the hospital specialist and GP can be found here

1. Scope

Prescribing and monitoring by hospital specialist consultants and monitoring by General Practitioners

2. Aim

To outline the details of prescription and the responsibilities for each person caring for the patient taking Pirfenidone (in conjunction with Policy “Pirfenidone – Treatment of Idiopathic Pulmonary Fibrosis”)

3. Introduction

Pirfenidone is an anti-fibrotic used for the treatment of Idiopathic Pulmonary Fibrosis

All patients who are to be considered for pirfenidone must be discussed at the Cambridge ILD MDT. It is then recommended as an option for treating idiopathic pulmonary fibrosis in line with the criteria as set out in NICE Technology Appraisal 282 and NICE Clinical Guideline 163, e.g. if:

- the patient has a forced vital capacity (FVC) between 50% and 80% predicted, or the patient is taking part in the Pirfenidone mild patient programme (FVC >80% predicted) and
- the manufacturer provides pirfenidone with the discount agreed in the patient access scheme.

Treatment should be discontinued if there is evidence of disease progression, defined as a decline in predicted FVC of 10% or more within any 12 month period or if the patient is unable to tolerate Pirfenidone due to side effects.

4. Abbreviations

ILD – Interstitial Lung Disease
FVC – forced vital capacity
FEV1 – forced expiratory volume in 1 second
UIP – Usual Interstitial Pneumonia
IPF – Idiopathic Pulmonary Fibrosis
MDT – Multi-Disciplinary Team
GP – General Practitioner
6MWT – six minute walk test

5. Dose and Administration

Upon initiating treatment, the dose should be titrated to the recommended daily dose of nine capsules per day over a 14-day period as follows:

- Days 1 to 7: 267 mg three times a day (801 mg/day)
- Days 8 to 14: 534 mg three times a day (1602 mg/day)
- Day 15 onward: 801 mg three times a day (2403 mg/day)

The recommended daily dose for patients with IPF is 801mg three times a day with food for a total of 2403 mg/day.

Doses above 2403 mg/day are not recommended for any patient.

Patients who miss 14 consecutive days or more of treatment should re-initiate therapy by undergoing the initial 2-week titration regimen up to the recommended daily dose. For treatment interruption of less than 14 consecutive days, the dose can be resumed at the previous recommended daily dose without titration.

A dose reduction of pirfenidone to 534 mg three times daily is required with concomitant use of high dose ciprofloxacin (750mg twice daily). For this reason concomitant use of ciprofloxacin should be avoided & a discussion with Hospital Specialist should be had if no alternative exists.

Further information can be found in the Summary of Product Characteristics - Pirfenidone & Policy "Pirfenidone – Treatment of Idiopathic Pulmonary Fibrosis")

6. Adverse Effects

The summary of product characteristics lists the following adverse reactions for pirfenidone as the most commonly reported (10% or higher): nausea, rash, fatigue, diarrhoea, dyspepsia and photosensitivity reaction. Pirfenidone is in the black triangle scheme and all adverse drug reactions should be reported via the Yellow Card Scheme.

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

Side Effect	**Action**	
	By GP	**By Hospital Specialist**
Gastro-intestinal disturbance – nausea, diarrhoea, indigestion	• Advise to take with food. Prescribe anti-reflux therapy. If symptoms persist discuss with Hospital Specialist.	• Reduce dose to 267-534mg 2-3 times a day with food; re-escalate as tolerated • If symptoms persist further stop treatment for 1-2 weeks
Photosensitivity reaction/skin rash	• Discuss with Hospital Specialist. • Advise to use of factor 50 sun block daily. • Advise to avoid sun exposure. • Avoid use of drugs that	• Reduce dose to 267mg three times a day. • If rash persists after 7 days stop drug for 15 days and then re-escalate as per initial titration scheme.

	may cause photosensitive skin rash e.g. Doxycycline	• If severe skin reaction stop pirfenidone and consider emollients or topical corticosteroids
Hepatic impairment – bruising, itchy skin, loss of appetite, dark urine	• Discuss with Hospital Specialist • Monitor liver function as per SCG (Section 10)	• Review as appropriate undertaking dose adjustment/drug cessation in accordance with policy 'Pirfenidone – Treatment of Idiopathic Pulmonary Fibrosis"
Weight loss	• Monitor – encourage increase in calories • Report sudden weight loss to Hospital Specialist	• Review as appropriate
Tiredness	• Encourage rest • Contact Hospital Specialist with overwhelming tiredness	• Review as appropriate • Consider dose reduction
Headache	• Manage with occasional simple analgesia • Contact Hospital Specialist if severe/frequent	• Review as appropriate
In case of any severe or life threatening side effect	• Immediately stop pirfenidone and contact Hospital Specialist	• Review as appropriate

Common side effects (may affect up to 1 in 10 people):
• infections of the throat or the airways going into the lungs and/or sinusitis
• bladder infections
• weight loss
• difficulty sleeping
• dizziness
• feeling sleepy

• changes in taste
• hot flushes
• shortness of breath
• cough
• stomach problems such as acid reflux, vomiting, feeling bloated, abdominal pain and discomfort, heart burn, feeling constipated and passing wind
• blood tests may show increased levels of liver enzymes
• skin problems such as itchy skin, skin redness or red skin, dry skin, skin rash
• muscle pain, aching joints/joint pains
• feeling weak or feeling low in energy
• chest pain
• sunburn.
Uncommon side effects (may affect up to 1 in 100 people):
• swelling of the face, lips and/or tongue, difficulty
• breathing or wheezing.
Rare side effects (may affect up to 1 in 1,000 people):
• blood tests may show decrease in white blood cells.

Further information can be found in the Summary of Product Characteristics

7. Cautions

- Concomitant use with Ciprofloxacin – reduce dose of pirfenidone to 534 mg three times a day with high dose ciprofloxacin (750mg twice daily). Discuss with Hospital specialist if no alternative to ciprofloxacin exists.
- Omeprazole and rifampicin may reduce the efficacy of pirfenidone
- Avoid exposure to direct sunlight
- Avoid consumption of grapefruit juice

8. Contraindications

- Hypersensitivity to the active substance within the drug or its excipients
- 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 dialysis
- Smoking

Further information can be found in the Summary of Product Characteristics

9. Interactions

- Avoid exposure to direct sunlight
- Several CYP enzymes are involved in the metabolism of pirfenidone, CYP1A2 being the most prominent CYP enzyme involved. Strong inducers and inhibitors of these enzymes may result in a reduced or increased exposure to pirfenidone, examples include ciprofloxacin (dose of pirfenidone to be reduced) and fluvoxamine (should be avoided), and smoking.
- Not all interactions noted in the SPC are likely to be clinically significant and not all inducers and inhibitors are mentioned by name. Advice from the specialist centre is therefore required.
- When in doubt, GPs are advised to seek the advice of the Hospital Specialist.
- **Contraindicated** - fluvoxamine
- **Avoid concomitant use with:**

Carbamazepine	Isoniazid	Phenytoin
Cimetidine	Nalidixic-acid	Primidone
Ciprofloxacin – see section 8. Dosing	Norfloxacin	Rifampicin
Clarithromycin	Oral-contraceptives	Ritonavir
Enoxacin	Phenobarbital	St Johns Wort
Erythromycin		

- **Use with caution:**

Amiodarone Amitriptyline Aprepitant Bupropion Chloramphenicol Cinacalcet Citalopram Clozapine Diclofenac	Diltiazem Disulfiram Duloxetine Entacapone Ethylestradiol Fenofibrate Fluconazole Fluoxetine Fluvastatin	Insulin Lansoprazole Levofloxacin Ketoconazole Methoxsalen Metronidazole Mexiletine Modafinil Moxifloxacin	Nicotine Omeprazole Paroxetine Probenecid Propafenone Quinidine Sertraline Sildenafil Terbinafine Topiramate Voriconazole Zafirlukast

Further information can be found in the Summary of Product Characteristics.

10. Monitoring Standards & Actions to take in the event of abnormal test results/symptoms

- See section 6 for management of adverse effects
- GP to inform Hospital Specialists as per contacts below if patient is suffering from any side effects
    - **GP monitoring of Hepatic Function (ALT/ AST/Alk Phos / Bilirubin):**

(At monthly intervals for 6 months and if stable every 3 months thereafter)

- If the **AST is more than 3 times upper limit (and less than 5 times upper limit)** after starting pirfenidone then:
    - Contact the ILD Team for advice who will manage as per policy

- If the **AST is less than or equal to 5 times upper limit** after starting pirfenidone **together with hyperbilirubinaemia and symptoms** then:
    - Discontinue treatment and contact the ILD team who will manage as per policy

- If the **AST is more than 5 times** then:
    - Discontinue treatment and contact the ILD team who will manage as per policy

11. Shared Care Responsibilities

a. Hospital specialist:

- Diagnosis of ILD in line NICE TAG282, Clinical Guideline 163 and Specialist Service Specifications
- Send a letter to the GP requesting shared care for the patient.
- Educate the patient on how to take the medicine and what to do if they feel unwell.
- Prescribe Pirfenidone
- Provide the patient with a blood monitoring booklet for recording results of liver function blood tests
- Arrange for delivery of the medicine
- Review the patient in clinic and via telephone calls
- Provide the patient with contact information should they require.

- Inform the GP after each clinic attendance if there is any change to treatment or monitoring.
- Inform GP of patients who do not attend clinic appointments.
- To provide any advice to the patient/carer/GP when requested.
- Report adverse effects to the Yellow Card Scheme

b. General Practitioner:

- Provide confirmation of whether agreed to participate in shared care within 14 days of receipt of the request for shared care.
- Take blood to monitor liver function at monthly intervals for 6 months and if stable every 3 months thereafter as per Section 10.
- Communicate results to the patients to be recorded in the 'Blood Monitoring Booklet'
- Ensure no interacting medication is prescribed without liaising with the specialist team first.
- Report any adverse events to the hospital specialist as outlined in sections 6 & 10, where appropriate
- Request advice from the hospital specialist when necessary.
- To ensure drug interactions & potential adverse effects of Pirfenidone are considered during consultations within primary care GP's should include details of Pirfenidone in the hospital only/3rd party prescriber section of the repeat medication template on their GP clinical system. (CCG medicines management team can provide details of how to do this for both SystemOne & EMIS web- if this process is unfamiliar).

c. Patient or parent/carer:

- Hold responsibility for their 'Blood monitoring Booklet' – to record their blood test results and bring to each clinic appointment.
- Make appointments for the scheduled blood tests to be taken.
- Report to the hospital specialist or GP if they do not have a clear understanding of their treatment.
- Patients must not exceed the recommended dose.
- Patients must attend their scheduled clinic and blood test appointments (where relevant).
- Must inform other clinical staff that they are receiving treatment.
- Report any adverse effects to the hospital specialist or GP.

12. Contact numbers for advice and support

Cambridge University Hospital Trust – Addenbrooke's Hospital		
Specialist	**Post**	**Telephone**

Professor Chilvers	Consultant	01223 762007
Caroline Owen	Respiratory Nurse Specialist	07872048641
Dr Christine Fiddler	Consultant Respiratory Physician	01223 217079
Medicines Information		01223 217502/217478

Papworth Hospital NHS Foundation Trust		
Specialist	**Post**	**Telephone**
Dr Helen Parfrey	ILD Consultant	01480 364521
Dr Muhunthan Thillai	ILD Consultant	01480 364530
Dr Nicky Simler	ILD Consultant	01480 364530
Dr Christine Fiddler	Consultant Respiratory Physician	01480 364521
ILD CNS	Specialist Nurse	01480 364184
Duncan Grady	Thoracic Directorate Pharmacist	01480 830541 pager 845
Medicines Information		01480 364179
Medicines Helpline (patients)		01480 364739

13. Equality and Diversity Statement

This document complies with the Cambridge University Hospital Trust service Equality and Diversity statement.

14. Disclaimer

It is your responsibility to check that this printed out copy is the most recent issue of this document.

15. Document management

Document ratification and history	
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NHS
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The information contained in this guideline is issued on the understanding that it is accurate based on the resources at the time of issue. For further information please refer to the most recent Summary of Product Characteristics
https://www.medicines.org.uk/emc/medicine/29932