SAFETY CHECKLIST FOR PRESCRIBING PHYSICIAN

Pirfenidone

This safety checklist contains key elements to follow when prescribing pirfenidone:

Indication for use

- I am satisfied that the patient is an adult with a diagnosis of idiopathic pulmonary fibrosis (IPF).
- I have started therapy at 267 mg three times a day and the patient has been advised that therapy will be titrated according to the recommendations of the Summary of Product Characteristics (SmPC).
- I have advised the patient to take pirfenidone with food and to avoid grapefruit and grapefruit juice while they are being treated with pirfenidone.

Before starting pirfenidone I have:

- Checked whether the patient is hypersensitive to pirfenidone.
- Checked whether the patient is on medication which could potentially interact adversely with pirfenidone.
- Arranged for adequate monitoring for abnormal liver function tests.

Drug-induced Liver Injury

Prior to initiation of treatment:

- ☐ The patient does not have severe hepatic impairment or end stage liver disease. Pirfenidone is contraindicated in patients with severe hepatic impairment or end stage liver disease.
- ☐ Liver function tests have been performed prior to initiation of treatment with Pirfenidone.
- ☐ I am aware that elevations of serum transaminases can occur during treatment with Pirfenidone.
- ☐ The patient is informed that serious liver injury may occur and that he/she should contact their prescribing physician or regular physician immediately for clinical evaluation and liver function tests if symptoms of liver injury including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice (as described in the patient information leaflet) occur.

During treatment:

- ☐ Liver function tests will be performed monthly in the first six months of treatment.
- ☐ Liver function tests will be performed every three months thereafter during treatment.
- ☐ Patients who develop liver enzyme elevations will be closely monitored and the dose of pirfenidone will be adjusted or treatment will be permanently discontinued if necessary (please refer to the Summary of Product Characteristics for recommendations).
- ☐ Prompt clinical evaluation and liver function tests will be performed if a patient develops symptoms or signs of liver injury (please refer to the Summary of Product Characteristics for recommendations).

Photosensitivity

- ☐ The patient is informed that pirfenidone is known to be associated with photosensitivity reactions and that preventive measures have to be taken.
- ☐ The patient is advised to avoid or reduce exposure to direct sunlight (including sunlamps).
- ☐ The patient is instructed to use a sunblock daily, to wear clothing that protects against sun exposure, and to avoid other medications known to cause photosensitivity.
- ☐ The patient is informed that he/she should report to the prescribing physician or regular physician if any new and significant skin rash occurs.

Reporting of adverse events

Healthcare professionals should report any adverse events suspected to be associated with the use of Pirfenidone according to national reporting requirements. If you are aware of any suspected adverse reactions associated with the use of Pirfenidone, including clinically significant photosensitivity reactions and skin rashes, drug-induced liver injury, clinically significant abnormal liver function tests and any other clinically significant ADRs, please report such information at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to Novumgen Limited. Please contact Novumgen Limited Medical Information by emailing safety@novumgen.com or by calling +44 (0)203 096 2886.

This educational material is provided by Novumengen Limited and is mandatory as a condition of the Marketing Authorisation in order to comply and minimize important selected risks.

Specific adverse drug reaction follow-up forms

Guided questionnaire for assessment of DILI

AER		Local Case ID	
Site No		Date of Birth (patient) (DD-MMM-YYYY)	
Patient ID/Initials		Race	☐ Caucasian ☐ Black ☐ Asian ☐ American Indian or ☐ Alaska Native Other (Specify): _____
Patient Gender		BMI	

1. Product information (dose information)

Product Name	Dose and Units	Frequency	Route	Dosage form
Start date:		**Last dose date:**		**Ongoing** ☐
How was Drug Regimen altered in response to the event?				
Not altered ☐				
Altered due to AE ☐ **Specify:** _____				
Reduced ☐		**Date:**		
		New dose (Unit):		
Temporally interrupted ☐		**Stopped date** **Restart date**		
Permanently discontinued ☐		**Date:**		
Rechallenge ☐		**Date:**		

1. All dates must be reported as DD-MMM-YYYY.
2. For an intermittent dose regimen (e.g cyclic therapy), if the event occurred between two cycles, enter the start date as the start date of first administration of the first cycle.
3. For a dose escalation regimen, enter the dose at the time of the event. This date is of particular importance for intermittent dosing regimen (e.g. cyclic therapy)

Product information (dose information) (Cont…)

Product Name	Dose and Units	Frequency	Route	Dosage form
Start date:		**Last dose date:**		**Ongoing** ☐
How was Drug Regimen altered in response to the event?				
Not altered ☐				
Altered due to AE ☐ **Specify:** _____				
Reduced ☐		**Date:**		
		New dose (Unit):		
Temporally interrupted ☐		**Stopped date** **Restart date**		
Permanently discontinued ☐		**Date:**		
Rechallenge ☐		**Date:**		

1. All dates must be reported as DD-MMM-YYYY.
2. For an intermittent dose regimen (e.g cyclic therapy), if the event occurred between two cycles, enter the start date as the start date of first administration of the first cycle.
3. For a dose escalation regimen, enter the dose at the time of the event. This date is of particular importance for intermittent dosing regimen (e.g. cyclic therapy)

2. Medical history

Hepatitis history including A, B, C, D and E	☐	Previous DILI (specify suspected drugs below)	☐
Autoimmune hepatitis	☐	Biliary non-obstructive	☐
Recent exposure to blood products/ body fluids/transfusion	☐	Fatty liver or steatohepatitis	☐
Dyslipidemia	☐	Heart failure	☐
Biliary obstructive disease	☐	Other causes of hyperbilirubinemia	☐
Recent Intravenous drug abuse	☐	Diabetes (specify if uncontrolled below)	☐
Malignancy	☐	Haemodynamic shock	☐
History of alcohol abuse	☐	Exposure to toxic agents	☐
Obesity	☐	Recent travel to countries with endemic hepatitis infections	☐
Other relevant conditions (specify below)	☐	Other relevant risk factors (specify below)	☐
Unknown			☐

If any item is checked above, please describe relevant details, i.e., onset date, signs and symptoms, laboratory values, duration, diagnostic tests, treatment and outcomes.

3. Concomitant Medication

Please provide relevant concomitant medications (including prescription medication, other OTC drugs, herbal and dietary supplements). Please ensure consistency with data reported on the standard SAE reporting form.

Product	Suspected	Total daily dose/Units	Start date	Ongoing	Last dose date prior to AE
	☐			☐	
	☐			☐	
	☐			☐	
	☐			☐	
	☐			☐	

1. All dates must be reported as DD-MMM-YYYY.
2. For an intermittent dose regimen (e.g cyclic therapy), if the event occurred between two cycles, enter the start date as the start date of first administration of the first cycle.
3. For a dose escalation regimen, enter the dose at the time of the event. This date is of particular importance for intermittent dosing regimen (e.g. cyclic therapy).

4. Clinical Sign and Symptoms

Signs and symptoms	Yes	Onset date	Ongoing	Resolution date
Nausea	☐		☐	
Vomiting	☐		☐	
Malaise	☐		☐	
Reduced appetite	☐		☐	
Fatigue	☐		☐	
Dark Urine	☐		☐	
Light colored feces	☐		☐	
Abdominal pain	☐		☐	
Jaundice	☐		☐	
Pruritis	☐		☐	
Hepatomegaly	☐		☐	
Splenomegaly	☐		☐	
Encephalopathy	☐		☐	
Hepatic dysfunction	☐		☐	
Ascites	☐		☐	
Esophageal varices	☐		☐	
Rash	☐		☐	
Fever	☐		☐	
Eosinophilia	☐		☐	
Other organ involvement specify below)	☐		☐	
Other (specify below)	☐		☐	

5. Liver Biochemical Tests

	ALT		AST		GGT		ALP		Total Bilirubin	
Reference range (Unit)	**Value**	**XULN**	**Value**	**XULN**	**Value**	**XULN**	**Value**	**XULN**	**Value**	**XULN**
Baseline										
Date										

6. Virology Tests:

Please specify if not done (ND) in the result section

Type of test	Date	Results
Hepatitis A- IgM		
Hepatitis A- IgG		
Hepatitis B		
HBsAg		
Anti- HBs		
Anti-HBc IgM		
HBeAg		
Anti-HBe		
HBV DNA		
Hepatitis C		
Anti-HCV		
HCVRNA		
Hepatitis D		
Hepatitis E		
EBV IgM		
EBV IgG		
CMV IgM		
CMB IgG		
Others infections (specify below)		
1. ***All dates must be reported as DD-MMM-YYYY***		

7. Autoantibodies for Immunologic Studies

Please specify if not done (ND) in the result section

Type of test	Date	Results
Antimitochondrial antibody (AMA)		
Antinuclear antibody (ANA)		
Anti-smooth-muscle antibody (ASMA)		
Antineutrophil cytoplasmic antibody (ANCA)		
Anti-liver/kidney microsomal antibody (anti-LKM)		
Other (Specify below)		

8. Hepatic Imaging and Liver Biopsy

Please specify if not done (ND) in the result section

Type of test	Date	Results
Ultrasound		
CT scan		
Magnetic resonance cholangiopancreatography		
Endoscopic retrograde cholangiopancreatography (ERCP)		
Hepatobiliary iminodiacetic acid (HIDA)		
Scan		
Liver Biopsy		
Other (Specify)		

1. ***All dates must be reported as DD-MMM-YYYY***

9. Treatments/Procedures for DILI

Treatment/ Procedure	Total daily dose/Units	Start date	Ongoing	Last dose date prior to AE
			☐	
			☐	
			☐	
			☐	
			☐	

1. E.g. glucocorticoid, ursodeoxycholic acid
2. All dates must be reported as DD-MMM-YYYY.
3. For an intermittent dose regimen (e.g cyclic therapy), if the event occurred between two cycles, enter the start date as the start date of first administration of the first cycle.
4. For a dose escalation regimen, enter the dose at the time of the event. This date is of particular importance for intermittent dosing regimen (e.g. cyclic therapy).

Completed By:

Name: _____ Position: _____

Date & Signature: _____

E-mail: _____