Part VI: Summary of the Risk Management Plan

Summary of Risk Management Plan for PIRFENIDONE 267 mg and 801 mg, film coated tablets[1] (Pirfenidone)

This is a summary of the risk management plan (RMP) for Pirfenidon ratiopharm 267mg und 801mg Filmtabletten and Pirfenidon Actavis 267mg und 801mg Filmtabletten (hereinafter referred to as Pirfenidone). The RMP details important risks of Pirfenidone, how these risks can be minimised, and how more information will be obtained about Pirfenidone's risks and uncertainties (missing information).

Pirfenidone's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Pirfenidone should be used.

Important new concerns or changes to the current ones will be included in updates of Pirfenidone's RMP.

I. The Medicine and What It is used for

Pirfenidone is authorised for the treatment of idiopathic pulmonary fibrosis in adults (see SmPC for the full indication). It contains pirfenidone as the active substance and it is given orally.

II. Risks Associated with the Medicine and Activities to Minimise or Further Characterise the Risks

Important risks of Pirfenidone, together with measures to minimise such risks and the proposed studies for learning more about Pirfenidone's risks, are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In the case of Pirfenidone, these measures are supplemented with *additional risk minimisation measures* mentioned under relevant important risks, below.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

[1] in AT: Pirfenidon ratiopharm 267mg und 801mg Filmtabletten or Pirfenidon Actavis 267mg und 801mg Filmtabletten

II.A List of Important Risks and Missing Information

Important risks of Pirfenidone are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of Pirfenidone. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine).

Table 12: Summary of Safety Concerns

List of important risks and missing information	
Important identified risks	• Drug-induced liver injury (DILI) • Photosensitivity reaction and rash
Important potential risks	• None
Missing information	• None

II.B Summary of Important Risks

Table 13: Summary of Pharmacovigilance Activities and Risk Minimisation Activities by Safety Concern

Important identified risk: Drug-induced liver injury (DILI)	
Evidence for linking the risk to the medicine	Scientific literature, SmPC, Esbriet EU RMP v12.1
Risk factors and risk groups	Subgroup analyses of specific liver-related laboratory outcomes in the pooled safety analyses, in relation to the effects of sex, age and baseline IPF severity was not possible as there were too few patients in these subgroups to draw meaningful conclusions. Risk groups or risk factors are dependent on the nature of the liver disorder although non-specific factors for all forms of hepatic dysfunction such as alcohol abuse are well recognized (Esbriet EU RMP, 2023).
Risk minimisation measures	Routine risk minimisation measures SmPC section 4.2, 4.3, 4.4, 4.8 and 5.2. PL section 2, 3 and 4. Legal status: Prescription only medicine. The treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of IPF. Additional risk minimisation measures Safety checklist

Additional pharmacovigilance activities	None
Important identified risk: Photosensitivity reaction and rash	
Evidence for linking the risk to the medicine	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. Incidence in patients has been derived from clinical studies in the E.U. and U.S. (Esbriet EU RMP, 2023).
Risk factors and risk groups	No specific groups or factors indicating increased risk of photosensitivity reaction or rash have been identified for either patients with IPF or those treated with pirfenidone. In the general population, risk factors for photosensitivity reactions include prolonged exposure to the sun and UV rays; diseases such as dermatomyositis and lupus erythematosus; and certain drugs and drug classes (e.g., antibiotics [quinolones, tetracyclines, sulfonamides]), NSAIDs, diuretics, chemotherapeutics agents and retinoids (Esbriet EU RMP, 2023).
Risk minimisation measures	Routine risk minimisation measures SmPC section 4.2, 4.4 and 4.8. PL section 2, 3 and 4. Legal status: Prescription only medicine. The treatment should be initiated and supervised by specialist physicians experienced in the diagnosis and treatment of IPF. Additional risk minimisation measures Safety checklist
Additional pharmacovigilance activities	None

II.C Post-Authorisation Development Plan

II.C.1 Studies Which Are Conditions of the Marketing Authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Pirfenidone.

II.C.2 Other Studies in Post-Authorisation Development Plan

There are no studies required for Pirfenidone.