

**IMPORTANT  
DRUG  
WARNING**

August 2019

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**Subject: Updated Safety Information with Use of ESBRIET® (Pirfenidone):**

- **Elevated liver enzymes and Drug-induced liver injury**
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Dear Health Care Provider:

The purpose of this letter is to inform you of important safety information for Esbriet® (pirfenidone, 5-methyl-1-phenyl-2-1[H]-pyridone), indicated for the treatment of Idiopathic Pulmonary Fibrosis (IPF).

**Updated Safety Information with Use of Esbriet®**

Based on the FDA's review of reports in the FDA Adverse Event Reporting System (FAERs) database and the literature on drug-induced liver injury associated with the use of pirfenidone, section 5.1 of the United States Prescribing Information (USPI) is now revised and contains the following:

- Cases of drug-induced liver injury (DILI) have been observed with Esbriet®. In the postmarketing period, non-serious and serious cases of DILI, including severe liver injury with fatal outcome, have been reported.

Genentech, a Member of the Roche Group considers that the benefit-risk profile of Esbriet® in the approved indication remains favorable based on the cumulative analysis of available global clinical and post-marketing safety data. The company will continue to monitor this risk with enhanced pharmacovigilance measures and will provide updates in the Periodic Safety Update Reports and Periodic Benefit Risk Evaluation Reports.

**Prescriber Action**

- Measure liver function tests promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice.
- The following recommendation remains unchanged in the updated USPI; refer to

the guidance in the enclosed full prescribing information.

- Patients should be informed about the need for periodic monitoring. Liver function tests (ALT, AST, and bilirubin) should be performed prior to the initiation of therapy with Esbriet® in all patients, then monthly for the first 6 months and every 3 months thereafter, and as clinically indicated.
- Esbriet should be used with caution in patients with mild (Child Pugh Class A) to moderate (Child Pugh Class B) hepatic impairment. Esbriet® is not recommended for use in patients with severe (Child Pugh Class C) hepatic impairment.
- Recommended dosage modifications, interruption, or discontinuation of Esbriet® due to liver enzyme elevations remain unchanged.

### **Reporting Adverse Events**

Health Care Providers should report any adverse events suspected to be associated with the use of Esbriet® to Genentech at 1-888-835-2555.

Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088) or online ([www.fda.gov/medwatch](http://www.fda.gov/medwatch)).

### **Company Contact Point**

Should you have any questions about the information in this letter or the safe and effective use of Esbriet®, please feel free to contact us at: Genentech Medical Information/Communications Department at (800) 821-8590.

This letter is not intended as a complete description of the benefits and risks related to the use of Esbriet®. Please refer to the enclosed [full prescribing information](#).

Sincerely,

A handwritten signature in blue ink that reads "Susan Begelman M.D.".

Susan Begelman, M.D.  
Vice President and Interim Head of U.S Medical Affairs