Clinical Policy Title:	pirfenidone
Policy Number:	RxA.378
Drug(s) Applied:	Esbriet®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2021
Line of Business Policy Applies to:	All lines of Business

Background

Pirfenidone (Esbriet®) is a pyridone. It is indicated for the treatment of idiopathic pulmonary fibrosis (IPF).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pirfenidone (Esbriet®)	IPF	Days 1 through 7: 267 mg orally three times daily with meal Days 8 through 14: 534 mg orally three times daily with meal Days 15 onward: 801 mg orally three times daily with meal	Days 1 through 7: 801 mg/day Days 8 through 14: 1602 mg/day Days 15 onward: 2403 mg/day

Dosage Forms

- Capsules: 267 mg
- Tablets: 267 mg, 801 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Idiopathic Pulmonary Fibrosis (must meet all)**:**

1. Diagnosis of IPF;
2. Prescribed by or in consultation with a pulmonologist;
3. Age ≥ 18 years;
4. Dose does not exceed:
   a. Days 1 through 7: 801 mg (3 capsules or 1 tablet) per day;
   b. Days 8 through 14: 1602 mg (6 capsules or 2 tablets) per day;
   c. Day 15 and onward: 2403 mg (9 capsules or 3 tablets) per day.

Approval duration

Commercial: 6 months

Medicaid: 6 months

II. Continued Therapy Approval

A. Idiopathic Pulmonary Fibrosis (must meet all)**:**

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed 2403 mg per day.

Approval duration

Commercial: 12 months

Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
IPF: Idiopathic Pulmonary Fibrosis
ULN: Upper Limit of Normal
ALT: Alanine Aminotransferase
AST: Aspartate Transaminase

APPENDIX B: Therapeutic Alternatives

- Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed warning(s):
  - None reported.

APPENDIX D: General Information

- Elevated liver enzymes and drug-induced liver injury has been observed with Esbriet®. ALT, AST, and bilirubin elevations have occurred with Esbriet® including cases of drug induced liver injury. In the post marketing period, non-serious and serious cases of drug-induced liver injury, including severe liver injury with fatal outcome, have been reported. Patients treated with Esbriet® had a higher incidence of ALT and/or AST elevations of ≥3x ULN (3.7%) compared with placebo patients (0.8%). Increases in ALT and AST ≥3x ULN were reversible with dose modification or treatment discontinuation.
- Conduct liver function tests (ALT, AST, and bilirubin) prior to the initiation of therapy with Esbriet®, monthly for the first 6 months, every 3 months thereafter, and as clinically indicated. Measure liver function promptly in patients who report symptoms that may indicate liver injury, including fatigue, anorexia, right upper abdominal discomfort, dark urine, or jaundice. Dosage modification or interruption may be necessary for liver enzyme elevations.
- Esbriet® is not recommended for use in patients with end stage renal disease.
- Photosensitivity and rash: Photosensitivity and rash have been noted with Esbriet®. Avoid exposure to sunlight and sunlamps. Wear sunscreen and protective clothing daily. Temporary dosage reductions or discontinuations may be required.

- Moderate (e.g., ciprofloxacin) and strong inhibitors of CYP1A2 (e.g., fluvoxamine) increase systemic exposure of Esbriet® and may alter the adverse reaction profile of Esbriet®. Discontinue fluvoxamine prior to administration or reduce to 267 mg three times a day. Consider dosage reduction with use of ciprofloxacin.

References

1. Esbriet® Prescribing Information. South San Francisco, CA: Genentech USA, Inc.; July 2019. Available at: www.esbriet.com. Accessed May 31, 2021.
2. Raghu G, Rochwerg B, Yuang Z, et al. An official ATS/ERS/JRS/ALAT clinical practice guideline: treatment of idiopathic pulmonary fibrosis, an update of the 2011 clinical practice guideline. Am J Respir Crit Care Med. 2015; 192(2): e3-e19.
3. Raghu G, Collard HR, Egan JJ, et al. An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. Am J Respir Crit Care Med. 2011; 183: 788-824.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
1. Policy title table was updated. 2. Line of Business Policy Applies to was update to all lines of business. 3. Dosing information: Dosing Regime updated to include “with meal”. Approval duration was updated to specify Medicaid and Commercial. 4. Continued Therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance..." 5. Added APPENDIX D: General Information. 6. References were updated.	7/22/2020	09/14/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. Appendix A was updated to include abbreviations ALT and AST. 4. Appendix D was updated to include “ Esbriet® is not recommended for...” 5. Appendix D was updated to include “Photosensitivity and rash: Photosensitivity and rash have been…” 6. Appendix D was updated to include “Moderate (e.g., ciprofloxacin) and strong inhibitors of CYP1A2...” 7. References were reviewed and updated.	5/31/2021	09/14/2021