

Managing Antifibrotic Therapy in Patients With Idiopathic Pulmonary Fibrosis (IPF)

Educating patients on potential adverse events of antifibrotic agents empowers them with strategies to minimize these side effects to help improve tolerability and adherence. Encourage patients to report any bothersome side effects so appropriate interventions can be made in a timely manner. Importantly, reassure your patients that side effects of antifibrotic therapy generally subside over time.

Antifibrotic Agents Approved for IPF

Drug	Nintedanib	Pirfenidone
Formulations	100 mg, 150 mg capsules	267 mg, 801 mg capsules
Dosing	150 mg twice daily	Days 1-7: 267 mg 3 times daily Days 8-14: 534 mg 3 times daily Days 15+: 801 mg 3 times daily
Significant Adverse Events	Most common: Diarrhea Others include: <ul style="list-style-type: none"> Nausea/vomiting Abdominal pain Fatigue Skin ulcer/rash Weight loss Decreased appetite Headache Bleeding Risk Potential embryo-fetal toxicity Elevated liver enzymes, hepatotoxicity 	Most common: Nausea, photosensitivity/rash, diarrhea Others include: <ul style="list-style-type: none"> Dyspepsia Abdominal pain Fatigue Dizziness Headache Weight loss Decreased appetite Arthralgia Elevated liver enzymes, hepatotoxicity
Liver Function Monitoring	Prior to initiation of treatment, monthly during the first 3 months of treatment, and periodically thereafter or as clinically indicated <ul style="list-style-type: none"> If AST or ALT >3 to ≤5 times ULN with no signs of liver damage, consider dose reduction (100 mg twice daily) or temporary treatment interruption If AST or ALT >5 times ULN or >3 times ULN with signs or symptoms of liver damage, discontinue therapy 	Prior to initiation of treatment, monthly during the first 6 months, then every 3 months thereafter, and as clinically indicated <ul style="list-style-type: none"> If AST or ALT >3 to ≤5 times ULN without hyperbilirubinemia, consider no change, dose reduction, or temporary treatment interruption If AST or ALT >3 to ≤5 times ULN with hyperbilirubinemia or AST or ALT >5 times ULN regardless of bilirubin levels, discontinue therapy
Potential Drug-Drug Interactions	<ul style="list-style-type: none"> Monitor for increased risk of bleeding with concomitant anticoagulant/antiplatelet use Monitor for tolerability of nintedanib with moderate to strong P-glycoprotein or CYP3A4 inhibitors (eg, ketoconazole, erythromycin). Dose reduction or therapy interruption may be required Avoid with moderate to strong P-glycoprotein or CYP3A4 inducers (carbamazepine, phenytoin, St John's wort) due to risk of decreased nintedanib efficacy 	<ul style="list-style-type: none"> Avoid with moderate to strong CYP1A2 inhibitors (eg, ciprofloxacin, fluvoxamine), if possible, due to risk of increased pirfenidone exposure. Discontinue fluvoxamine prior to pirfenidone initiation. If fluvoxamine is required, pirfenidone dose reduction to 267 mg 3 times daily is recommended. If ciprofloxacin is required, pirfenidone dose reduction to 534 mg 3 times daily is recommended when ciprofloxacin doses 750 mg/day or higher Avoid smoking due to risk of decreased pirfenidone efficacy

ALT = alanine aminotransferase; AST = aspartate aminotransferase; ULN = upper limit of normal.

Interventions for Specific Adverse Events Related to Antifibrotic Therapy

Adverse Event	Interventions
Diarrhea	<ul style="list-style-type: none"> Antidiarrheal agent Take with high protein foods Small, frequent meals Adequate hydration Dose reduction or temporary treatment interruption
Nausea/Vomiting	<ul style="list-style-type: none"> Antiemetics Take with high protein foods Small, frequent meals Adequate hydration Dose reduction or temporary treatment interruption
Dyspepsia	<ul style="list-style-type: none"> Antacids Small, frequent meals Dose reduction or temporary treatment interruption
Photosensitivity/Rash	<ul style="list-style-type: none"> Sun-protective clothing, sunscreen (SPF ≥50) Minimize sun exposure Dose reduction or temporary treatment interruption
Crippling fatigue	<ul style="list-style-type: none"> Dose reduction or temporary treatment interruption

References:

- Lederer DJ, Martinez FJ. Idiopathic pulmonary fibrosis. *N Engl J Med*. 2018;378:1811-1123.
Nintedanib [prescribing information]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2020.
Pirfenidone [prescribing information]. South San Francisco, CA: Genentech; 2016.
Shaw J, Marshall T, Morris H, et al. Idiopathic pulmonary fibrosis: a holistic approach to disease management in the antifibrotic age. *J Thorac Dis*. 2017;11:4700-4707.