Medications for Idiopathic Pulmonary Fibrosis

IPF Part 2

Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease that gets worse over time. Scarring of the walls of the alveolar sacs (interstitium) causes the lungs to stiffen and reduces the ability of the lungs to absorb oxygen. This leads to shortness of breath that occurs with less and less exercise. While there is no cure for IPF, there are medications that can help with symptoms and slow progression of the disease. Treatment of IPF is important because lung function and symptoms of people with IPF typically worsen over time. There are different kinds of treatments available for people suffering from IPF. This fact sheet discusses medications that are used to help treat IPF. For more information about IPF and other ways to manage and live with it in addition to medication, see parts 1 and 3 at www.thoracic.org/patients.

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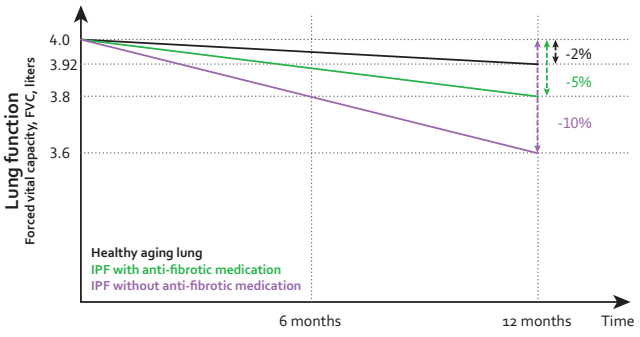
What anti-fibrotic drugs are available for the long-term treatment of IPF?

Pirfenidone and nintedanib are two anti-fibrotic drugs that are used for the long-term treatment of IPF. Anti-fibrotic means that the drugs block scarring. Scar formation in the lungs is complex and involves many different types of cells. By decreasing the formation of scar tissue in IPF, pirfenidone and nintedanib slow the decline in lung function. These are both approved for use in many countries, including the US.

What benefit can I expect from anti-fibrotic drugs?

Both anti-fibrotic drugs slow down the worsening of IPF, but neither are able to cure the disease or reverse existing fibrosis. A healthy person loses around 35 milliliters (ml) of lung function volume per year with increasing age. Those affected by IPF who are not treated with an anti-fibrotic drug lose, on average, around 200-400 milliliters (ml) of their vital capacity (lung function) per year. This is a loss of up to 10% of the total lung function volume each year. People who are treated with an anti-fibrotic drug lose, on average, around 100-200 ml of their vital capacity per year, or about half of the loss that is seen in people not taking an antifibrotic drug. This slowing of lung function decline in people treated with pirfenidone or nintedanib has been confirmed in several large clinical research studies that include more than 2800 people with IPF. However, it is important to note that not everyone with IPF experiences benefit from these medications and that both medications can have associated side effects. (Figure 1)

Figure 1. *Decline in lung function in healthy adults (black, nonsmokers), in patients with IPF treated with antifibrotic medication (green), and in patients with IPF not treated with anti-fibrotic medication (purple).*



Anti-fibrotic therapy might reduce shortness of breath over time, and some people may have a decrease in cough severity, but these benefits have not been seen consistently in all people taking part in the research studies. Some, but not all, studies have suggested that people treated with anti-fibrotic medications may need to be admitted to the hospital less often. Further, people on these medications may live longer than without these medications. Taking both drugs together is not yet well studied; it is unknown if there would be additional benefit or harm to this approach.

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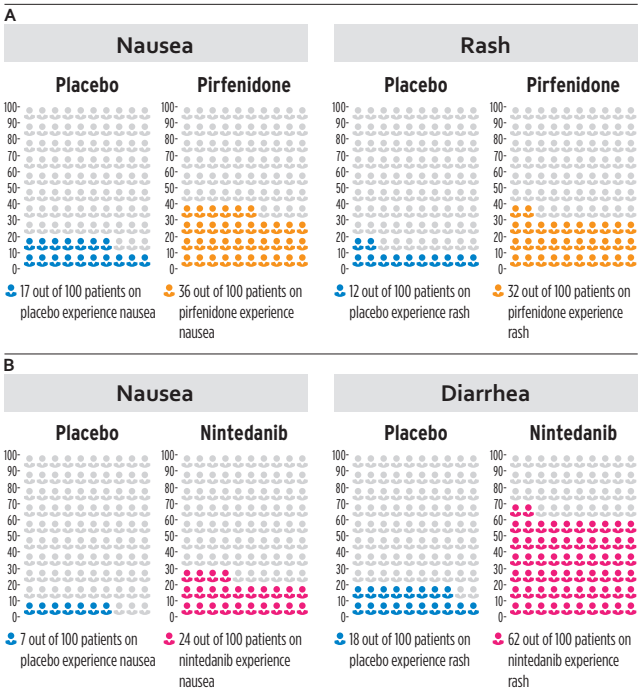
How do I take pirfenidone (brand name Esbriet®) and what side effects can occur?

People with IPF who are prescribed pirfenidone will typically take tablets or capsules three times daily with food. You will usually be started on one 267 mg tablet or capsule taken three times per day, and will be instructed to gradually increase the dose to 801 mg three times per day. During this period, your lung specialist will ask you about side effects that might occur and check for abnormal liver blood tests. Blood tests are usually performed less often after the first few months in those who are tolerating a stable dose without significant side effects. Side effects of pirfenidone that occur in more than 10% of people include nausea, acid reflux (heartburn), vomiting, decreased appetite, weight loss, headache, dizziness, fatigue, and skin problems such as a "photosensitivity" rash that develops in reaction to sun exposure (Figure 2). Overall, side effects from pirfenidone occur frequently, but usually these can be controlled sufficiently so that most patients can continue treatment (Figure 3). Talk to your healthcare provider about possible side effects and concerns you may have about your medication.

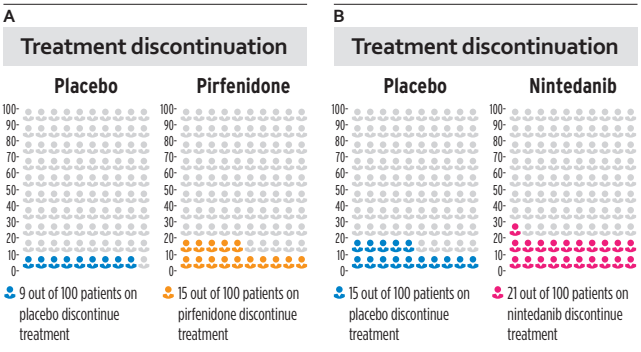
Figure 2. *Most common side effects from pirfenidone (A) and nintedanib (B).*



How do I take nintedanib (brand name Ofev®) and what side effects can occur?

People with IPF who are prescribed nintedanib will typically take one 150 mg tablet twice daily with food. The dose can be reduced to 100 mg tablets if side effects occur. The most common side effect of nintedanib is diarrhea, which occurs in about two thirds of patients. Additional side effects can include decreased appetite, weight loss, nausea, vomiting, abdominal pain, and abnormal liver blood tests (Figure 2). Your doctor will monitor your liver using simple blood tests that need to be repeated more frequently in the first few months of treatment and typically monthly thereafter. Overall, side effects from nintedanib occur often, but usually these can be controlled well enough that most can continue treatment (Figure 3). Talk to your IPF healthcare team about possible side effects and concerns you may have about your medication.

Figure 3. *Number of patients that discontinue treatment due to side effects from pirfenidone (A) or nintedanib (B) in clinical trials.*



How can I manage common side effects of pirfenidone and nintedanib?

Nausea, diarrhea, or loss of appetite occur in up to 50% of people with IPF taking anti-fibrotic drugs. Therefore, management of these side effects with medications or a dietary change is often needed. Your IPF healthcare team or a dietician can provide advice about how to manage these symptoms. This is particularly important for any weight loss, either as a consequence of your disease or from side effects of the anti-fibrotic medication. For patients taking pirfenidone, it is essential to wear sun-protective clothing (e.g., long sleeves, wide-brimmed hat) and sunblock to prevent a bad sunburn.

These medicines can interact with other medications or supplements. It is also important to check with your physician or pharmacist before starting any new medications or supplements to make sure these are safe to take along with your anti-fibrotic drug.

How do I know if the anti-fibrotic drug is working?

Despite using these medications, your lung function is still likely to get worse over time, and your shortness of breath will likely increase. The goal of anti-fibrotic treatment is to slow this progression, and preserve your lung function as much as possible. As a result, your

physical performance and quality of life will likely be better in the future.

How long do I have to take the anti-fibrotic drug?

Anti-fibrotic medications can be continued for as long as they are considered effective. The treatment can also be changed from pirfenidone to nintedanib, or vice versa, if severe side effects occur, or if one drug is considered to be ineffective. Decisions about whether to change or discontinue anti-fibrotic medications should be made along with your lung specialist and healthcare team.

What happens if I don't want to be treated with an anti-fibrotic drug?

You might decide not to take any medications for IPF. This may be because you suffer from other severe diseases, or you have concerns about possible side effects or have had significant side effects that appear to outweigh potential benefit from the drugs. Sometimes your lung specialist will advise you not to use anti-fibrotic treatment. Regardless of whether you take an anti-fibrotic medication or not, it is important to remember that there are other strategies that can help manage your disease. Other ways to help manage IPF are covered in Part 3 found at www.thoracic.org/patients.

Which drugs should I not take for the treatment of IPF?

Currently, only pirfenidone and nintedanib are approved for the long-term treatment of IPF. Although you can find suggestions for a variety of other treatments on the Internet, these lack proven benefit and are not recommended at this time. We advise that you discuss your questions related to such alternative treatments with your lung specialist.

What drugs are used to treat acute exacerbations of IPF?

Different medications are sometimes used for a short period of time if patients experience a sudden worsening of their symptoms. This situation can occur with a variety of predisposing factors, with a resulting increase in the amount of inflammation in the lungs. These short-term medications most often include antibiotics against lung infections and corticosteroids for the treatment of inflammation.

Are there medications that relieve the symptoms of IPF?

Medications that can relieve symptoms include opiate medications such as morphine to treat severe shortness of breath, cough suppressants, and medications against anxiety. Although these can help reduce symptoms, these do not affect the underlying fibrosis itself.

Will there be new drugs available soon?

For many decades, studies of potential medications for IPF showed no benefit, and some of these treatments were even found to be harmful. Pirfenidone and nintedanib are the first and only drugs to date that have been shown to reliably slow the progression of lung fibrosis. There is no medication to cure IPF, but research is ongoing to find more effective and better tolerated treatments. It is therefore still important that we continue to research new ways for the treatment of IPF. Taking part in and supporting clinical trials might help you or other people affected by IPF in the future. You can find ongoing clinical trials listed on the Pulmonary Fibrosis Foundation and the clinicaltrials.gov webpages below. Please talk to your lung specialist to get more information on new clinical trials that are testing potential treatments of IPF.

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Rx *Action Steps*

- ✔ If you have been diagnosed with IPF ask your lung specialist about antifibrotic drugs.
- ✔ Do not take any medicines for IPF without discussing them with your lung specialist.
- ✔ Take medicines regularly as prescribed and talk to your IPF healthcare team about any concerns you have about the medicines including side effects.
- ✔ Talk about other non-drug therapies you can do for IPF.

Healthcare Provider's Contact Number:

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For More Information

American Thoracic Society

- www.thoracic.org/patients/
  - Flexible bronchoscopy
  - Oxygen therapy
  - Part 1: What is Idiopathic Pulmonary Fibrosis?
  - Part 3: Nondrug Treatments for Idiopathic Pulmonary Fibrosis
- https://trials.pulmonaryfibrosis.org/
- http://clinicaltrials.gov/

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