New Drug Overview

Jascayd (nerandomilast)

PDL Category: Idiopathic Pulmonary Fibrosis

Introduction

Disease Background:

- Idiopathic pulmonary fibrosis (IPF) is a distinct kind of idiopathic interstitial pneumonia, a category of conditions that cause interstitial lung disease (ILD). IPF is classified as a chronic fibrosing interstitial pneumonia, that is a progressing disease limited to the lung and results from an abnormal wound healing activity causing a deposition of changed extracellular matrix as well as scarring and disturbance of alveolar design (*Richeldi et al 2025*).
  - It is a serious long-term disease where the tissue around the air sacs in the lungs are affected. Tissue in the lung becomes thick and stiff, which can result in persistent scarring in the lungs (fibrosis). Fibrosis, or this permanent scarring, results in having a harder time in breathing (*NIH 2023*).
- IPF generally affects adults 55 to 75 years of age, and affects men more than women. Risk factors for IPF include cigarette smoking, older age, being male, family history, exposure to certain environments (such as livestock or pine wood dust), or exposure to certain viral proteins and antibodies to viruses, among others (*Richeldi et al 2025).*
- Typically non-specific symptoms of the pulmonary system are observed, including chronic dry cough and dyspnea. Fatigue may also occur (*Richeldi et al 2025).*
  - The progression of IPF varies for each patient, with scarring that may happen quickly in some or slowly in others. The disease may stay stable for long periods of time in some or gets worse quickly in others (*NIH 2023*).
  - Acute exacerbations are seen in 5-20% of patients. Acute exacerbations are characterized as worsening of clinical symptoms, as well as objective findings that may include fever or worsening of oxygenation and radiographic discoveries. During the period of the disease, acute exacerbations can occur at any time. (*Richeldi et al 2025).*
- There is currently no cure for IPF; however, supportive care strategies such as smoking cessation, pulmonary rehabilitation, and vaccination for respiratory infections are suggested (*King 2026*, *NIH 2023).* Two antifibrotic medications FDA-approved in 2014 are available and appear to be associated with slowing progression of the disease and reducing acute exacerbation frequency. There may also be a mortality benefit (*King 2026*).

- Progressive pulmonary fibrosis (PPF) is a specific type of progressive and fibrotic disease that occurs in cases of ILD other than in IPF that is described per clinical symptoms, lung function, and imaging of the chest irrespective of the underlying disorder (*Kang and Song 2023*).
  - It is an ILD that results in signs of fibrosis with confirmation of progression over time.
    - It is estimated that about 13% to 40% of non-IPF fibrosing ILDs progress within 2 years, even with appropriate management of the disease.

- Jascayd was FDA approved in 2025.

Pharmacology/Usage

- Jascayd (nerandomilast) is a phosphodiesterase 4 (PDE4) inhibitor, with at least nine-fold preferential inhibition of the PDE4B isoenzyme over PDE4A, PDE4C, and PDE4D. PDE4 hydrolyzes and inactivates cyclic adenosine monophosphate (cAMP). Nerandomilast exerts both anti-fibrotic and immunomodulatory effects as PDE4B inhibition elevates intracellular cAMP levels and reduces the expression of pro-fibrotic growth factors and inflammatory cytokines, which are overexpressed in idiopathic pulmonary fibrosis and progressive pulmonary fibrosis.

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Jascayd (nerandomilast)
• For the treatment of idiopathic pulmonary fibrosis (IPF) in adult patients. • For the treatment of progressive pulmonary fibrosis (PPF) in adult patients.	✔

(Prescribing information: Jascayd 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Jascayd (nerandomilast)	Film-Coated Tablets	Oral	BID, approximately 12 hours apart, with or without food.	• Do not reduce dosage when used concomitantly with pirfenidone • Reduce dosage to 9mg BID for patients who are unable to tolerate the 18mg BID dose, except in patients who concomitantly use with pirfenidone. • Swallow tablets whole or disperse in water. • If a dose is missed, advise the patient to take the next dose at the next scheduled time. Do not make up for a missed dose. • Jascayd use is not recommended in patients with end stage renal disease or severe hepatic impairment.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The efficacy of Jascayd for IPF was assessed in two randomized, double-blind, placebo-controlled trials (FIBRONEER-IPF and Trial 2).

- FIBRONEER-IPF included adult patients with IPF (N=1,177) with or without background antifibrotic treatments (nintedanib or pirfenidone).
  - They were randomized to receive Jascayd (9mg BID or 18mg BID) or placebo until the last patient received treatment for 52 weeks (blinded trial duration up to 91 weeks; end of trial duration up to 109 weeks). Randomization was stratified by the presence or absence of background antifibrotic treatments (nintedanib or pirfenidone) at baseline
  - This trial included patients with a mean age of 70 years (range 42 to 90 years) who were mostly males (83%) and White (68%).
  - At baseline, the mean forced vital capacity (FVC) was 78% of predicted normal. In addition, 78% were on stable antifibrotic treatment (nintedanib 46%, pirfenidone 32%) and 22% were not on either treatment (15% treatment naïve, 7% previously discontinued treatment).
- Trial 2 was a 12-week trial that enrolled adult patients (N=147) with IPF with or without background antifibrotic treatments (nintedanib or pirfenidone).
  - They were randomized to receive Jascayd 18mg BID or placebo for 12 weeks. Randomization was stratified by the presence or absence of background antifibrotic treatments (nintedanib or pirfenidone) at baseline
  - This trial included patients with a mean age of 70 years (range 40 to 85 years) who were mostly male (77%) and White (78%).
  - At baseline, the mean FVC was 78% of predicted normal. In addition, 50% of the patients were on stable antifibrotic treatment (nintedanib 29%, pirfenidone 21%).

- In both studies, patients were required to have a diagnosis of IPF based on ATS/ERS/JRS/ALAT criteria. The diagnosis was confirmed by the investigator based on chest high-resolution computed tomography (HRCT) scan and, if available, lung biopsy, and usual interstitial pneumonia (UIP) or probable UIP HRCT pattern consistent with the clinical diagnosis of IPF.
  - Patients were also required to be greater than or equal to 40 years of age with an FVC ≥45% of predicted and a carbon monoxide diffusing capacity (DLCO, corrected for hemoglobin) ≥25% of predicted.
  - Prior to visit 1 and during screening, patients had to be on stable treatment with nintedanib or pirfenidone (no dose changes for at least 12 weeks) and planned to stay on this background antifibrotic treatment after randomization. Alternatively, patients were required to be naïve to or have previously discontinued nintedanib or pirfenidone for at least 8 weeks and did not plan to start or restart background antifibrotic treatment.
- The primary endpoint in FIBRONEER-IPF was the absolute change from baseline in FVC in milliliters (mL) at 52 weeks.
  - In this study population, there was less decline in absolute change from baseline in FVC in patients who received Jascayd as compared with patients who received placebo (accounting for mortality), and this reduction in decline was statistically significant.
    - The adjusted mean decline in patients receiving Jascayd 18mg or Jascayd 9mgs was -106ml and -122ml, respectively, whereas in the placebo group, an adjusted mean decline of -170ml was observed. The respective treatment differences compared with the placebo group were 64ml and 48ml.
    - In this trial, the results of the primary endpoint across subgroups by background antifibrotic treatment (nintedanib, pirfenidone, or none) for Jascayd 18mg vs placebo were consistent with the overall population. Efficacy was not observed in patients who received Jascayd 9mg BID with pirfenidone as background antifibrotic treatment.
- In Trial 2, patients taking Jascayd 18mg BID compared to placebo, with or without background antifibrotic treatments, had a reduction in FVC decline at week 12 of 91ml.
- The key secondary endpoint in the FIBRONEER-IPF trial was time to first occurrence of any of the components of the composite endpoint over the blinded duration of the trial (up to 91 weeks): acute IPF exacerbation, hospitalization for respiratory cause, or death.
  - Acute IPF exacerbation was defined as acute worsening or development of dyspnea typically less than one month duration, computed tomography with new bilateral ground-glass opacity, and/or consolidation superimposed on a

background pattern consistent with IPF, and deterioration not fully explained by cardiac failure or fluid overload. Neither acute IPF exacerbations nor respiratory hospitalizations were adjudicated.
    - Overall, there was no statistically significant treatment difference in hazard ratio (HR) for the Jascayd 18mg or 9mg groups compared to placebo for the key secondary composite endpoint (Jascayd 18mg and 9mg respectively: HR 1.17 and HR 1.03).
    - An event occurred in 21.7% of the Jascayd 18mg group, 20.2% in the Jascayd 9mg group, and 20.4% in the placebo group (*Richeldi et al 2025a*)
- Survival was assessed.
    - In the FIBRONEER-IPF study population, the HR for all-cause mortality, assessed until the end of trial (up to 109 weeks), did not demonstrate a significant treatment difference for Jascayd 18mg or 9mg compared to placebo (HR 0.66 and HR 0.95, respectively).

- The efficacy of Jascayd for PPF was assessed in a randomized, double-blind, placebo-controlled trial (FIBRONEER-ILD).
    - This study enrolled adult patients (N=1,178) with PPF with or without background treatment with nintedanib who were randomized to Jascayd 9mg BID, Jascayd 18mg BID, or placebo until the last patient received treatment for 52 weeks (blinded trial duration up to 109 weeks; end of trial duration up to 114 weeks). Randomization was stratified by the presence or absence of nintedanib therapy and by HRCT pattern using central review.
    - Enrolled patients had a mean age of 66 years (range 26 to 88), while 56% were male and 58% were White. At baseline, the mean FVC was 70% of predicted normal, 44% were on stable treatment with nintedanib, and 56% of patients were not treated with nintedanib (44% were treatment naïve and 12% previously discontinued nintedanib treatment).
    - On baseline HRCT, 71% of patients had UIP or UIP-like fibrotic pattern and 29% of patients had other fibrotic patterns. The underlying clinical IDL diagnoses were autoimmune ILDs (28%), hypersensitivity pneumonitis (20%), unclassifiable idiopathic interstitial pneumonia (20%), idiopathic nonspecific interstitial pneumonia (19%), and other ILDs (14%).
    - Patients with PPF were enrolled if they had relevant fibrosis (greater than 10% fibrotic features) on HRCT and presented with clinical signs of progression. Patients were required to be ≥18 years of age and to have an FVC ≥45% of predicted and a DLCO ≥25% of predicted. Prior to visit 1 and during screening, patients had to be on stable therapy with nintedanib and planned to stay on this background PPF therapy after randomization. Alternatively, patients were required to be naïve to or have previously discontinued nintedanib for at least 8 weeks and did not plan to start or restart background PPF treatment.
    - The primary endpoint in this study was the absolute change from baseline in FVC in mL at 52 weeks.
        - In this study population, there was less decline in absolute change from baseline in FVC in patients who received Jascayd compared with patients who received placebo (accounting for mortality), and this reduction in decline was statistically significant. The adjusted mean decline in patients receiving Jascayd 18mg or Jascayd 9mg was -86mL and -69mL, respectively, whereas in the placebo group, an adjusted mean decline of -152mL was observed. The respective treatment difference compared with the placebo group was 65mL and 83mL. FVC results across relevant subgroups were similar.
    - The key secondary endpoint in this trial was the time to the first occurrence of any of the components of the composite endpoint over the blinded duration of the trial (up to 109 weeks): acute ILD exacerbation, hospitalization for respiratory cause, or death.
        - Acute ILD exacerbation was defined as acute worsening or development of dyspnea typically less than 1 month duration, computed tomography with new bilateral ground-glass opacity and/or consolidation superimposed on a background pattern consistent with fibrosing ILD, and deterioration not fully explained by cardiac failure or fluid overload. Neither acute ILD exacerbations nor respiratory hospitalizations were adjudicated.

- Overall, there was no statistically significant treatment difference in the hazard ratio (HR) for the Jascayd 18mg or 9mg groups compared to placebo for the key secondary composite endpoint (Jascayd 18mg or 9mg groups, respectively, compared to placebo: HR 0.77 and HR 0.88).
- In this study population, the HRs for all-cause mortality, assessed until the end of the trial, for Jascayd 18mg and 9mg compared to placebo were 0.51 and 0.51, respectively. These results were not prespecified for multiplicity control.

Clinical guidelines

- Note that guidelines do not include Jascayd as the guidelines were published prior to Jascayd being FDA approved.
- **Idiopathic Pulmonary Fibrosis (an Update) and Progressive Pulmonary Fibrosis in Adults: An Official American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Association Latino Americana de Torax (ALAT) Clinical Practice Guideline** (*Raghu et al 2022*)**.**
  - Recommendations include not using antacids for respiratory outcome improvements in patients with IPF.
  - Treatment considerations for IPF include nintedanib and pirfenidone, while non-pharmacologic considerations include oxygen supplementation and pulmonary rehabilitation.
  - It is recommended to obtain further data on pirfenidone efficacy and safety for non-IPF interstitial lung disease (ILD) manifesting progressive pulmonary fibrosis (PPF) in general and specific types of non-IPF ILD manifesting PPF, as well as for nintedanib for specific types of non-IPF ILD manifesting PPF.
  - Nintedanib use is suggested for PPF treatment if patients have failed standard management for fibrotic ILD, other than IPF.
- **An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of idiopathic pulmonary fibrosis. An update of the 2011 Clinical Practice Guideline** (*Raghu et al 2015*).
  - It is recommended against using certain treatments for IPF, including anticoagulants, imatinib, ambrisentan, and the combination of prednisone, azathioprine, and N-acetylcysteine.
  - The authors recommend using nintedanib and pirfenidone for treatment of IPF.

Safety summary

- **Contraindications:** None.

- **Box Warning:** None.

- **Warnings and precautions:** None.

- **Common adverse drug reactions:**
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Jascayd 18mg BID) minus reported % incidence for placebo in patients with IPF. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included diarrhea (25%), COVID-19 (1%), upper respiratory tract infection (3%), depression (2%), weight decreased (3%), decreased appetite (4%), nausea (1%), fatigue (1%), headache (2%), vomiting (1%), back pain (2%), and dizziness (0%).
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Jascayd 9mg BID) minus reported % incidence for placebo for all grades in patients with IPF. Please note that an incidence of 0% means the incidence was the same as or less than placebo.

- The most frequently reported adverse events included nausea diarrhea (14%), COVID-19 (4%), upper respiratory tract infection (1%), depression (1%), weight decreased (2%), decreased appetite (4%), nausea (2%), fatigue (2%), headache (1%), vomiting (0%), back pain (1%), and dizziness (1%).

- **Drug interactions:**
  - Nerandomilast is a CYP3A substrate.
    - Reduce the dosage to 9mg BID when used concomitantly with strong CYP3A inhibitors.
    - Avoid the use of Jascayd with strong or moderate CYP3A inducers.
  - Concomitant use of Jascayd with pirfenidone decreases exposure of nerandomilast. When Jascayd was used concomitantly with pirfenidone in patients with IPF in a phase-3 study, efficacy was not observed with the Jascayd 9mg BID dosage.
    - The recommended dosage of Jascayd is 18mg BID when used concomitantly with pirfenidone. Do not reduce the dosage to 9mg BID.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use in pregnant women to assess for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are maternal and fetal risks associated with untreated IPF and PPF during pregnancy. Based on findings from animal studies, Jascayd may increase the risk for fetal loss. Advise pregnant women and females of reproductive potential of the potential risk of fetal loss.
  - The safety and efficacy of use have not been established in the pediatric population.

Conclusion

- Idiopathic pulmonary fibrosis (IPF) is a distinct kind of idiopathic interstitial pneumonia, a category of conditions that cause interstitial lung disease (ILD). IPF is classified as a chronic fibrosing interstitial pneumonia, that is a progressing disease limited to the lung and results from an abnormal wound healing activity causing a deposition of changed extracellular matrix as well as scarring and disturbance of alveolar design (*Richeldi et al 2025*).
- Progressive pulmonary fibrosis (PPF) is a specific type of progressive and fibrotic disease that occurs in cases of ILD other than in IPF that is described per clinical symptoms, lung function, and imaging of the chest irrespective of the underlying disorder (*Kang and Song 2023*).
- Jascayd is a PDE4 inhibitor indicated for:
  - The treatment of IPF in adult patients.
  - The treatment of PPF in adult patients.
- The efficacy of Jascayd for IPF was assessed in two randomized, double-blind, placebo-controlled trials.
  - FIBRONEER-IPF included adult patients (N=1,177) with IPF with or without background antifibrotic treatments (nintedanib or pirfenidone) who were randomized to receive Jascayd 9mg or 18mg, or placebo.
    - The primary endpoint was the absolute change from baseline in FVC at 52 weeks.
      - Results suggested that there was less decline in absolute change from baseline in FVC in the Jascayd group compared to placebo, and this reduction in decline was statistically significant.
      - Note that efficacy was not observed in patients who received Jascayd 9mg BID with pirfenidone as background antifibrotic treatment. Thus, the recommended dosage of Jascayd is 18mg BID when used concomitantly with pirfenidone.
    - The main secondary endpoint was time to first occurrence of any of the components of the composite endpoint over the blinded duration of the trial: acute IPF exacerbation, hospitalization for respiratory cause, or death.

        - Overall, there was no statistically significant treatment difference in HR for the Jascayd 18mg or 9mg groups compared to placebo for this endpoint (HR 1.17 and HR 1.03, respectively).
        - The HR for all-cause mortality, a secondary endpoint, did not demonstrate a significant treatment difference for Jascayd 18mg or 9mg as compared with placebo.
    - Trial 2 was a 12-week trial that included adults (N=147) with IPF with or without background antifibrotic treatments who were randomized to Jascayd 18mg or placebo.
        - Patients in the Jascayd 18mg group compared to placebo, with or without background antifibrotic treatments, had a reduction in FVC decline at week 12 of 91mL.
- The efficacy of Jascayd for PPF was assessed in one randomized, double-blind, placebo-controlled trial.
    - The study enrolled adults with PPF with or without background treatment with nintedanib, and the primary endpoint was the absolute change from baseline in FVC in mL at 52 weeks.
        - Results suggested that there was less decline in absolute change from baseline in FVC in patients receiving Jascayd compared with placebo, and this reduction in decline was statistically significant.
- Guidelines do not currently include Jascayd (nerandomilast) but do recommend pirfenidone or nintedanib.
- Jascayd offers providers another treatment option, and use has been studied with and without background antifibrotic treatments (nintedanib or pirfenidone). Comparator treatments with Jascayd include Ofev (nintedanib) and Esbriet (pirfenidone).

- There is no evidence to suggest that Jascayd is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Jascayd remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

- **PDL Placement:**
    - ☐ Preferred
    - ☒ Non-Preferred with Conditions

References

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Publication Date: February 2026.