

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

218764Orig1s000

LABELING

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use JASCAYD safely and effectively. See full prescribing information for JASCAYD.

JASCAYD® (nerandomilast tablets), for oral use

Initial U.S. Approval: 2025

INDICATIONS AND USAGE

JASCAYD is a phosphodiesterase 4 (PDE4) inhibitor indicated for the treatment of idiopathic pulmonary fibrosis in adult patients. (1)

DOSAGE AND ADMINISTRATION

- **Recommended Dosage:** 18 mg orally twice daily approximately 12 hours apart with or without food. (2.1)
- Reduce JASCAYD to 9 mg twice daily for patients who are unable to tolerate 18 mg twice daily, except in patients taking concomitant pirfenidone. (2.1, 7.1)
- Swallow tablets whole or dispersed in water. (2.1)
- See full prescribing information for administration instructions for patients who have difficulty swallowing tablets. (2.3)

DOSAGE FORMS AND STRENGTHS

Tablets: 9 mg and 18 mg (3)

CONTRAINDICATIONS

None. (4)

ADVERSE REACTIONS

Most common adverse reactions ($\geq 5\%$) are diarrhea, COVID-19, upper respiratory tract infection, depression, weight decreased, decreased appetite, nausea, fatigue, headache, vomiting, back pain, and dizziness. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Boehringer Ingelheim Pharmaceuticals, Inc. at (800) 542-6257 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

Strong CYP3A Inhibitors: Reduce JASCAYD dosage to 9 mg twice daily. (2.2, 7.1)

Moderate or Strong CYP3A Inducers: Avoid concomitant use with JASCAYD. (7.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 10/2025

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

JASCAYD is indicated for the treatment of idiopathic pulmonary fibrosis (IPF) in adult patients.

2 DOSAGE AND ADMINISTRATION

2.1 Recommended Dosage and Administration Instructions

The recommended dosage of JASCAYD is 18 mg twice daily, administered orally approximately 12 hours apart, with or without food.

- Recommended dosage of JASCAYD is 18 mg twice daily when used concomitantly with pirfenidone. Do not reduce dosage to 9 mg twice daily [see *Drug Interactions* (7.1)].
- Reduce JASCAYD to 9 mg twice daily for patients who are unable to tolerate 18 mg twice daily, except in patients who concomitantly use JASCAYD with pirfenidone.

Administration Instructions

Swallow JASCAYD tablets whole or dispersed in water [see *Dosage and Administration* (2.3) and *Clinical Pharmacology* (12.3)].

Missed Dose(s)

If a dose of JASCAYD is missed, advise the patient to take the next dose at the next scheduled time. Advise the patient to not make up for a missed dose.

Maximum Recommended Dosage

The maximum recommended dosage of JASCAYD is 18 mg twice daily.

2.2 Dosage Modification of JASCAYD for Concomitant Use With CYP3A Inhibitors

Strong CYP3A Inhibitors

Reduce JASCAYD dosage to 9 mg twice daily when used concomitantly with strong CYP3A inhibitors [see *Drug Interactions* (7.1)].

Moderate and Weak CYP3A Inhibitors

No dosage modification is recommended for JASCAYD when used concomitantly with moderate or weak CYP3A inhibitors.

2.3 Administration Instructions for Patients Who Have Difficulty Swallowing Tablets

Disperse JASCAYD tablet in water and administer as follows:

- Place approximately 100 mL (3 to 4 ounces) of non-carbonated, room temperature water in a glass. Do not use any other liquids.
- Place a JASCAYD tablet in the water, without crushing, and stir regularly for approximately 15 to 20 minutes until the tablet is dispersed into very small pieces (the tablet will not completely dissolve).
- Drink the dispersion within 2 hours of mixing.
- If the dispersion is not drunk immediately, stir again before drinking.
- Rinse the glass with approximately 100 mL (3 to 4 ounces) of water and drink to ensure the full dose is administered.

3 DOSAGE FORMS AND STRENGTHS

Tablets:

- 9 mg, light yellow, oval, biconvex, film-coated tablets debossed with the Boehringer Ingelheim company symbol on one side and “F9” on the other side.
- 18 mg, light red, oval, biconvex, film-coated tablets debossed with the Boehringer Ingelheim company symbol on one side and “F18” on the other side.

4 CONTRAINDICATIONS

None.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in clinical trials of another drug and may not reflect the rates observed in practice.

The safety of JASCAYD was based on a randomized, placebo-controlled, double-blind trial (FIBRONEER-IPF), which included 1,177 adult patients with IPF who were randomized in a 1:1:1 ratio to receive JASCAYD 9 mg twice daily, JASCAYD 18 mg twice daily, or matching placebo. Patients received JASCAYD or placebo with or without background antifibrotic treatment (nintedanib or pirfenidone) for at least 52 weeks [see *Clinical Studies (14)*]. The median duration of exposure was 14 months in each treatment arm.

Discontinuation due to adverse reactions occurred more frequently in patients treated with JASCAYD (with or without background antifibrotic treatment) 18 mg (15%) and 9 mg (12%) compared to placebo (11%). The most frequent adverse reaction leading to discontinuation of JASCAYD 18 mg and 9 mg was diarrhea (6% and 2%, respectively).

Table 1 lists the most common adverse reactions from the studied population with an incidence of greater than or equal to 5% in JASCAYD-treated patients and more common than the placebo group.

Table 1 Adverse Reactions with JASCAYD with Incidence of $\geq 5\%$ and More Common than Placebo in Patients¹ with IPF (FIBRONEER-IPF Trial)

	JASCAYD 18 mg BID n=392	JASCAYD 9 mg BID n=392	Placebo n=393
Diarrhea	42%	31%	17%
COVID-19	13%	16%	12%
Upper respiratory tract infection	13%	11%	10%
Depression ²	12%	11%	10%
Weight decreased	11%	10%	8%
Decreased appetite	9%	9%	5%
Nausea	8%	9%	7%
Fatigue	7%	8%	6%

Headache	7%	6%	5%
Vomiting	6%	5%	5%
Back pain	6%	5%	4%
Dizziness	5%	6%	5%

¹Studied population including patients who received JASCAYD with or without background antifibrotic treatment (nintedanib or pirfenidone)

²Includes depression, depressed mood, depression rating scale score increased, suicidal ideation, adjustment disorder with depressed mood, depressive symptom

BID: twice daily; COVID-19: infection with SARS-CoV-2 virus

Specific Adverse Reactions of JASCAYD with or without Concomitant Use of Nintedanib or Pirfenidone

Diarrhea

Diarrhea was more common in patients using JASCAYD with concomitant nintedanib. In patients taking nintedanib, diarrhea occurred in 62%, 50%, and 28% of patients treated with JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively. In patients using concomitant pirfenidone, diarrhea occurred in 24% and 8% of patients treated with JASCAYD 18 mg twice daily, and placebo, respectively. In patients without concomitant antifibrotic treatment, diarrhea occurred in 26%, 17%, and 8% of patients using JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively.

Diarrhea was the most common adverse reaction associated with treatment discontinuation, and most common with JASCAYD used concomitantly with nintedanib: discontinuation occurred in 13%, 2%, and 1% of patients treated with JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively. No treatment discontinuations due to diarrhea occurred in patients treated with background pirfenidone and JASCAYD 18 mg twice daily or background pirfenidone with placebo. Diarrhea leading to treatment discontinuation occurred in 1% of patients treated with JASCAYD 18 mg twice daily and in no patients treated with JASCAYD 9 mg or placebo without concomitant antifibrotic treatment.

In most patients treated with JASCAYD, diarrhea was of mild to moderate intensity and generally occurred within the first 3 months of treatment.

Weight Decrease

Weight decrease was most common in patients who received JASCAYD concomitantly with nintedanib in the studied population: in patients taking nintedanib, weight decrease occurred in 16%, 14%, and 12% of patients treated with JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively. In patients using concomitant pirfenidone, weight decrease occurred in 6% and 5% of patients treated with JASCAYD 18 mg twice daily and placebo, respectively. In patients without background antifibrotic therapy, weight decrease occurred in 8%, 2%, and 6% of patients treated with JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively.

Decreased Appetite

In patients taking nintedanib, decreased appetite occurred in 7%, 10%, and 4% in JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively. In patients using concomitant pirfenidone, decreased appetite occurred in 13% and 10% of patients treated with JASCAYD 18 mg twice daily and placebo, respectively. In patients without concomitant antifibrotic treatment, decreased appetite occurred in 9%, 6%, and 0% of patients treated with JASCAYD 18 mg twice daily, JASCAYD 9 mg twice daily, and placebo, respectively.

Less Common Adverse Reactions

Less common adverse reactions in the studied population following administration of JASCAYD included asthenia (5% JASCAYD 18 mg twice daily, 4% JASCAYD 9 mg twice daily, and 2% placebo), amylase increased (1% JASCAYD 18 mg twice daily, 1% JASCAYD 9 mg twice daily, and 0% placebo), and vasculitis (1% JASCAYD 18 mg twice daily, 1% JASCAYD 9 mg twice daily, and 0% placebo).

7 DRUG INTERACTIONS

7.1 Effects of Other Drugs on JASCAYD

Strong CYP3A Inhibitors

Reduce the dosage of JASCAYD to 9 mg twice daily when used concomitantly with strong CYP3A inhibitors [see *Dosage and Administration (2.2)*].

Nerandomilast is a CYP3A substrate. Concomitant use of JASCAYD with a strong CYP3A inhibitor increases exposure of nerandomilast, which may increase the risk of JASCAYD adverse reactions [see *Clinical Pharmacology (12.3)*].

Moderate or Strong CYP3A Inducers

Avoid use of JASCAYD with strong or moderate CYP3A inducers.

Nerandomilast is a CYP3A substrate. Concomitant use of JASCAYD with moderate or strong CYP3A inducers is expected to decrease exposure of nerandomilast, which may decrease the efficacy of JASCAYD [see *Clinical Pharmacology (12.3)*].

Pirfenidone

Recommended dosage of JASCAYD is 18 mg twice daily when used concomitantly with pirfenidone. Do not reduce the dosage to 9 mg twice daily [see *Dosage and Administration (2.1)*].

Concomitant use of JASCAYD with pirfenidone decreases exposure of nerandomilast in patients with IPF [see *Clinical Pharmacology (12.3)*]. When JASCAYD was used concomitantly with pirfenidone in patients with IPF in FIBRONEER-IPF, efficacy was not observed with the JASCAYD 9 mg twice daily dosage [see *Clinical Studies (14)*].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on JASCAYD use in pregnant women to evaluate 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 idiopathic pulmonary fibrosis during pregnancy (*Clinical Considerations*).

Based on findings from animal reproduction studies, JASCAYD may increase the risk for fetal loss. In an embryo-fetal development study in rats, oral administration of nerandomilast to pregnant rats during organogenesis at an exposure approximately 5 times the maximum recommended human dose (MRHD) of 36 mg/day resulted in an increase in embryo-fetal losses (*see Data*). Advise pregnant women and females of reproductive potential of the potential risk of fetal loss.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general

population, the estimated background risk of major birth defects is 2% to 4% and miscarriage in clinically recognized pregnancies is 15% to 20%.

Clinical Considerations

Disease-Associated Maternal and/or Embryo/Fetal Risk

Untreated IPF can lead to respiratory failure and mortality in the mother and intrauterine growth restriction, preterm birth, fetal hypoxia, and neonatal death.

Data

Animal Data

In an embryo-fetal development study in pregnant rats dosed by the oral route during the period of organogenesis from gestation days 6 to 17, nerandomilast caused an increase in embryo-fetal losses (pre- and post-implantation loss and decreased mean number of live fetuses) at an exposure that was approximately 5 times the MRHD (on an AUC basis with a maternal oral dose of 6 mg/kg/day). Maternal toxicity, as evidenced by decreased body weight gains and adverse clinical signs, was observed at exposures approximately 7 times the MRHD (on an AUC basis with a maternal oral dose of 9 mg/kg/day). No fetal or maternal toxicities were observed at exposures up to 3 and 5 times the MRHD (on an AUC basis with maternal oral doses of 3 mg/kg/day and 6 mg/kg/day), respectively.

In an embryo-fetal development study in pregnant rabbits dosed by the oral route during the period of organogenesis from gestation days 7 to 19, no effects on maternal or fetal development were observed at an exposure that was approximately 24 times the MRHD (on an AUC basis with a maternal oral dose of 15 mg/kg/day).

In a prenatal and postnatal development study in pregnant rats dosed by the oral route during the periods of gestation and lactation from gestation day 6 to lactation day 20, nerandomilast had no effects on delivery or the growth and development of offspring at an exposure that was approximately 2 times the MRHD (on an AUC basis with a maternal oral dose of 3 mg/kg/day).

8.2 Lactation

Risk Summary

There are no data on the presence of nerandomilast or its metabolite in human milk, the effects on the breastfed infant, or the effects on milk production. Nerandomilast is present in animal milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk (*see Data*).

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for JASCAYD and any potential adverse effects on the breastfed infant from JASCAYD or from the underlying maternal condition.

Data

In a prenatal and postnatal development study in pregnant rats dosed by the oral route during the periods of gestation and lactation from gestation day 6 to lactation day 20, nerandomilast was present in the plasma of rat pups during the lactation period. In a single dose milk secretion study in lactating rats dosed with radiolabeled nerandomilast by the oral route, similar concentrations of total radioactivity were observed in the milk and plasma of lactating females, with the maximum radioactive concentration observed at 1 hour post dose that was significantly reduced by 24 hours post dose. The concentration of total radioactivity in animal milk does not necessarily predict the concentration of drug in human milk.

8.4 Pediatric Use

The safety and effectiveness of JASCAYD for the treatment of idiopathic pulmonary fibrosis have not been established in pediatric patients.

8.5 Geriatric Use

There were 930 patients 65 years of age and older in the FIBRONEER-IPF trial [see *Clinical Studies (14)*]. Of the total number of JASCAYD-treated patients in this trial, 623 (79%) were 65 years of age and older, while 251 (32%) were 75 years of age and older. No overall differences in safety or effectiveness of JASCAYD have been observed between patients 65 years of age and older and younger adult patients.

8.6 Renal Impairment

JASCAYD has not been investigated in patients with end stage renal disease (eGFR <15 mL/min/1.73 m²). Use of JASCAYD is not recommended in patients with end stage renal disease (eGFR <15 mL/min/1.73 m²).

The recommended dosage in patients with mild (eGFR ≥60 to <90 mL/min/1.73 m² according to CKD-EPI), moderate (eGFR ≥30 to <60 mL/min/1.73 m²), or severe renal impairment (eGFR ≥15 to <30 mL/min/1.73 m²) is the same as that in patients with normal renal function [see *Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

JASCAYD has not been investigated in patients with severe (Child-Pugh Class C) hepatic impairment. Use of JASCAYD is not recommended in patients with severe (Child-Pugh Class C) hepatic impairment.

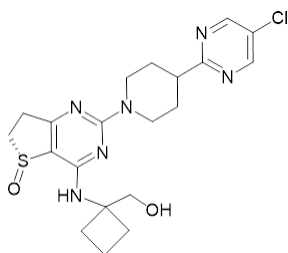
The recommended dosage in patients with mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment is the same as that in patients with normal hepatic function [see *Clinical Pharmacology (12.3)*].

10 OVERDOSAGE

In the event of an overdose with JASCAYD, monitor the patient for any signs or symptoms of adverse reactions and provide appropriate symptomatic treatment. Consider contacting the Poison Help line (1-800-222-1222) or a medical toxicologist for additional overdose management recommendations.

11 DESCRIPTION

JASCAYD (nerandomilast tablets), for oral administration, contain nerandomilast, a phosphodiesterase 4 (PDE4) inhibitor. The chemical name of nerandomilast is [1-[[[(5R)-2-[4-(5-chloropyrimidin-2-yl)-1-piperidyl]-5-oxo-6,7-dihydrothieno[3,2-d]pyrimidin-4-yl]amino]cyclobutyl]methanol. Nerandomilast has one chiral center and is the R-stereoisomer. Its structural formula is:



Nerandomilast is a white to off-white to light yellow powder with an empirical formula of C₂₀H₂₅ClN₆O₂S and a molecular weight of 449 g/mol. At or below pH 3, nerandomilast is very slightly to slightly soluble in water, and above pH 3 it is practically insoluble.

Each film-coated tablet of JASCAYD contains 9 mg or 18 mg of nerandomilast and the following inactive ingredients: croscarmellose sodium, ferric oxide red (18 mg tablets only), ferric oxide yellow (9 mg tablets only), ferrousferrous oxide (18 mg tablets only), hydroxypropyl cellulose, hypromellose, lactose monohydrate, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol, and talc. Each JASCAYD tablet contains less than 5 mg of sodium.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Nerandomilast is an inhibitor of phosphodiesterase 4 (PDE4) with at least nine-fold preferential inhibition of the PDE4B isoenzyme over PDE4A, PDE4C and PDE4D based on *in vitro* data. 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 IPF.

12.2 Pharmacodynamics

Exposure-Response

Increases in nerandomilast steady state trough concentrations were associated with better efficacy, as indicated by a smaller reduction in forced vital capacity (FVC) from baseline over 52 weeks.

Cardiac Electrophysiology

At 2.1 times the maximal concentration provided by the maximum recommended dose of nerandomilast, clinically significant QTc interval prolongation was not observed.

12.3 Pharmacokinetics

Nerandomilast exposure increased in a dose proportional manner following administration of single doses of 0.0032 to 2.6 times a single dose of 18 mg and multiple doses of 0.056 to 1 times the maximum recommended dose of 18 mg twice daily. Following administration of multiple doses of 18 mg twice daily, C_{max} increases 1.3-fold and AUC_{tau} increases 1.38-fold. Nerandomilast steady state is reached in approximately 4 days.

No clinically relevant differences in nerandomilast pharmacokinetics were observed between healthy subjects and patients with IPF.

Absorption

The absolute oral bioavailability of nerandomilast is 73%. Nerandomilast median (min, max) time to maximum plasma concentration (T_{max}) is 1 to 1.25 hours (range 0.5 to 4 hours).

Effect of Food

No clinically relevant differences in nerandomilast pharmacokinetics were observed following administration with a high-fat meal (1000 calories, 50% fat).

Distribution

Nerandomilast steady state apparent (oral) central volume of distribution is 93 L (CV 37%). *In vitro*, nerandomilast plasma protein binding is 77% and is not concentration dependent. Nerandomilast blood-to-plasma ratio is approximately 0.6 to 0.8.

Elimination

The geometric mean (CV%) elimination half-life of nerandomilast is 17 hours (46%) with an apparent (oral) clearance of 15.2 L/h.

Metabolism

Nerandomilast is primarily metabolized by CYP3A and to a lesser extent by multiple UGT enzymes.

After oral administration of nerandomilast, chiral inversion from the pharmacologically active R-enantiomer to the pharmacologically inactive S-enantiomer occurs via metabolism. The S-enantiomer was identified as a minor metabolite of nerandomilast. The R-enantiomer is the predominant circulating enantiomer.

Excretion

After a single oral dose of radiolabeled nerandomilast, approximately 58% of the dose was recovered in feces (14% as unchanged nerandomilast) and 36% of the dose was recovered in urine (13% as unchanged nerandomilast).

Specific Populations

No clinically significant differences in the pharmacokinetics of nerandomilast were observed based on age (range: 18 to 90 years), body weight (range: 34 to 136 kg), sex, race (66% White and 32.5% Asian), mild (eGFR ≥ 60 to < 90 mL/min/1.73 m² [calculated according to Chronic Kidney Disease Epidemiology Collaboration]), moderate (eGFR ≥ 30 to < 60 mL/min/1.73 m²), or severe renal impairment (eGFR ≥ 15 to < 30 mL/min/1.73 m²), or mild (Child-Pugh Class A) or moderate (Child-Pugh Class B) hepatic impairment.

Subjects with end stage renal disease or severe hepatic impairment (Child-Pugh Class C) have not been studied [see *Use in Specific Populations* (8.6, 8.7)].

Drug Interaction Studies

Strong CYP3A Inhibitors: Nerandomilast C_{max} increased by 1.3-fold and AUC increased by 2.2-fold following concomitant administration with itraconazole (a strong CYP3A and P-gp inhibitor) 200 mg oral solution once daily for 4 days [see *Drug Interactions* (7.1)].

Pirfenidone: Nerandomilast trough concentrations at steady state (C_{trough,ss}) decreased by approximately 50% following concomitant administration with pirfenidone in patients with IPF [see *Drug Interactions* (7.1)].

Other Drugs: No clinically significant differences in nerandomilast C_{trough,ss} were observed when used concomitantly with nintedanib. No clinically significant differences in the pharmacokinetics of the following drugs were observed when used concomitantly with nerandomilast: oral midazolam (CYP3A4 substrate), pirfenidone, and nintedanib.

In Vitro Studies

CYP450 Enzymes: Nerandomilast is a CYP3A4 substrate. Nerandomilast does not inhibit CYP3A4, CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, and CYP2D6.

Transporter Systems: Nerandomilast is a P-glycoprotein (P-gp) substrate, but is not a substrate of BCRP, OATP1B1, OATP1B3, OAT1, OAT3, and OCT2. Nerandomilast is an inhibitor of P-gp, MATE1, MATE2-K, but is not expected to cause clinically significant interactions. Nerandomilast is not an inhibitor of BCRP, OAT1, OAT3, OCT2, OATP1B1, or OATP1B3.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

The carcinogenic potential of nerandomilast was assessed in Tg.rasH2 mice and Wistar Han rats. No evidence of tumorigenicity was observed in male and female Tg.rasH2 mice that received nerandomilast for 26 weeks at oral doses up to 60 and 100 mg/kg/day, respectively. No evidence of tumorigenicity was observed in male or female rats that received nerandomilast for up to 102 weeks at oral doses up to 2 mg/kg/day (approximately 2 times the MRHD on an AUC basis).

Mutagenesis

Nerandomilast was not mutagenic or clastogenic in the following assays: *in vitro* bacterial reverse mutation (Ames) assay, *in vitro* chromosomal aberration assay in human peripheral blood lymphocytes, and *in vivo* rat micronucleus assay.

Impairment of Fertility

Nerandomilast had no effect on fertility in male or female rats at oral doses up to 6 mg/kg/day (approximately 3 or 4 times the MRHD on an AUC basis, respectively). Decreased mating, pregnancy, and fertility indices at the highest tested dose of 9 mg/kg/day (approximately 4 or 9 times the MRHD on an AUC basis) were attributed to excessive general toxicity.

Sexually mature female monkeys administered nerandomilast by the oral route for 39 weeks showed sporadic menstrual cycle prolongation at dose levels of 10 mg/kg/day and 30 mg/kg/day (approximately 3- and 10 times the MRHD on an AUC basis, respectively). Menstrual cycles were not affected in monkeys at oral doses of 3 mg/kg/day (equivalent to the MRHD on an AUC basis).

14 CLINICAL STUDIES

The efficacy of JASCAYD was evaluated in two randomized, double-blind, placebo-controlled trials (FIBRONEER-IPF [NCT05321069] and Trial 2 [NCT04419506]).

FIBRONEER-IPF enrolled a total of 1,177 adult patients with IPF with or without background antifibrotic treatments (nintedanib or pirfenidone). They were randomized in a 1:1:1 ratio to receive JASCAYD 9 mg twice daily, JASCAYD 18 mg twice daily, or placebo twice daily 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. The FIBRONEER-IPF trial consisted of 83% male and 17% female patients with a mean age of 70 years (age range: 42 to 90 years). The study population included 68% White, 32% Asian, and <1% Black or African American. For ethnicity, 8% of patients identified as Hispanic or Latino. At baseline, the mean FVC was 78% of predicted normal; 78% of the patients 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 a total of 147 adult patients with IPF with or without background antifibrotic treatments (nintedanib or pirfenidone) and were randomized 2:1 to receive JASCAYD 18 mg twice daily or placebo twice daily for 12 weeks. Randomization was stratified by the presence or absence of background antifibrotic treatments (nintedanib or pirfenidone) at baseline. The study population in Trial 2 consisted of 77% male, and mean age of 70 years (age range: 40 to 85 years). The study population included 78% White and 22% Asian. For ethnicity, 9% of patients identified as Hispanic or Latino. At baseline, the mean

FVC was 78% of predicted normal; 50% of the patients were on stable antifibrotic treatment (nintedanib 29%, pirfenidone 21%).

In both the FIBRONEER-IPF trial and Trial 2, patients were required to have a diagnosis of IPF based on ATS/ERS/JRS/ALAT criteria. 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 greater than or equal to 45% of predicted and a carbon monoxide diffusing capacity (DLCO, corrected for hemoglobin) greater than or equal to 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 re-start background antifibrotic treatment. Patients with active vasculitis, severe depression or suicidal behavior or ideation, or use of immunomodulatory medications (other than prednisone ≤ 15 mg/day or equivalent) were excluded.

Change from Baseline in Forced Vital Capacity

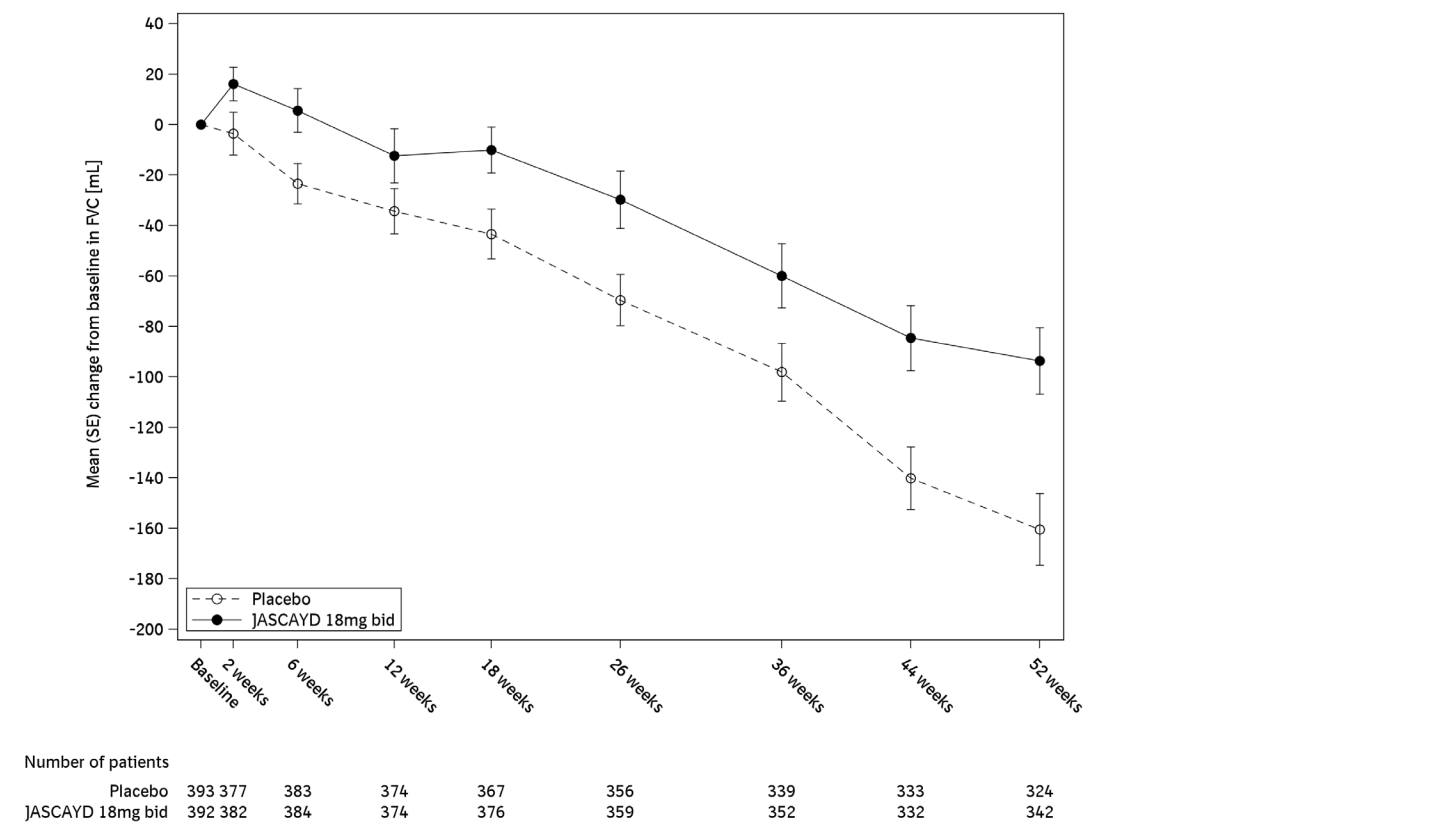
The primary endpoint in FIBRONEER-IPF trial was the absolute change from baseline in forced vital capacity (FVC) in milliliters (mL) at 52 weeks for JASCAYD compared with placebo.

In the FIBRONEER-IPF 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 18 mg or JASCAYD 9 mg was -106 mL and -122 mL, respectively, whereas in the placebo group, an adjusted mean decline of -170 mL was observed. The respective treatment differences compared with the placebo group were 64 mL (95% CI: 25, 102) and 48 mL (95% CI: 10, 86).

In the FIBRONEER-IPF trial, the results of the primary endpoint across subgroups by background antifibrotic treatment (nintedanib, pirfenidone, or none) for JASCAYD 18 mg versus placebo were consistent with the overall population. Efficacy was not observed in patients who received JASCAYD 9 mg twice daily with pirfenidone as background antifibrotic treatment [*see Drug Interactions (7.1)*].

Figure 1 shows the change in FVC from baseline over time in patients who received JASCAYD 18 mg twice daily compared to placebo in the FIBRONEER-IPF trial.

Figure 1 Change from Baseline in FVC (mL) in Adults with IPF over 52 weeks with JASCAYD 18 mg Compared to Placebo (FIBRONEER-IPF)



Display based on descriptive means and standard errors for change from baseline values from patients with results that were available at each week.
bid = twice daily

In Trial 2, patients taking JASCAYD 18 mg twice daily compared to placebo, with or without background antifibrotic treatments, had a reduction in FVC decline at Week 12 of 91 mL (95% CI: 44, 138).

Time To First Acute IPF Exacerbation, First Hospitalization for Respiratory Cause, Or Death

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.

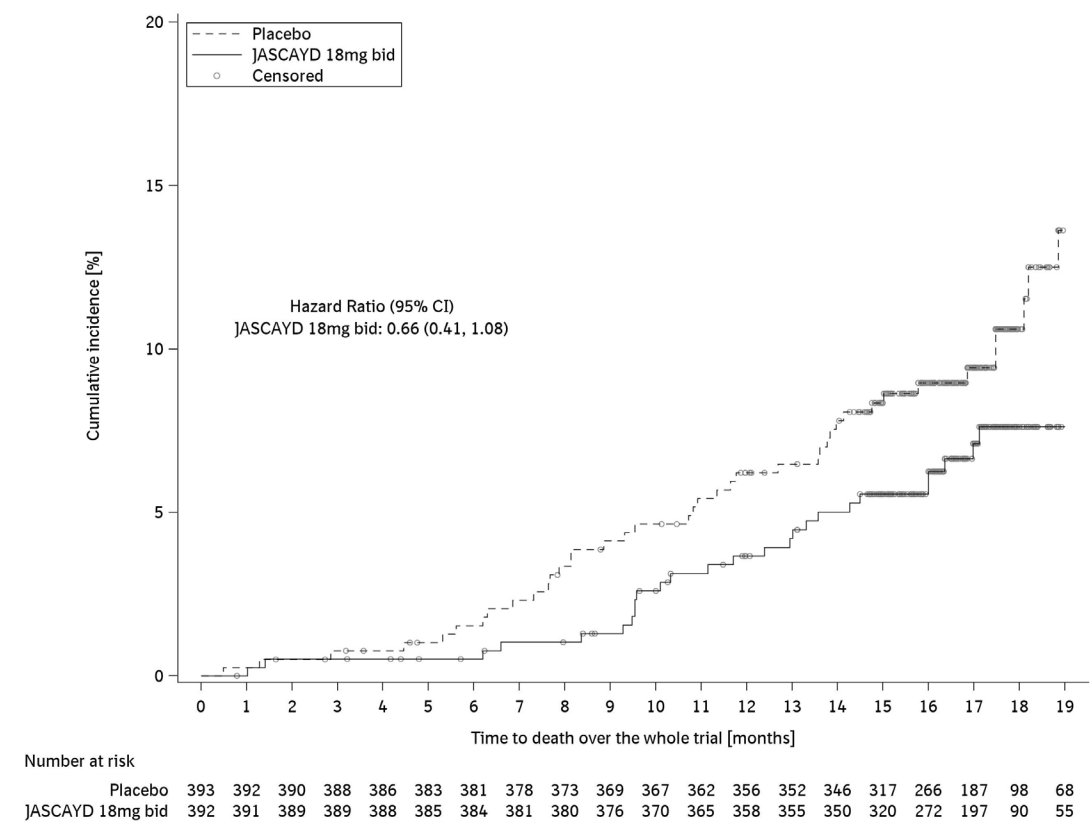
Overall, there was no statistically significant treatment difference in hazard ratio (HR) for the JASCAYD 18 mg or 9 mg groups compared to placebo for the key secondary composite endpoint (JASCAYD 18 mg and 9 mg, respectively: HR 1.17 [95% CI: 0.86, 1.59] and HR 1.03 [95% CI: 0.75, 1.41]).

Survival

In the FIBRONEER-IPF study population, the hazard ratio for all-cause mortality, assessed until the end of trial (up to 109 weeks), did not show a significant treatment difference for JASCAYD 18 mg or 9 mg compared to placebo (HR: 0.66 [95% CI: 0.41, 1.08] and HR 0.95 [95% CI: 0.61, 1.49], respectively).

Figure 2 shows the cumulative incidence of death in adults with IPF in the FIBRONEER-IPF trial for JASCAYD 18 mg and placebo.

Figure 2 Cumulative Incidence of Death in Adults with IPF (FIBRONEER-IPF)



bid = twice daily

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

JASCAYD tablets are supplied as follows:

Tablet Strength	Tablet Description	Package Configuration	NDC
9 mg	light yellow, oval, biconvex, film-coated tablets debossed with the Boehringer Ingelheim company symbol on one side and “F9” on the other side	Bottles of 60 with child-resistant closure	0597-2465-41

18 mg	light red, oval, biconvex, film-coated tablets debossed with the Boehringer Ingelheim company symbol on one side and “F18” on the other side	Bottles of 60 with child-resistant closure	0597-7313-21
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Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature]. Store in the original container to protect from light.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Pregnancy

Advise female patients to contact their healthcare provider if they become pregnant or suspect they may be pregnant during treatment with JASCAYD. Advise female patients of the potential risk of fetal loss [see *Use in Specific Populations (8.1)*].

Missed Dose

Inform patients that if they miss a dose of JASCAYD, they should take the next dose at the next scheduled time. Advise patients to not make up for a missed dose or exceed the recommended dosage of 18 mg twice daily [see *Dosage and Administration (2.1)*].

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COL11694AJ032025

PATIENT INFORMATION
JASCAYD (JASS-kayd)
(nerandomilast tablets)
for oral use

What is JASCAYD?

JASCAYD is a prescription medicine used to treat adults with a lung disease called idiopathic pulmonary fibrosis (IPF). It is not known if JASCAYD is safe and effective in children.

Before you take JASCAYD, tell your healthcare provider about all of your medical conditions, including if you:

- have kidney problems.
- have liver problems.
- are pregnant or plan to become pregnant. JASCAYD may cause loss of your pregnancy (miscarriage). It is not known if JASCAYD can harm your unborn baby. Tell your healthcare provider right away if you become pregnant or think you are pregnant while taking JASCAYD.
- are breastfeeding or plan to breastfeed. It is not known if JASCAYD passes into your breastmilk. You and your healthcare provider should decide if you will take JASCAYD or breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. JASCAYD may affect the way other medicines work, and other medicines may affect how JASCAYD works. Know the medicines you take. Keep a list of them and show it to your healthcare provider or pharmacist when you get a new medicine.

How should I take JASCAYD?

- Take JASCAYD exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much JASCAYD to take and when to take it.
- Take JASCAYD either with or without food.
- Swallow JASCAYD tablets whole.
- If you cannot swallow JASCAYD tablets whole:
 - Place 3 to 4 ounces (about 100 mL) of non-carbonated, room temperature water in a glass. Do not use any other liquids.
 - Place a JASCAYD tablet in the water, without crushing the tablet, and stir regularly for about 15 to 20 minutes until the tablet is in very small pieces (the tablet will not completely dissolve).
 - Drink the JASCAYD and water mixture within 2 hours of mixing.
 - If you do not drink the mixture right away, stir the mixture again before drinking.
 - Rinse the glass with 3 to 4 ounces (about 100 mL) of water and drink to make sure that you have taken the full dose of JASCAYD.
- If you miss a dose of JASCAYD, take your next dose at your regular time. **Do not** take the missed dose.
- **Do not** take more than two 18 mg JASCAYD tablets in 1 day.
- If you take too much JASCAYD, call your healthcare provider or Poison Help line at 1-800-222-1222, or go to the nearest hospital emergency room right away.

What are the possible side effects of JASCAYD?

The most common side effects of JASCAYD include:

- | | | |
|-------------------------------------|----------------------|-------------|
| ○ diarrhea | ○ weight loss | ○ headache |
| ○ COVID-19 | ○ decreased appetite | ○ vomiting |
| ○ upper respiratory tract infection | ○ nausea | ○ back pain |
| ○ depression | ○ fatigue | ○ dizziness |

These are not all of the possible side effects of JASCAYD. For more information, ask your healthcare provider or pharmacist. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store JASCAYD?

- Store JASCAYD at room temperature between 68°F to 77°F (20°C to 25°C).
- Store JASCAYD in the original child-resistant container to protect it from light.

Keep JASCAYD and all medicines out of the reach of children.

General information about the safe and effective use of JASCAYD.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use JASCAYD for any condition for which it was not prescribed. Do not give JASCAYD to other people, even if they have the same symptoms you have. It may harm them. You can ask your healthcare provider or pharmacist for information about JASCAYD that is written for health professionals.

What are the ingredients in JASCAYD?

Active ingredient: nerandomilast

Inactive ingredients: croscarmellose sodium, ferric oxide red (18 mg tablets only), ferric oxide yellow (9 mg tablets only), ferrousferic oxide (18 mg tablets only), hydroxypropyl cellulose, hypromellose, lactose monohydrate, magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol, and talc.

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For more information about JASCAYD, including current Prescribing Information and patient support, go to www.jascayd.com or call Boehringer Ingelheim Pharmaceuticals, Inc. at 1-800-542-6257, or scan the code to go to www.jascayd.com.



This Patient Information has been approved by the U.S. Food and Drug Administration.

Approved: 10/2025



CareConnect4Me™ is here to help you get started on JASCAYD and provide support along the way, Monday - Friday, from 8:00 AM to 8:00 PM ET. For assistance, call 1-844-JASCAYD.

18 mg
(nerandomilast tablets)
Jascayd®

NDC 0597-7313-21

Jascayd®
(nerandomilast tablets)

18 mg

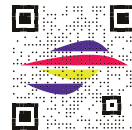
R_x only

60 tablets



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Scan the code for information about taking JASCAYD or to access current Prescribing Information.



GTIN 00005977313214
SN 12345678901234
EXP YYYY-MMM-DD
LOT 123456A



Jascayd®
(nerandomilast tablets)

18 mg

Each tablet contains 18 mg of nerandomilast.

Recommended Dosage:
See Prescribing Information.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Store in the original container to protect from light.

Keep out of reach of children.

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3 0 5 9 7 7 3 1 3 2 1 5

NDC 0597-7313-21

Jascayd®
(nerandomilast tablets)

18 mg

R_x only

60 tablets



Jascayd®
(nerandomilast tablets)

18 mg

Jascayd®
(nerandomilast tablets)

18 mg

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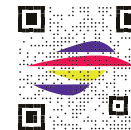
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CT14617A

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P058954-001





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9 mg

Jascayd®
(nerandomilast tablets)

NDC 0597-2465-41

Jascayd®
(nerandomilast tablets)

9 mg

R_x only

60 tablets



Jascayd®
(nerandomilast tablets)

9 mg

Each tablet contains 9 mg of nerandomilast.

Recommended Dosage:
See Prescribing Information.

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].

Store in the original container to protect from light.

Keep out of reach of children.

CareConnect4Me™ is here to help you get started on JASCAYD and provide support along the way, Monday - Friday, from 8:00 AM to 8:00 PM ET. For assistance, call 1-844-JASCAYD.



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Scan the code for information about taking JASCAYD or to access current Prescribing Information.



GTIN 00005972465413
SN 12345678901234
EXP YYYY-MMM-DD
LOT 123456A



NDC 0597-2465-41

Jascayd®
(nerandomilast tablets)

9 mg

R_x only

60 tablets



Jascayd®
(nerandomilast tablets)

9 mg

Jascayd®
(nerandomilast tablets)

9 mg

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P058949-001

NDC 0597-7313-21

60 tablets



(nerandomilast tablets)

18 mg

R_x only

Reference ID: 5672859

Each tablet contains 18 mg of nerandomilast.

Recommended Dosage:
See Prescribing Information.

Store at 20°C to 25°C
(68°F to 77°F).

Store in the original container
to protect from light.

Keep out of reach of children.

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LOT

123456A



P058953-001

L14615A

EXP

YYYY-MMM-DD



NDC 0597-2465-41

60 tablets

 **Jascayd[®]**
(nerandomilast tablets)

9 mg

R_x only

Reference ID: 5672859

Each tablet contains 9 mg of nerandomilast.

Recommended Dosage:
See Prescribing Information.

Store at 20°C to 25°C
(68°F to 77°F).

Store in the original container
to protect from light.

Keep out of reach of children.

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CareConnect4Me™ is here to help you get started on JASCAYD and provide support along the way, Monday - Friday, from 8:00 AM to 8:00 PM ET. For assistance, call 1-844-JASCAYD.

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L14623A

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/s/

KATHLEEN M DONOHUE
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