HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use ZEGFROVY safely and effectively. See full prescribing information for ZEGFROVY.

ZEGFROVY™ (sunvozertinib) tablets, for oral use
Initial U.S. Approval: 2025

----------INDICATIONS AND USAGE----------
ZEGFROVY is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. (1, 2.1)
This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s). (1)

----------DOSAGE AND ADMINISTRATION----------
Recommended dosage: 200 mg orally once daily taken with food. (2.2)

----------DOSAGE FORMS AND STRENGTHS----------
Tablets: 150 mg and 200 mg. (3)

----------CONTRAINDICATIONS----------
None. (4)

----------WARNINGS AND PRECAUTIONS----------
- Interstitial Lung Disease (ILD)/Pneumonitis: Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold ZEGFROVY in patients with suspected ILD/pneumonitis and permanently discontinue ZEGFROVY if ILD/pneumonitis is confirmed. (2.3, 5.1)
- Gastrointestinal Adverse Reactions: Administer ZEGFROVY with food to reduce gastrointestinal adverse reactions. Monitor patients for nausea, vomiting and diarrhea and provide supportive care, including anti-diarrheals, anti-emetics, or fluid replacement, as indicated. Withhold, reduce the dose, or permanently discontinue ZEGFROVY based on severity. (2.3, 5.2)
- Dermatologic Adverse Reactions: Monitor patients for rash and dermatologic adverse reactions. Instruct patients to use alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream during treatment with ZEGFROVY and to avoid the use of irritating skin products (e.g., products containing retinol or retinoic acid, benzoyl peroxides). Withhold, reduce the dose, or permanently discontinue ZEGFROVY based on severity. (2.3, 5.3)
- Ocular Toxicity: Promptly refer patients presenting with eye symptoms suggestive of keratitis to an ophthalmologist. Advise discontinuation of contact lenses until ocular symptoms are evaluated. Withhold, reduce the dose, or permanently discontinue ZEGFROVY based on severity. (2.3, 5.4)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective non-hormonal contraception. (5.5, 8.1, 8.3)

----------ADVERSE REACTIONS----------
- The most common (≥20%) adverse reactions were: diarrhea, rash, decreased appetite, stomatitis, fatigue, nausea, paronychia, vomiting, constipation, musculoskeletal pain, pruritus, dry skin, urinary tract infection, abdominal pain and decreased weight. (6.1)
- The most common (≥2%) Grade 3 or 4 laboratory abnormalities were: decreased lymphocytes, increased lipase, decreased hemoglobin, increased amylase, increased creatine kinase, decreased neutrophils, decreased potassium, increased aspartate aminotransferase, increased alanine aminotransferase, decreased sodium, increased magnesium, and increased alkaline phosphatase. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Dizal (Jiangsu) Pharmaceutical Co., Ltd. at +1-855-482-0653 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- Strong CYP3A Inhibitors: Avoid concomitant use. If concomitant use cannot be avoided, reduce ZEGFROVY dose. (2.4, 7.1)
- Strong and Moderate CYP3A Inducers: Avoid concomitant use. If concomitant use cannot be avoided, increase ZEGFROVY dose. (2.4, 7.1)
- P-gp or BCRP Substrates: Monitor for increased adverse reactions during concomitant use with ZEGFROVY. (7.2)
- Hormonal Contraceptives: Avoid concomitant use. (7.2)

----------USE IN SPECIFIC POPULATIONS----------
- Lactation: Advise not to breastfeed. (8.2)

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

Revised: 07/2025

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

ZEGFROVY is indicated for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test *[see Dosage and Administration (2.1)]*, whose disease has progressed on or after platinum-based chemotherapy.

This indication is approved under accelerated approval based on overall response rate and duration of response *[see Clinical Studies (14)]*. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).

2. DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for treatment with ZEGFROVY for locally advanced or metastatic NSCLC based on the presence of EGFR exon 20 insertion mutations in tumor tissue *[see Clinical Studies (14)]*. Information on FDA-approved tests is available at: http://www.fda.gov/CompanionDiagnostics.

2.2 Recommended Dosage

The recommended dosage of ZEGFROVY is 200 mg orally once daily with food *[see Warnings and Precautions (5.2)]* until disease progression or unacceptable toxicity. Swallow ZEGFROVY tablets whole. Do not split, crush, chew, or dissolve the tablets. Take ZEGFROVY at the same time each day.

Missed Dose

If a dose of ZEGFROVY is missed within 12 hours, take the dose. If a dose of ZEGFROVY is missed by more than 12 hours, skip the missed dose and take the next dose at the regularly scheduled time.

Vomiting

If a ZEGFROVY dose is vomited, do not take an additional dose. Take the next dose at the regularly scheduled time.

2.3 Dosage Modifications for Adverse Reactions

Reduce the dose of ZEGFROVY to 150 mg orally once daily with food, for the management of adverse reactions. Permanently discontinue ZEGFROVY in patients unable to tolerate 150 mg orally once daily.

The recommended dosage modifications for adverse reactions are provided in Table 1.

Table 1: Recommended Dosage Modifications of ZEGFROVY for Adverse Reactions

Adverse Reaction	Severity*	Dose Modifications
Interstitial Lung Disease (ILD)/Pneumonitis *[see Warnings and Precautions (5.1)]*	Any Grade	• Withhold ZEGFROVY if ILD/pneumonitis is suspected. • Permanently discontinue ZEGFROVY if ILD/pneumonitis is confirmed.
Nausea or Vomiting *[see Warnings and Precautions (5.2)]*	Grade 1	• Administer supportive care including anti-emetics.
	Grade 2	• Administer supportive care including anti-emetics. • Withhold ZEGFROVY until recovery to Grade ≤1; then resume ZEGFROVY at the same dose.
	Grade 3 or 4	• Administer supportive care including anti-emetics.

Adverse Reaction	Severity*	Dose Modifications
		• Withhold ZEGFROVY until recovery to Grade ≤1; then resume ZEGFROVY at the next lower dose.
Diarrhea *[see Warnings and Precautions (5.2)]*	Grade 1	• Administer supportive care including anti-diarrheals (i.e., loperamide).
	Grade 2 or 3	First occurrence • Administer supportive care and anti-diarrheals (i.e., loperamide). • Withhold ZEGFROVY until recovery to Grade ≤1; then resume ZEGFROVY at the same dose level. Recurrence • Withhold ZEGFROVY until recovery to Grade ≤1; then resume ZEGFROVY at the next lower dose.
	Grade 4	First occurrence • Withhold ZEGFROVY and provide supportive care and anti-diarrheals (i.e., loperamide). • If resolved to Grade ≤1 within 3 weeks, resume ZEGFROVY at the next lower dose. • If not resolved to Grade ≤1 within 3 weeks, permanently discontinue ZEGFROVY. Recurrence • Permanently discontinue ZEGFROVY.
Dermatologic Adverse Reactions *[see Warnings and Precautions* (5.3)*]*	Grade 2	• Administer supportive care. • Reassess within 3 weeks, if rash does not improve, consider ZEGFROVY dose reduction.
	Grade 3	• Withhold ZEGFROVY and administer supportive care. • Upon recovery to Grade ≤1, resume ZEGFROVY at the next lower dose. • If no improvement within 3 weeks, permanently discontinue ZEGFROVY.
	Grade 4	• Permanently discontinue ZEGFROVY.
Ocular Toxicity *[see Warnings and Precautions (5.4)]*	Any Grade	• Withhold ZEGFROVY if ulcerative keratitis is suspected. • Permanently discontinue ZEGFROVY if ulcerative keratitis is confirmed.
Other Adverse Reactions *[see Adverse Reaction (6.1)]*	Grade 3 or 4	• Withhold ZEGFROVY. • If resolved to Grade ≤1 within 3 weeks, resume ZEGFROVY at the same dose or the next lower dose. • If not resolved to Grade ≤1 within 3 weeks, permanently discontinue ZEGFROVY.

* Adverse reactions graded by the National Cancer Institute Common Terminology Criteria for Adverse Events Version 5.0 (NCI CTCAE v5.0).

2.4 Dosage Modifications for Drug Interactions

Strong CYP3A Inhibitors

Avoid concomitant use of strong CYP3A inhibitors. If concomitant use cannot be avoided, reduce the ZEGFROVY dose from 200 mg to 150 mg *[see Drug Interactions (7.1)]*.

After discontinuing a CYP3A inhibitor, resume the ZEGFROVY dose (after 3 to 5 half-lives of the CYP3A inhibitor) that was taken prior to initiating the CYP3A inhibitor.

Strong and Moderate CYP3A Inducers

Avoid concomitant use of strong and moderate CYP3A inducers. If concomitant use cannot be avoided, increase the ZEGFROVY dose from 200 mg to 400 mg *[see Drug Interactions (7.1)].*

After discontinuing a CYP3A inducer, resume the ZEGFROVY dose (7 to 14 days after discontinuing the CYP3A inducer) that was taken prior to initiating the CYP3A inducer.

3. DOSAGE FORMS AND STRENGTHS

Tablets:

- 150 mg: yellow, biconvex film-coated tablets, debossed with “150” on one side and Dizal company logo on the other side.
- 200 mg: yellow, biconvex film-coated tablets, debossed with “200” on one side and Dizal company logo on the other side.

4. CONTRAINDICATIONS

None.

5. WARNINGS AND PRECAUTIONS

5.1 Interstitial Lung Disease/Pneumonitis

ZEGFROVY can cause severe and life-threatening interstitial lung disease (ILD)/pneumonitis.

In the safety population *[see Adverse Reactions (6.1)]*, ILD/pneumonitis occurred in 1.7% of patients. The median time to first onset for ILD/pneumonitis was 61 days (range: 35 to 86 days). ZEGFROVY was discontinued due to ILD/pneumonitis in 0.8% of patients.

Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (e.g., dyspnea, cough, and fever). Immediately withhold ZEGFROVY in patients with suspected ILD/pneumonitis and permanently discontinue ZEGFROVY if ILD/pneumonitis is confirmed *[see Dosage and Administration (2.3)]*.

5.2 Gastrointestinal Adverse Reactions

ZEGFROVY can cause severe gastrointestinal adverse reactions including diarrhea, nausea, and vomiting.

In the safety population *[see Adverse Reactions (6.1)],* serious gastrointestinal adverse reactions occurred in 1.7% of patients, including 0.8% Grade 3 nausea. Diarrhea occurred in 73% of patients who received ZEGFROVY, including 2.5% Grade 3. Diarrhea leading to dosage interruption or dose reduction occurred in 5% of patients and required permanent discontinuation of ZEGFROVY in 0.8% of patients. Nausea and vomiting occurred in 43% of patients, including 3.3% Grade 3 events. Nausea and vomiting leading to dosage interruption or dose reduction occurred in 7% of patients and permanent discontinuation of ZEGFROVY in 0.8% of patients.

Administer ZEGFROVY with food to reduce gastrointestinal adverse reactions. Monitor patients for gastrointestinal toxicity, and provide supportive care, including anti-diarrheals, anti-emetics, or fluid replacement, as indicated. Withhold, reduce the dose, or permanently discontinue ZEGFROVY based on severity *[see Dosage and Administration (2.3)]*.

5.3 Dermatologic Adverse Reactions

ZEGFROVY can cause severe rash including acneiform dermatitis and pruritus.

Based on the safety population *[see Adverse Reactions (6.1)]*, dermatologic adverse reactions occurred in 68% of patients including 9% acneiform dermatitis. Grade 3 dermatologic adverse reactions were 7% rash, 0.8% acneiform dermatitis, and 0.8% pruritus.

Instruct patients to use alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream during treatment with ZEGFROVY and to avoid the use of irritating skin products (e.g., products containing retinol or retinoic acid, benzoyl peroxides).

Withhold, reduce the dose, or permanently discontinue ZEGFROVY based on severity *[see Dosage and Administration (2.3)].*

5.4 Ocular Toxicity

ZEGFROVY can cause ocular toxicity including keratitis, dry eye symptoms, blurred vision, and visual impairment.

Based on the safety population *[see Adverse Reactions (6.1)],* ocular toxicity occurred in 13% of patients who received ZEGFROVY, including keratitis (0.8%).

Promptly refer patients with new or worsening eye symptoms to an ophthalmologist. Advise discontinuation of contact lenses until ocular symptoms are evaluated. Withhold, reduce the dose, or permanently discontinue ZEGFROVY based on severity *[see Dosage and Administration (2.3)].*

5.5 Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, ZEGFROVY can cause fetal harm when administered to a pregnant woman.

In animal reproduction studies, oral administration of sunvozertinib to pregnant animals during the period of organogenesis resulted in structural abnormalities at concentrations below the human exposure at the recommended dose based on area under the curve (AUC) *[see Use in Specific Populations (8.1)]*.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ZEGFROVY and for 2 weeks after the last dose, since ZEGFROVY can render some hormonal contraceptives ineffective *[see Drug Interactions (7.2)]*. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEGFROVY and for 2 weeks after the last dose *[see Use in Specific Populations (8.1, 8.3)]*.

6. ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Interstitial Lung Disease/Pneumonitis *[see Warnings and Precautions (5.1)]*
- Gastrointestinal Adverse Reactions *[see Warnings and Precautions (5.2)*]
- Dermatologic Adverse Reactions *[see Warnings and Precautions (5.3)]*
- Ocular Toxicity *[see Warnings and Precautions (5.4)]*

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 the clinical trials of another drug and may not reflect the rates observed in practice.

The pooled safety populations described in *WARNINGS AND PRECAUTIONS* reflect exposure to ZEGFROVY as a single agent at a dose of 200 mg orally once daily in 121 patients with locally advanced or metastatic NSCLC from two clinical trials WU-KONG1 (NCT03974022) *[see Clinical*

Studies (14)] and WU-KONG2 (n=3). Among 121 patients who received ZEGFROVY, 56% were exposed for 6 months or longer and 28% were exposed for greater than one year. In this pooled safety population, the most common (≥20%) adverse reactions were diarrhea, rash, decreased appetite, stomatitis, fatigue, nausea, paronychia, vomiting, constipation, musculoskeletal pain, pruritus, dry skin, urinary tract infection, abdominal pain and decreased weight. The most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes, increased lipase, decreased hemoglobin, increased amylase, increased creatine kinase, decreased neutrophils, decreased potassium, increased aspartate aminotransferase, increased alanine aminotransferase, decreased sodium, increased magnesium, and increased alkaline phosphatase.

EGFR Exon 20 Insertion Mutation-Positive Locally Advanced or Metastatic NSCLC Previously Treated with Platinum-Based Chemotherapy

The safety of ZEGFROVY was evaluated in WU-KONG1B *[see Clinical Studies (14)]* in patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations in a multinational, open-label, dose randomization clinical trial. Eligible patients must have had disease progression on or after platinum-based chemotherapy and received ZEGFROVY 200 mg orally once daily until disease progression or intolerable toxicity. The median age of patients who received ZEGFROVY was 62 years (range: 35-88); 67% were females; 65% were Asian and 33% were White; 97% were not of Hispanic or Latino ethnicity.

Serious adverse reactions occurred in 41% of patients who received ZEGFROVY. Serious adverse reactions in ≥2% of patients who received ZEGFROVY were pneumonia (9%); dyspnea (4.4%); and pancreatitis, device related infection and rash (2.2% each). Fatal adverse reactions occurred in 2.2% of patients who received ZEGFROVY including thrombosis (1.1%) and COVID-19 infection (1.1%).

Permanent discontinuation of ZEGFROVY due to adverse reactions occurred in 8% of patients. Adverse reactions leading to treatment discontinuation of ZEGFROVY in ≥2% of patients were pneumonia and rash (2.2% each).

Dosage interruption of ZEGFROVY due to adverse reactions occurred in 48% of patients. Adverse reactions requiring dosage interruption of ZEGFROVY in ≥5% of patients were vomiting (9%), pneumonia (8%), and rash (8%).

Dose reduction of ZEGFROVY due to adverse reactions occurred in 23% of patients. Adverse reactions requiring dose reduction of ZEGFROVY in ≥3% of patients were rash (4.4%) and diarrhea (3.3%).

Table 2 summarizes the adverse reactions in WU-KONG1B.

Table 2: Adverse Reactions (≥10%) in Patients with Locally Advanced or Metastatic NSCLC Who Received ZEGFROVY in WU-KONG1B

Adverse Reaction	ZEGFROVY N=91	
	All grades[1] (%)	Grade 3 or 4 (%)
Gastrointestinal disorders		
Diarrhea*	73	2.2
Stomatitis*	40	2.2
Vomiting*	35	0
Nausea	32	2.2

Adverse Reaction	ZEGFROVY N=91	
	All grades[1] (%)	Grade 3 or 4 (%)
Constipation	27	0
Weight decreased	26	3.3
Abdominal pain*	19	1.1
Abdominal distension	16	0
Skin and subcutaneous tissue disorders		
Rash*	60	8
Paronychia*	30	0
Pruritus	26	1.1
Dry skin*	21	0
Metabolism and nutrition disorders		
Decreased appetite	52	0
General disorders and administration site conditions		
Fatigue*	41	1.1
Edema*	11	0
Malaise	11	1.1
Musculoskeletal and connective tissue disorders		
Musculoskeletal pain*	26	2.2
Infections and infestations		
Urinary tract infection*	24	1.1
Pneumonia*	25	11
Eye disorders		
Ocular toxicity*	18	0
Nervous system disorders		
Peripheral neuropathy*	14	0
Cardiac disorders		
Arrhythmia*	12	1.1

[1]NCI CTCAE v5.0.
*Grouped Terms

Clinically relevant adverse reactions in <10% of patients who received ZEGFROVY were: cough, dizziness, dyspnea, dry eye and keratitis.

Table 3 summarizes the laboratory abnormalities in WU-KONG1B.

Table 3: Selected Laboratory Abnormalities (≥20%) That Worsened from Baseline in Patients with Locally Advanced or Metastatic NSCLC Who Received ZEGFROVY in WU-KONG1B

Laboratory Abnormality	ZEGFROVY[1] N=91	
	All Grades[2] (%)	Grade 3 or 4 (%)
Chemistry		
Creatinine increased	62	0
Creatine kinase increased	57	8
Lipase increased	47	13
Aspartate aminotransferase increased	44	4.4
Amylase increased	37	9
Sodium decreased	33	3.4
Albumin decreased	32	0
Potassium decreased	29	3.4
Alanine aminotransferase increased	28	4.4
Magnesium increased	23	4.4
Alkaline phosphatase increased	21	2.2
Hematology		
Hemoglobin decreased	61	12
Lymphocytes decreased	54	20
Neutrophils decreased	41	4.4
Urinalysis		
Urine protein increased	38	0

[1]The denominator used to calculate the rate varied from 89 to 90 based on the number of patients with a baseline and at least one post-treatment value.

[2]NCI CTCAE v5.0

Other Clinical Trials Experience

The following adverse reactions occurred following administration of ZEGFROVY: Interstitial Lung Disease (ILD)/Pneumonitis

7. DRUG INTERACTIONS

7.1 Effect of Other Drugs on ZEGFROVY

Table 4 describes drug interactions where coadministration with another drug affects ZEGFROVY.

Table 4: Effect of Other Drugs on ZEGFROVY

Strong CYP3A Inhibitors	
Prevention or Management	• Avoid concomitant use with strong CYP3A inhibitors.

	• If concomitant use cannot be avoided, reduce ZEGFROVY dose as recommended *[see Dosage and Administration (2.4)]* and monitor for increased ZEGFROVY adverse reactions.
Mechanism and Clinical Effect(s)	• Sunvozertinib is a CYP3A substrate. • Concomitant use with strong CYP3A inhibitors increases sunvozertinib exposure *[see Clinical Pharmacology (12.3)],* which may increase the risk of ZEGFROVY-associated adverse reactions.
Strong or Moderate CYP3A Inducers	
Prevention or Management	• Avoid concomitant use with strong and moderate CYP3A inducers. • If concomitant use cannot be avoided, increase ZEGFROVY dose as recommended *[see Dosage and Administration (2.4)].*
Mechanism and Clinical Effect(s)	• Sunvozertinib is a CYP3A substrate. • Concomitant use with strong or moderate CYP3A inducers decreases sunvozertinib exposure *[see Clinical Pharmacology (12.3)],* which may reduce effectiveness of ZEGFROVY.

7.2 Effect of ZEGFROVY on Other Drugs

Table 5 describes drug interactions where coadministration with ZEGFROVY affects another drug.

Table 5: Effect of ZEGFROVY on Other Drugs

Hormonal Contraceptives (CYP3A Substrates)	
Prevention or Management	• Avoid concomitant use of ZEGFROVY with hormonal contraceptives. • Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ZEGFROVY and for 2 weeks after the last dose.
Mechanism and Clinical Effect(s)	• Sunvozertinib is an inducer of CYP3A4. • Concomitant use of ZEGFROVY with CYP3A substrates decreased their plasma concentrations *[see Clinical Pharmacology (12.3)]*, where minimal concentration changes may lead to therapeutic failure of hormonal contraceptives.
P-gp or BCRP Substrates	
Prevention or Management	• Monitor for increased adverse reactions of P-gp or BCRP substrates, where minimal concentration changes may lead to serious adverse reactions, when coadministered with ZEGFROVY.
Mechanism and Clinical Effect(s)	• Sunvozertinib is an inhibitor of P-gp and BCRP. • ZEGFROVY increases exposure of P-gp or BCRP substrates *[see Clinical Pharmacology (12.3)],* which may increase the risk of adverse reactions associated with these substrates.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings from animal studies and its mechanism of action *[see Clinical Pharmacology (12.1)],* ZEGFROVY can cause fetal harm when administered to a pregnant woman. There are no available data on the use of ZEGFROVY in pregnant women to inform a drug-associated risk. Oral administration of sunvozertinib to pregnant animals during the period of organogenesis resulted in structural abnormalities at concentrations below the human exposure at the recommended dose based on AUC (*see Data*). Advise pregnant women and females of reproductive potential of the potential risk to a fetus.

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

Data

Animal Data

In an embryo-fetal development study, pregnant rats received oral doses of 10, 20, or 40 mg/kg/day of sunvozertinib during the period of organogenesis (gestation day 6 to 17). Sunvozertinib caused maternal toxicity (decreased body weight and food consumption) and embryo-fetal toxicity (skeletal variations) at 40 mg/kg/day (0.6 times the human exposure at the recommended dose based on AUC).

In an embryo-fetal development study, pregnant rabbits received oral doses of 0.5, 1.5, or 5 mg/kg/day of sunvozertinib during the period of organogenesis (gestation day 6 to 19). Sunvozertinib caused maternal toxicity (decreased body weight and food consumption) and embryo-fetal toxicities including an increased incidence of visceral malformations in the heart and lung at ≥0.5 mg/kg/day (0.02 times the human exposure at the recommended dose based on AUC) and skeletal variations at ≥1.5 mg/kg/day (0.07 times the human exposure at the recommended dose based on AUC).

8.2 Lactation

Risk Summary

There are no data on the presence of sunvozertinib or its metabolites in human milk or their effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with ZEGFROVY and for 2 weeks after the last dose.

8.3 Females and Males of Reproductive Potential

Based on animal data and mechanism of action, ZEGFROVY can cause fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1)]*.

Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating ZEGFROVY.

Contraception

Females

Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ZEGFROVY and for 2 weeks after the last dose. ZEGFROVY may render hormonal contraceptives ineffective *[see Drug Interactions (7.2)]*.

Males

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZEGFROVY and for 2 weeks after the last dose *[see Use in Specific Populations (8.1)]*.

Infertility

Females

Based on animal studies, ZEGFROVY may impair fertility in females. The reversibility of the effects on female fertility was not assessed *[see Nonclinical Toxicology (13.1)]*.

Males

Based on animal studies, ZEGFROVY may impair fertility in males. The effects on male fertility were reversible *[see Nonclinical Toxicology (13)]*.

8.4 Pediatric Use

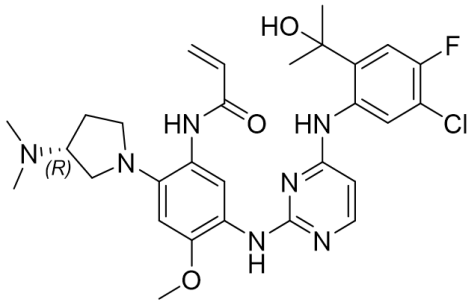
The safety and effectiveness of ZEGFROVY in pediatric patients have not been established.

8.5 Geriatric Use

Of the 121 patients who received ZEGFROVY 200 mg in clinical studies, 43% were 65 years and over, and 9% were 75 years and over. No overall difference in effectiveness was observed between patients who were ≥65 years of age and younger patients. There was a higher incidence of adverse reactions of Grade ≥3 (69% vs. 52%) and serious adverse reactions (48% vs. 38%) in patients at 65 years and older as compared to those younger than 65 years.

11. DESCRIPTION

ZEGFROVY (sunvozertinib) is a kinase inhibitor. The molecular formula for sunvozertinib is $C_{29}H_{35}ClFN_7O_3$, and the molecular weight is 584.09 g/mol. The chemical name of sunvozertinib is *N*-{5-[(4-{[5-chloro-4-fluoro-2-(1-hydroxy-1-methylethyl)phenyl]amino}pyrimidin-2-yl)amino]-2-[(*3R*)-3-(dimethylamino)pyrrolidin-1-yl]-4-methoxyphenyl}prop-2-enamide. Sunvozertinib has one chiral carbon with *R*-configuration. The chemical structure of sunvozertinib is shown below:



ZEGFROVY tablets contain 150 mg or 200 mg of active ingredient sunvozertinib. Inactive ingredients in ZEGFROVY core tablets are colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, and microcrystalline cellulose. The tablet coating consists of hypromellose 2910, iron oxide yellow, titanium dioxide, and triacetin.

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Sunvozertinib is a kinase inhibitor of the epidermal growth factor receptor (EGFR) that binds to and inhibits EGFR exon 20 insertion mutations at similar concentrations as wild-type EGFR.

In cultured cell models, sunvozertinib inhibited EGFR phosphorylation in cells expressing different EGFR exon 20 insertion mutation variants at approximately 2- to 10-fold lower concentrations than wild-type EGFR signaling inhibition. Sunvozertinib exhibited anti-tumor activity against xenograft models of NSCLC with EGFR exon 20 insertion mutations.

12.2 Pharmacodynamics

Exposure Response Relationships

No clinically significant exposure-response relationships for overall response rate (ORR) were observed over the exposure range between sunvozertinib 200 mg and 300 mg (1.5 times the approved recommended dose).

Cardiac Electrophysiology

At 1.5 times the approved recommended dose, a clinically significant QTc interval prolongation was not observed.

12.3 Pharmacokinetics

Sunvozertinib pharmacokinetics were observed at steady state at the approved recommended dosage and are presented as geometric mean (CV%) unless otherwise specified.

Sunvozertinib total systemic exposure (AUC) and maximum concentration (C_{max}) increase approximately dose-proportionally across the dose range of 50 mg (0.25 times the approved recommended dose) to 400 mg (2 times the approved recommended dose). Steady state is reached within 15 days and the mean accumulation of AUC was approximately 3-fold. The steady-state C_{max} and AUC of sunvozertinib were 412 (45%) ng/mL and 8,060 (42%) h*ng/mL, respectively.

Absorption

Sunvozertinib median (minimum, maximum) time to maximum plasma concentration (t_{max}) is approximately 6 hours (3, 10 hours).

Effect of Food

No clinically significant differences in sunvozertinib AUC and C_{max} were observed following administration of sunvozertinib with a high-fat meal (approximately 1,000 calories, approximately 50% fat).

Distribution

The apparent (oral) volume of distribution is 2,116 L (81%). Sunvozertinib plasma protein binding ranges from approximately 89% to 94% in vitro.

Elimination

Sunvozertinib elimination half-life is 50 hours (27%) with an apparent (oral) clearance of 29 L/h (54%).

Metabolism

Sunvozertinib is primarily metabolized by CYP3A and forms the active demethylated metabolite, DZ0753. DZ0753 AUC represents 10% of the parent AUC.

Excretion

Following a single oral dose of radiolabeled sunvozertinib, 79% of the dose was recovered in feces (7.3% unchanged) and 10% in urine (5.6% unchanged).

Specific Populations

No clinically significant differences in the pharmacokinetics of sunvozertinib were observed based on age (19 to 96 years), sex, race (Asian 62%, White 28%, Black or African American 8%), body weight (30 to 118 kg), smoking status, mild to moderate renal impairment (CLcr 30 to 89 mL/min, estimated by Cockcroft-Gault), and mild (bilirubin ≤ ULN and AST > ULN or bilirubin >1 to 1.5 x ULN and any AST) to moderate (bilirubin ≥1.5 to 3 x ULN and any AST) hepatic impairment. The effect of severe hepatic impairment (total bilirubin >3 x ULN and any AST) and severe renal impairment (CLcr 15 to 29 mL/min) on the pharmacokinetics of sunvozertinib has not been studied.

Drug Interaction Studies

Clinical Studies and Model-Informed Approaches

Strong CYP3A Inhibitors: Sunvozertinib AUC increased by 1.5-fold and C_{max} by 1.3-fold following concomitant administration of itraconazole (strong CYP3A inhibitor) 200 mg once daily.

Strong and Moderate CYP3A Inducers: Sunvozertinib AUC decreased by 48% and C_{max} by 38% following concomitant administration of carbamazepine (strong CYP3A inducer) 300 mg twice daily.

Sunvozertinib AUC is predicted to decrease by 44% following concomitant administration of efavirenz (moderate CYP3A inducer) 600 mg once daily.

CYP3A Substrates: Midazolam (sensitive CYP3A substrate) AUC decreased by 23% and C_{max} by 15% following concomitant administration of ZEGFROVY.

P-glycoprotein (P-gp) Substrates: Digoxin (P-gp substrate) AUC increased by 1.4-fold and C_{max} by 1.2-fold following concomitant administration of ZEGFROVY.

BCRP Substrates: Rosuvastatin (BCRP substrate) AUC increased by 1.4-fold and C_{max} by 1.6-fold following concomitant administration of ZEGFROVY.

Other Drugs:

No clinically significant effect on sunvozertinib pharmacokinetics is predicted following concomitant administration of fluconazole (moderate CYP3A inhibitor) 200 mg once daily.

No clinically significant effect on sunvozertinib pharmacokinetics is predicted following concomitant administration of dexamethasone (weak CYP3A inducer) 8 mg once daily.

No clinically significant effect on the pharmacokinetics of desipramine (CYP2D6 substrate) is predicted when used concomitantly with ZEGFROVY.

No clinically significant effect on sunvozertinib pharmacokinetics was observed when used concomitantly with acid reducing agents (e.g. proton pump inhibitor).

In Vitro Studies

CYP450 Enzymes: Sunvozertinib induces CYP2C8.

Transporter Systems: Sunvozertinib is a substrate of P-gp. Sunvozertinib inhibits OATP1B1.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Carcinogenicity studies have not been conducted with sunvozertinib.

Mutagenesis

Sunvozertinib was not genotoxic in the bacterial reverse mutation (Ames) assay, an in vitro chromosome aberration assay, or an in vivo micronucleus assay in rats.

Impairment of Fertility

Fertility studies have not been conducted with sunvozertinib. In repeat-dose toxicology studies of up to 4-weeks duration in dogs, oral administration of sunvozertinib caused vaginal epithelial atrophy and degeneration of the seminiferous tubule in the testes at doses as low as 8 mg/kg/day (≥0.2 times the human exposure at the recommended dose based on AUC). The reversibility of the findings in females was not assessed. The findings in males were reversible.

14. CLINICAL STUDIES

EGFR Exon 20 Insertion Mutation-Positive Locally Advanced or Metastatic NSCLC Previously Treated with Platinum-Based Chemotherapy

The efficacy of ZEGFROVY was evaluated in WU-KONG1B (NCT03974022), a multinational, open-label, dose randomization clinical trial. Eligible patients had locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations with disease progression on or after platinum-based chemotherapy and Eastern Cooperative Oncology Group (ECOG) of score 0 or 1. Patients with previously treated and stable intracranial metastases were eligible to enroll. Patients with measurable disease at baseline were randomized to receive either ZEGFROVY 200 mg (n=85) or ZEGFROVY at an unapproved dose orally once daily with food until disease progression or intolerable toxicity.

The major efficacy outcome measure was overall response rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST v 1.1) as evaluated by a blinded independent review committee (BIRC). An additional efficacy outcome measure was duration of response (DOR) by BIRC.

The efficacy population had the following demographic characteristics: the median age was 61 years (range: 35 to 88 years); 67% were female; 65% were Asian; 33% were White; and 2% were other races or had race not reported; 2% were of Hispanic or Latino ethnicity; 71% had never smoked. At baseline, 61% had ECOG performance status of 1; 96% had metastatic disease; 94% had adenocarcinoma histology; and 25% had brain metastases. All patients had received prior platinum-based chemotherapy, 42% had received prior anti-PD-(L)1 therapy, and 14% had received prior amivantamab.

All 85 patients in the efficacy population had EGFR exon 20 insertion mutations in tumor based prospective local or central laboratory testing. Tumor samples from patients were tested retrospectively using Life Technologies Corporation Oncomine™ Dx Express Test. In these tumor samples, 68% (58/85) were positive for EGFR exon 20 insertion mutations, 2.4% (2/85) did not have an EGFR exon 20 insertion mutation identified, and 29% (25/85) did not generate reportable results.

Efficacy results are summarized in Table 6.

Table 6: Efficacy Results of WU-KONG1B Study

Efficacy Parameter	**ZEGFROVY (N=85)**
Overall Response Rate (ORR), % (95% CI[a])	46 (35, 57)
Complete Response, %	6
Partial Response, %	40
Duration of Response (DOR)	N=39
Median[b], months (95% CI)	11.1 (8.2, NE)
Patients with DOR ≥6 months	72%

CI = confidence interval
[a]95% CI for ORR was calculated based on Clopper-Pearson exact CI method.
[b]Kaplan-Meier estimate using confirmed responses.

16. HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

ZEGFROVY tablets are supplied in bottles with a child-resistant cap as follows:

Tablet Strength	Description	Quantity	NDC Code
150 mg	Yellow, biconvex film-coated tablets, debossed with “150” on one side and Dizal company logo on the other side.	30	24538-101-01
200 mg	Yellow, biconvex film-coated tablets, debossed with “200” on one side and Dizal company logo on the other side.	30	24538-102-01

Storage and Handling

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

17. PATIENT COUNSELING INFORMATION

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

Interstitial Lung Disease/Pneumonitis

Advise patients that ZEGFROVY can cause interstitial lung disease/pneumonitis. Advise patients to immediately contact their healthcare provider for new or worsening respiratory symptoms *[see Warnings and Precautions (5.1)].*

Gastrointestinal Toxicity

Advise patients that ZEGFROVY can cause gastrointestinal toxicity, including nausea, vomiting, and diarrhea. Advise patients to take ZEGFROVY with food to reduce gastrointestinal adverse reactions. Advise patients to immediately contact their healthcare provider for symptoms of gastrointestinal toxicity *[see Warnings and Precautions (5.2)].*

Dermatologic Adverse Reactions

Advise patients that ZEGFROVY can cause dermatologic adverse reactions, including rash and pruritus. Advise patients to use alcohol-free (e.g., isopropanol-free, ethanol-free) emollient cream during treatment with ZEGFROVY and to avoid the use of irritating skin products (e.g., products containing retinol or retinoic acid, benzoyl peroxides). Advise patients to immediately contact their healthcare provider for symptoms of dermatologic adverse reactions *[see Warnings and Precautions (5.3)].*

Ocular Toxicity

Advise patients that ZEGFROVY can cause ocular toxicity. Advise patients to contact their healthcare provider if they develop eye symptoms. Advise discontinuation of contact lenses until symptoms are evaluated *[see Warnings and Precautions (5.4)]* and at least one week after symptoms have resolved.

Embryo-Fetal Toxicity

Advise females of reproductive potential of the potential risk to a fetus and to inform their healthcare provider of a known or suspected pregnancy *[see Warnings and Precautions (5.5), Use in Specific Populations (8.1)]*.

Advise females of reproductive potential to use effective non-hormonal contraception during treatment with ZEGFROVY and for 2 weeks after the last dose *[see Use in Specific Populations (8.3)],* since ZEGFROVY can render some hormonal contraceptives ineffective *[see Drug Interactions (7.2)]*.

Advise males with female partners of reproductive potential to use effective contraception during treatment with ZEGFROVY and for 2 weeks after the last dose *[see Use in Specific Populations (8.3)]*.

Lactation

Advise women not to breastfeed during treatment with ZEGFROVY and for 2 weeks after the last dose *[see Use in Specific Populations (8.2)]*.

Infertility

Advise females and males of reproductive potential that ZEGFROVY may impair fertility *[see Use in Specific Populations (8.3) and Nonclinical Toxicology (13.1)]*.

Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products *[see Drug Interactions (7.1, 7.2)].*

Manufactured for:

Dizal (Jiangsu) Pharmaceutical Co., Ltd.

Shanghai, 201203, China

PATIENT INFORMATION
ZEGFROVY (zeg-FROH-vee)
(sunvozertinib)
tablets, for oral use

What is ZEGFROVY?

ZEGFROVY is a prescription medicine used to treat adults with non-small cell lung cancer (NSCLC):

- that has spread to nearby tissues (locally advanced) or to other parts of the body (metastatic), **and**
- has a certain abnormal epidermal growth factor receptor (EGFR) gene, **and**
- whose disease has worsened while on or after chemotherapy that contains platinum.

Your healthcare provider will perform a test to make sure that ZEGFROVY is right for you.

It is not known if ZEGFROVY is safe and effective in children.

Before taking ZEGFROVY, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of eye or vision problems.
- are pregnant or plan to become pregnant. ZEGFROVY can harm your unborn baby.
  Females who are able to become pregnant:
  - Your healthcare provider should do a pregnancy test before you start treatment with ZEGFROVY.
  - You should use an effective form of non-hormonal birth control (contraception) during treatment with ZEGFROVY and for 2 weeks after your last dose of ZEGFROVY.
  - Talk to your healthcare provider about birth control methods that might be right for you during this time.
  - Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with ZEGFROVY.

  Males who have female partners who are able to become pregnant:
  - You should use effective birth control (contraception) during treatment with ZEGFROVY and for 2 weeks after your last dose of ZEGFROVY.
- are breastfeeding or plan to breastfeed. It is not known if ZEGFROVY passes into your breast milk. Do not breastfeed during treatment with ZEGFROVY and for 2 weeks after your last dose of ZEGFROVY. Talk to your healthcare provider about the best way to feed your baby during treatment with ZEGROVY.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ZEGFROVY may affect the way other medicines work and other medicines may affect how ZEGFROVY works.

How should I take ZEGFROVY?

- Take ZEGFROVY exactly as your healthcare provider tells you.
- Do not change your dose or stop taking ZEGFROVY unless your healthcare provider tells you to.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with ZEGFROVY if you develop certain side effects.
- Take your prescribed dose of ZEGFROVY 1 time a day at the same time each day.
- Take ZEGFROVY with food.
- Swallow ZEGFROVY tablets whole. Do not split, crush, chew, or dissolve the tablets.
- If you miss a dose of ZEGFROVY, take it as soon as you remember within 12 hours. If it has been more than 12 hours, skip the missed dose and take your next dose at your regularly scheduled time.
- If you vomit after taking a dose of ZEGFROVY, do not take an extra dose. Take your next dose at your regularly scheduled time.

What are the possible side effects of ZEGFROVY?

ZEGFROVY may cause serious side effects, including:

- **Lung problems.** ZEGFROVY can cause lung problems that can be severe and life-threatening. Symptoms may be similar to those from lung cancer. Tell your healthcare provider right away if you develop new or worsening symptoms of lung problems during treatment with ZEGFROVY, including shortness of breath or trouble breathing, cough, or fever.
- **Stomach and intestinal (gastrointestinal) problems.** ZEGFROVY can cause stomach and intestinal problems that can be severe, including diarrhea, nausea, and vomiting. Tell your healthcare provider right away if you get any of these symptoms during treatment with ZEGFROVY. Your healthcare provider may prescribe medicines as needed, or recommend drinking fluids or other treatments, to help treat your symptoms.
- **Skin problems.** ZEGFROVY can cause severe skin rashes. Use alcohol-free (such as isopropanol-free or ethanol-free) moisturizing cream during treatment with ZEGFROVY. Avoid use of irritating skin products, such as

skin products containing retinol or retinoic acid, and benzoyl peroxide. Tell your healthcare provider right away if you develop any skin reactions, including small, raised skin bumps that look like acne or itchy skin.

- **Eye problems.** Your healthcare provider may send you to see an eye specialist (ophthalmologist) if you develop new or worsening eye problems during treatment with ZEGFROVY. You should not use contact lenses until your eye symptoms are checked by a healthcare provider and for at least 1 week after your eye symptoms have resolved. Tell your healthcare provider right away if you develop any new or worsening symptoms of eye problems, including:
  - eye pain
  - eye redness
  - light sensitivity
  - feeling like something is in your eyes
  - increased tears
  - discharge from your eyes
  - eye irritation
  - dry eyes
  - eye crusting
  - blurred vision
  - loss of vision
  - vision problems

The most common side effects of ZEGFROVY include:

- diarrhea
- rash
- decreased appetite
- mouth sores
- feeling very tired
- nausea
- infected skin around the nail
- vomiting
- constipation
- muscle or joint pain
- itchy skin
- dry skin
- urinary tract infection
- stomach-area pain
- decreased weight

The most common severe abnormal lab test results with ZEGFROVY include:

- decreased white blood cell and red blood cell counts
- increased pancreas enzyme levels
- increased creatine kinase levels
- decreased potassium and salt (sodium) levels
- increase liver enzyme levels
- increased magnesium levels

ZEGFROVY may affect fertility in females and males, which may affect your ability to have a child. Talk to your healthcare provider if this is a concern for you.

These are not all of the possible side effects of ZEGFROVY.

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 ZEGFROVY?

- Store ZEGFROVY at room temperature between 68°F to 77°F (20°C to 25°C).

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

General information about the safe and effective use of ZEGFROVY.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ZEGFROVY for a condition for which it was not prescribed. Do not give ZEGFROVY to other people, even if they have the same symptoms that you have. It may harm them.

You can ask your pharmacist or healthcare provider for information about ZEGFROVY that is written for health professionals.

What are the ingredients in ZEGFROVY?

Active ingredient: sunvozertinib

Inactive ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, lactose monohydrate, magnesium stearate, and microcrystalline cellulose. Tablet coating contains: hypromellose 2910, iron oxide yellow, titanium dioxide, and triacetin.

Manufactured for: Dizal (Jiangsu) Pharmaceutical Co., Ltd., Shanghai, 201203, China

For more information, call +1-855-482-0653.

This Patient Information has been approved by the U.S. Food and Drug Administration. Issued: 07/2025