**HIGHLIGHTS OF PRESCRIBING INFORMATION**

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

**ATEBRIOZ™ (zilurgisertib) tablets, for oral use**

**Initial U.S. Approval: 2026**

## INDICATIONS AND USAGE

ATEBRIOZ is an activin receptor-like kinase-2 (ALK2) inhibitor indicated to reduce the volume of total new heterotopic ossification (HO) in adults and pediatric patients aged 12 years and older with fibrodysplasia ossificans progressiva (FOP). (1)

## DOSAGE AND ADMINISTRATION

- Recommended starting dosage: 100 mg orally once daily with or without food. (2.2)
- Administer ATEBRIOZ tablets whole or crushed. If crushed, mix 4 tablets (100 mg total) with four tablespoons (60 mL) of water, orange juice, apple sauce, or plain yogurt. (2.2)

## DOSAGE FORMS AND STRENGTHS

Tablets: 25 mg of zilurgisertib. (3)

## CONTRAINDICATIONS

Pregnancy. (4, 5.1, 8.1)

## WARNINGS AND PRECAUTIONS

Embryo-Fetal Toxicity: Can cause fetal harm. Verify females of reproductive potential are not pregnant prior to initiating ATEBRIOZ and advise of the potential risk to a fetus and to use effective contraception. Advise the patient to discontinue ATEBRIOZ immediately if pregnancy occurs during treatment and to contact their healthcare provider. (5.1, 8.1, 8.3)

## ADVERSE REACTIONS

Most common adverse reactions (≥ 10%): headache, arthralgia, upper respiratory tract infection, epistaxis, and nausea. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Mirum Pharmaceuticals, Inc. at 1-855-MRM-4YOU or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.**

## DRUG INTERACTIONS

CYP3A4 Inhibitors: Reduce ATEBRIOZ dosage to 50 mg orally once daily when used concomitantly with a strong CYP3A4 inhibitor. (2.3, 7.1)

CYP3A4 Inducers: Avoid concomitant use of ATEBRIOZ with strong or moderate CYP3A4 inducers. (7.1)

MATE1 and MATE2-K Substrates: Avoid concomitant use of ATEBRIOZ with MATE1 and MATE2-K substrates (e.g., metformin). (7.2)

## USE IN SPECIFIC POPULATIONS

Lactation: Breastfeeding is not recommended. (8.2)

**See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.**

**Revised: 9/2026**

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**FULL PRESCRIBING INFORMATION: CONTENTS***



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

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# FULL PRESCRIBING INFORMATION

## 1. INDICATIONS AND USAGE

ATEBRIOZ is indicated to reduce the volume of total new heterotopic ossification (HO) in adults and pediatric patients aged 12 years and older with fibrodysplasia ossificans progressiva (FOP).

## 2. DOSAGE AND ADMINISTRATION

### 2.1. Pregnancy Testing Prior to Treatment with ATEBRIOZ

Verify that females of reproductive potential are not pregnant prior to initiating ATEBRIOZ *[see Contraindications (4), Warnings and Precautions (5.1), and Use in Specific Populations (8.1, 8.3)]*.

### 2.2. Recommended Dosage and Administration

The recommended dosage of ATEBRIOZ is 100 mg orally once daily with or without food *[see Clinical Pharmacology (12.3)]*.

Administer ATEBRIOZ tablets whole or crushed. If crushed, mix 4 tablets (100 mg total) with four tablespoons (60 mL) of water, orange juice, apple sauce, or plain yogurt and administer immediately. Do not store the mixture for future use. Do not administer ATEBRIOZ with grapefruit, pomelo, or juices containing these fruits.

### 2.3. Dosage Modification for CYP3A4 Inhibitors

Reduce the ATEBRIOZ dosage to 50 mg orally once daily when used concomitantly with a strong CYP3A4 inhibitor. No change in ATEBRIOZ dosage is needed when used concomitantly with a mild or moderate CYP3A4 inhibitor *[see Drug Interactions (7.1)]*.

## 3. DOSAGE FORMS AND STRENGTHS

ATEBRIOZ Tablets: 25 mg of zilurgisertib, film-coated, white to off-white, round, debossed with "INCY" on one side and "25" on the other side.

## 4. CONTRAINDICATIONS

ATEBRIOZ is contraindicated in pregnancy. ATEBRIOZ can cause fetal harm when administered to a pregnant woman *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1, 8.3)]*.

# 5. WARNINGS AND PRECAUTIONS

## 5.1. Embryo-Fetal Toxicity

ATEBRIOZ is contraindicated during pregnancy. Based on its mechanism of action and findings from animal reproduction studies, ATEBRIOZ can cause fetal harm when administered to a pregnant woman. Oral administration of zilurgisertib to pregnant rats during the period of organogenesis resulted in adverse outcomes, including embryofetal lethality, decreased fetal weight, and skeletal malformations at exposures ≥ 3-times the human exposure at the clinical dose of 100 mg *[see Use in Specific Populations (8.1) and Clinical Pharmacology (12.1)]*. For females of reproductive potential, verify that the patient is not pregnant prior to initiation of treatment. Advise females of reproductive potential to use effective contraception during treatment with ATEBRIOZ and for one week after the final dose. Advise patients to discontinue ATEBRIOZ immediately if pregnancy occurs during treatment and to contact their healthcare provider *[see Use in Specific Populations (8.1, 8.3)]*.

# 6. ADVERSE REACTIONS

## 6.1. Clinical Trial 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 safety of ATEBRIOZ was evaluated in a 24-week, multicenter, randomized, double-blind, placebo-controlled trial (Study 1; NCT05090891). Sixty-three patients (28 adults and 35 pediatric patients 12 years of age and older) with FOP were randomized to ATEBRIOZ 100 mg (n = 32) or placebo (n = 31) once daily for 24 weeks. Patients who completed the 24-week double-blind period entered the 292-week open-label extension *[see Clinical Studies (14)]*. The adverse reactions reported by ≥ 10% of ATEBRIOZ-treated adults and pediatric patients aged 12 years and older and more frequently than placebo through Week 24 are listed in Table 1.

**Table 1: Adverse Reactions Occurring in ≥ 10% of Adults and Pediatric Patients Aged 12 Years and Older with FOP Receiving ATEBRIOZ and more Frequently than Placebo in Study 1 Through Week 24**

| **Adverse Reaction** | **ATEBRIOZ (N = 32) n (%)** | **Placebo (N = 31) n (%)** |
|---|---|---|
| Headache | 7 (22) | 5 (16) |
| Arthralgia | 7 (22) | 3 (10) |
| Upper respiratory tract infection | 7 (22) | 3 (10) |
| Epistaxis | 4 (13) | 0 |
| Nausea | 4 (13) | 1 (3) |

**Clinically Significant Adverse Reactions Occurring in < 10% of Patients with FOP**

In patients receiving ATEBRIOZ 100 mg orally once daily through Week 24, adverse reactions occurring in < 10% of patients included gastroenteritis, gastroesophageal reflux disease, iron deficiency anemia, rash (3 patients each), and alopecia (2 patients). None of these events were reported in the placebo group.

Laboratory Findings

*Increases in Serum Iron, Hemoglobin, and Transferrin Saturation*

Compared to placebo, ATEBRIOZ-treated patients experienced mean increases in serum iron, hemoglobin, and transferrin saturation levels; the mean values for all three measures remained within the normal range. No significant differences in mean ferritin change from baseline was observed between ATEBRIOZ- and placebo-treated patients, including patients who took iron supplements. Based on the data through Week 100, the increases in serum iron and transferrin saturation with ATEBRIOZ were not associated with signs or symptoms of iron overload.

# 7. DRUG INTERACTIONS

## 7.1. Effect of Other Drugs on ATEBRIOZ

Strong CYP3A4 Inhibitors

Reduce the ATEBRIOZ dosage to 50 mg once daily when used concomitantly with a strong CYP3A4 inhibitor *[see Dosage and Administration (2.3)]*.

ATEBRIOZ is a CYP3A4 substrate. Strong CYP3A4 inhibitors increase zilurgisertib exposure *[see Clinical Pharmacology (12.3)]*, which may increase the risk of ATEBRIOZ adverse reactions.

Strong and Moderate CYP3A4 Inducers

Avoid concomitant use of ATEBRIOZ with strong or moderate CYP3A4 inducers.

Strong or moderate CYP3A4 inducers decrease zilurgisertib plasma concentrations *[see Clinical Pharmacology (12.3)]*, which may reduce the effectiveness of ATEBRIOZ.

## 7.2. Effect of ATEBRIOZ on Other Drugs

MATE1 and MATE2-K Substrates

Avoid concomitant use of ATEBRIOZ with MATE1 and MATE2-K substrates (e.g., metformin). If unavoidable, monitor for adverse reactions and consider dose reduction of the substrates if appropriate, according to their approved prescribing information.

ATEBRIOZ is a MATE1 and MATE2-K inhibitor. ATEBRIOZ may increase exposure of substrates of MATE1 and MATE2-K, which may increase the risk of adverse events of MATE1 and MATE2-K substrates.

# 8. USE IN SPECIFIC POPULATIONS

## 8.1. Pregnancy

Risk Summary

ATEBRIOZ is contraindicated during pregnancy. Based on findings from animal reproduction studies and its mechanism of action, ATEBRIOZ can cause fetal harm when administered to a pregnant woman *[see Clinical Pharmacology (12.1)]*. There are no available data on the use of ATEBRIOZ during pregnancy to evaluate for a drug associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.

In animal reproduction studies, oral administration of zilurgisertib to pregnant rats during the period of organogenesis resulted in adverse outcomes, including embryofetal lethality, decreased fetal body weight, lower viability, and skeletal malformations (one or more fused sacral centra) at exposures ≥ 3-times the clinical exposure *(see Data)*. Advise pregnant women of the potential risk to a fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defects, loss, and other adverse outcomes. 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 a preliminary embryofetal developmental toxicity study, zilurgisertib was administered once daily orally to pregnant rats at doses of 1, 10, 50, 200 mg/kg during the period of organogenesis (gestation days 6 to 17). Zilurgisertib caused complete post-implantation loss at 200 mg/kg (14-times the clinical exposure based on AUC at the clinical dose of 100 mg). Increased post-implantation loss (early and late resorptions), decreased number of viable fetuses, low fetal body weight, and fetal skeletal malformations (one or more fused sacral centra) were observed at a dose of 50 mg/kg (approximately 3 times the human exposure based on AUC at the clinical dose of 100 mg).

In a pre- and post-natal development study, zilurgisertib was administered orally to pregnant rats at doses of 10, 20, and 40 mg/kg/day from implantation (gestation day 6) through lactation day 20. Maternal effects, including difficult parturition and dystocia were observed in dams administered 40 mg/kg/day (approximately 2-times the clinical exposure by AUC). Adverse developmental effects included low pup viability and malformations (bilateral retinal folds, small eye bulge, ventricular septal defect), reflex deficits (no pupillary light reflex on post-natal day 21), and lower femur width and length, abnormal tail morphology, kidney pelvic dilatation, and decreased mating index in the offspring at doses ≥ 20 mg/kg/day (at exposures equivalent to clinical exposures by AUC).

## 8.2. Lactation

Risk Summary

There are no data on the presence of zilurgisertib in human milk, the effects on the breastfed infant, or the effects on milk production. During the lactation period of the pre- and post-natal development study in rats, zilurgisertib was detected in rat pup plasma. Because of the potential for serious adverse reactions, including effects on bone development, in a breastfed infant, advise patients that breastfeeding is not recommended during treatment with ATEBRIOZ and for at least one week after the final dose.

## 8.3. Females and Males of Reproductive Potential

Based on animal data and mechanism of action, ATEBRIOZ can cause fetal harm when administered to pregnant women *[see Use in Specific Populations (8.1) and Clinical Pharmacology (12.1)]*.

Pregnancy Testing

Verify that the patient is not pregnant prior to initiating ATEBRIOZ *[see Dosage and Administration (2.1), Contraindications (4), and Warnings and Precautions (5.1)]*.

Contraception

*Females*

Advise females of reproductive potential to use effective contraception during treatment with ATEBRIOZ and for one week after the final dose.

## 8.4. Pediatric Use

The safety and effectiveness of ATEBRIOZ to reduce the volume of total new HO have been established in pediatric patients aged 12 years and older with FOP. Use of ATEBRIOZ for this indication is supported by evidence from an adequate and well-controlled study in 35 pediatric patients aged 12 to 16 years with FOP *[see Adverse Reactions (6.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*. The safety and effectiveness of ATEBRIOZ have not been established in pediatric patients younger than 12 years of age.

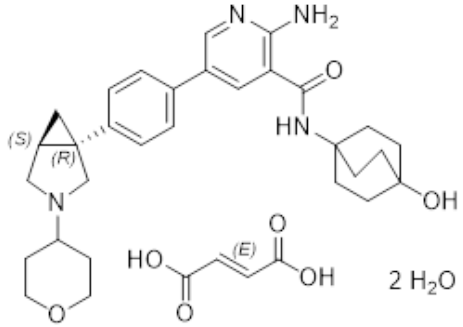
## 8.5. Geriatric Use

Clinical studies of ATEBRIOZ did not include sufficient numbers of patients 65 years of age and older to determine whether they respond differently from younger adult patients.

# 11. DESCRIPTION

ATEBRIOZ contains the active moiety zilurgisertib, an activin receptor–like kinase-2 (ALK-2) inhibitor, in the form of zilurgisertib fumarate dihydrate. The chemical name of zilurgisertib fumarate dihydrate is 2-amino-N-(4-hydroxybicyclo[2.2.2]octan-1-yl)-5-(4-((1R,5S)-3-(tetrahydro-2H-pyran-4-yl)-3-azabicyclo[3.1.0]hexan-1-yl)phenyl)nicotinamide fumarate dihydrate. Zilurgisertib fumarate dihydrate has a molecular formula of $C_{30}H_{38}N_4O_3$ $C_4H_4O_4$

$2H_2O$ and a molecular weight of 654.76 g/mol. Zilurgisertib fumarate dihydrate has the following chemical structure:




ATEBRIOZ (zilurgisertib) tablets, for oral use, is a white to off-white film-coated tablet that is round in appearance and debossed with "INCY" on one side and "25" on the other side. Each tablet contains 25 mg of zilurgisertib (equivalent to 32.55 mg of zilurgisertib fumarate dihydrate) and the following inactive ingredients, colloidal silicon dioxide, crospovidone, magnesium stearate, mannitol, and microcrystalline cellulose. The tablet coating consists of polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

# 12. CLINICAL PHARMACOLOGY

## 12.1. Mechanism of Action

FOP is a progressive disease caused by a monoallelic gain-of-function mutation in the activin A receptor, Type I (ACVR1) gene that codes the ALK2 Type I receptor in the bone morphogenetic protein (BMP) signaling pathway. Patients with FOP have constitutively active ALK2 signaling that causes HO. Zilurgisertib is an oral, and selective inhibitor of both wild-type ALK2 and pathogenic ALK2 (R206H mutation). Target engagement of zilurgisertib inhibits ALK2 mediated signaling and reduces endochondral bone formation.

## 12.2. Pharmacodynamics

Exposure-Response Relationships

The exposure-response relationship and time course of the pharmacodynamic response for the effectiveness and safety of zilurgisertib have not been fully characterized.

Cardiac Electrophysiology

Clinically significant QT interval prolongation was not observed at concentrations up to 6.7 times the mean maximum concentrations achieved with the recommended daily dose of ATEBRIOZ.

## 12.3. Pharmacokinetics

Zilurgisertib pharmacokinetics are presented as geometric mean (coefficient of variation [%CV]), unless otherwise specified.

In patients with FOP receiving zilurgisertib 100 mg once daily, the steady-state zilurgisertib AUC was 11980 nM·h (30.4%) and $C_{max}$ was 893 nM (35.4%). Following multiple doses, zilurgisertib exposure was slightly greater than dose-proportional at doses above 50 mg and steady-state was achieved by Day 5. Zilurgisertib exhibited a median accumulation ratio of 1.7-fold.

Absorption

Following a single dose of 100 mg zilurgisertib in healthy subjects, the median (minimum to maximum) time to peak zilurgisertib plasma concentration ($T_{max}$) was 2.1 hours (2.0 to 4.0 hours).

*Effect of Food*

Administration of a single dose of 100 mg zilurgisertib with a high-fat, high-calorie meal (50% calories from fat) had no clinically meaningful effect on zilurgisertib pharmacokinetics.

Distribution

The protein binding of zilurgisertib was 62.6%. The in vitro blood-to-plasma ratio was 1.04. The geometric mean (%CV) apparent volume of distribution (Vz/F) of zilurgisertib was 694 L (35.4%) after a single dose of 100 mg zilurgisertib in patients with FOP.

Elimination

After a single dose of 100 mg zilurgisertib in patients with FOP, the apparent clearance (CL/F) of zilurgisertib was 17.6 L/h (28.7%) and the elimination half-life ($t_{½}$) of zilurgisertib was 27.4 hours (23%).

*Metabolism*

Zilurgisertib is predominantly metabolized by CYP3A4 and to a minor extent by CYP2D6.

*Excretion*

Following a single oral 400 mg dose of radiolabeled zilurgisertib, 49% of the dose was recovered in feces (10% unchanged) and 38.5% in urine (28% unchanged).

Specific Populations

No clinically significant differences in the systemic exposure of zilurgisertib were observed based on age (12 to 80 years), sex (67% males, 33% females), race (74% White, 15% Black/African American, 6.5% Asian, and 2.6% other) or body weight (25 to 135 kg).

*Pediatric Patients*

In pediatric patients with FOP (12 to 16 years of age), the estimated steady-state AUC and $C_{max}$ for zilurgisertib was 11478 nM·h and 883 nM, respectively. Zilurgisertib accumulated with a median ratio of 1.6 following once daily dosing.

*Patients with Renal Impairment*

No significant difference in the exposure of zilurgisertib was observed in patients with mild renal impairment (eGFR 60-89 mL/min/1.73 $m^2$, MDRD) compared to healthy subjects with normal renal function. Zilurgisertib exposure ($AUC_{0-\infty}$) was approximately 64% higher in patients with moderate renal impairment (eGFR 30 to 59 mL/min/1.73 $m^2$), approximately 70% higher in

patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 $m^2$), and approximately 47% and 68% higher in patients with end-stage renal disease before and after hemodialysis (eGFR <15 mL/min/1.73 $m^2$), respectively, than in healthy subjects with normal renal function.

*Patients with Hepatic Impairment*

The zilurgisertib $C_{max}$ and AUC in patients with moderate hepatic impairment was comparable to healthy subjects with normal hepatic function. In patients with severe hepatic impairment, zilurgisertib AUC was 25% higher and $C_{max}$ was similar to that in subjects with normal hepatic function.

Drug Interaction Studies

*Clinical Studies and Model-Informed Approaches*

*Strong CYP3A4 Inhibitors:* Coadministration of itraconazole (a strong CYP3A4 inhibitor) increased the geometric mean $C_{max}$ and AUC of zilurgisertib 1.28-fold and 2.13-fold, respectively *[see Dose and Administration (2.3) and Drug Interactions (7.1)]*.

*Moderate CYP3A4 Inhibitors:* Coadministration of zilurgisertib with moderate CYP3A4 inhibitors (ciprofloxacin, erythromycin, and fluconazole) is predicted to increase the $C_{max}$ and AUC of zilurgisertib 1.09-1.13 and 1.50-1.78-fold, respectively.

*Strong CYP3A4 Inducers:* Coadministration of rifampin (a strong CYP3A4 inducer) decreased zilurgisertib $C_{max}$ and AUC by 56% and 79%, respectively *[see Drug Interactions (7.1)]*.

*Moderate CYP3A4 Inducers:* Concomitant use of efavirenz (a moderate CYP3A4 inducer) is predicted to decrease zilurgisertib $C_{max}$ and AUC by 25% and ~60%, respectively *[see Drug Interactions (7.1)]*.

*Strong and Moderate CYP2D6 Inhibitors:* Coadministration of paroxetine (a strong CYP2D6 inhibitor) and duloxetine is predicted to have negligible effect on zilurgisertib exposure.

*In Vitro Studies*

*Cytochrome P450 (CYP) Enzymes:* Zilurgisertib is a substrate of CYP3A4. Zilurgisertib does not inhibit CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2E1, CYP3A4, or CYP2D6 at clinically relevant concentrations. Zilurgisertib is not an inducer of CYP1A2, CYP2B6, or CYP3A4.

*Transporter Systems:* Zilurgisertib is a substrate of P-gp, BCRP and MRP2, but P-gp, BCRP or MRP2 inhibitors are not expected to affect zilurgisertib exposure at clinically relevant concentrations. Zilurgisertib is not a substrate of key hepatic transporters OATP, OAT, or OCT families. Zilurgisertib is not a substrate for renal transporters MATE1 and MATE2-K. Zilurgisertib is an inhibitor of MATE1 and MATE2-K and an inhibitor of OATP1B1, OATP1B3 and OCT2. Zilurgisertib is not an inhibitor of OAT1 or OAT3.

# 13. NONCLINICAL TOXICOLOGY

## 13.1. Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term carcinogenicity studies have not been conducted with zilurgisertib. In a 6-month repeat-dose toxicity study, rats orally administered zilurgisertib developed dose-dependent basophilic foci of cellular alterations (potential preneoplastic findings) and hepatic iron accumulation in the liver (at exposures comparable to clinical exposure). The liver findings in rats are consistent with the pharmacologic effects of zilurgisertib on iron homeostasis secondary to ALK2 inhibition. Chronic hepatic iron overload has been associated with hepatocarcinogenesis in animal models and in certain human disease states. The clinical relevance of these findings, including the potential carcinogenic risk in humans treated with zilurgisertib, is uncertain.

Zilurgisertib is not mutagenic based on the results of a bacterial mutagenicity assay. Zilurgisertib was not clastogenic in either an in vivo micronucleus assay or a comet assay in rats, and no genotoxic effects were observed in a 28-day oral toxicity study in rats.

In a fertility and early embryonic development study, zilurgisertib was administered orally to male rats at 0.3, 3, 15 or 60 mg/kg/day prior to and throughout mating and to female rats at 1, 10, 50 mg/kg/day or 200 mg/kg/day prior to mating and up to the implantation day (gestation day 7). Zilurgisertib had no effect on fertility or reproductive function in either male or female rats at doses up to 60 mg/kg/day and 200 mg/kg/day, respectively (9-and 11-times the human exposure based on AUC at the clinical dose of 100 mg, respectively).

# 14. CLINICAL STUDIES

The effectiveness of ATEBRIOZ was evaluated in a randomized, double-blind, placebo-controlled trial (Study 1; NCT05090891). Inclusion criteria included clinical diagnosis of FOP, patient-reported FOP disease activity within 1 year of the screening visit (i.e., FOP flare-ups, worsening joint function, or radiographic progression of HO), and a baseline Cumulative Analogue Joint Involvement Scale (CAJIS) score ≤ 23.

Sixty-three patients (28 adults and 35 pediatric patients aged 12 years of age and older) with FOP were randomized 1:1 to treatment with ATEBRIOZ 100 mg or placebo once daily for 24 weeks followed by a 292-week open label extension (OLE) period of ATEBRIOZ 100 mg treatment. Randomization was stratified by baseline CAJIS score (< 18 or 18-23).

The median age of enrolled patients was 16 years (range: 12 to 64 years), 56% were 12 to 16 years of age, 51% were female, 56% were White, 5% were Black/African American, 29% were Asian, 2% were multiracial, and 10% were race not reported or missing; 19% identified as Hispanic or Latino ethnicity. All patients had a baseline CAJIS score of ≤ 23 and 84% of patients had a score < 18 (range: 2-22). At baseline, the mean (SD) total volume of all HO lesions was 333.3 (257.1) $cm^3$ in the zilurgisertib group and 374.4 (376.5) $cm^3$ in the placebo group.

Efficacy was established based on the effect of ATEBRIOZ on total new HO lesion volume (assessed by whole-body computed tomography [WBCT], excluding the head) compared to placebo during the double-blind period. Total new HO lesion volume includes expansion of baseline HO lesion burden as well as any new discrete HO that developed during the 24-week

double-blind period. At Week 24, the mean change (SD) from baseline in total new HO volume was −3.2 $cm^3$ (19.9) in the zilurgisertib group and +24.6 $cm^3$ (51.9) in the placebo group, resulting in a Hodges-Lehmann treatment difference of −15.8 $cm^3$ (95% CI: -32.1, -6.0).

## 16. HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

ATEBRIOZ contains 25 mg of zilurgisertib and is available as a round, white to off-white film-coated tablet debossed on one side with "INCY" and "25" on the other side in bottles of 120 tablets with child-resistant closure (NDC 79378-029-16). Dispense in a tight container (See USP).

Storage and Handling

Store ATEBRIOZ tablets at 20ºC to 25ºC (68ºF to 77ºF); excursions permitted between 15ºC and 30ºC (59ºF and 86ºF) [see USP Controlled Room Temperature].

## 17. PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Administration Information

- Instruct patients to take ATEBRIOZ orally once daily with or without food.
- Inform patients and/or caregivers that ATEBRIOZ may be swallowed whole or crushed and mixed with liquid or soft food *[see Dosage and Administration (2.2)]*.

Embryo-Fetal Toxicity

ATEBRIOZ can cause fetal harm and is contraindicated during pregnancy. Advise females to immediately stop ATEBRIOZ and contact their healthcare provider if pregnancy occurs during treatment *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.1)]*.

Advise female patients of reproductive potential to use effective contraception, during treatment with ATEBRIOZ and for one week after the final dose *[see Use in Specific Populations (8.3)]*.

Lactation

Advise females not to breastfeed during treatment with ATEBRIOZ and for at least one week after the final dose *[see Use in Specific Populations (8.2)]*.

Drug Interactions

Advise patients to inform their healthcare providers of all concomitant medications, herbal and dietary supplements *[see Drug Interactions (7.1)]*.

Manufactured for:
Mirum Pharmaceuticals, Inc.
Foster City, CA 94404

Licensed from:
Incyte Corporation
Wilmington, DE 19803

ATEBRIOZ is a trademark of Incyte.



LB00332v1

**MEDICATION GUIDE**

**ATEBRIOZ™ (ah-TEB-ree-oz)**

**(zilurgisertib)**

**tablet, for oral use**

**What is the most important information I should know about ATEBRIOZ?**

**ATEBRIOZ can cause serious side effects, including:**

**Harm to your unborn baby including birth defects if taken during pregnancy. Females who are pregnant must not take ATEBRIOZ.**

- **Females who can become pregnant or plan to become pregnant:**
  - Your healthcare provider will ask you to take a pregnancy test before starting treatment with ATEBRIOZ to verify that you are not pregnant.
  - Use effective birth control (contraception) during treatment with ATEBRIOZ and for 1 week after the last dose of ATEBRIOZ. Talk to your healthcare provider about birth control methods that may be right for you.
  - If you become pregnant or think you may be pregnant during treatment with ATEBRIOZ, **stop taking ATEBRIOZ immediately and call your healthcare provider right away.**

**What is ATEBRIOZ?**

ATEBRIOZ is a prescription medicine used to reduce the amount of new abnormal bone growth outside of the skeleton (heterotopic ossification [HO]) in adults and pediatric patients aged 12 years and older with fibrodysplasia ossificans progressiva (FOP):

It is not known if ATEBRIOZ is safe and effective in children younger than 12 years of age.

**Who should not take ATEBRIOZ?**

**Do not** take ATEBRIOZ if you are pregnant. (See "**What is the most important information I should know about ATEBRIOZ?**")

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

- are breastfeeding or plan to breastfeed.
  - It is not known if ATEBRIOZ passes into your breast milk.
  - Breastfeeding is not recommended during treatment with ATEBRIOZ and for at least 1 week after the last dose of ATEBRIOZ.
  - Talk to your healthcare provider about the best way to feed your baby during this time.

**Tell your healthcare provider about all the medicines you take**, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ATEBRIOZ and certain other medicines can interact with each other, sometimes causing serious side effects.

Know the medicines you take. Keep a list of them to show to your healthcare provider and pharmacist when you get a new medicine.

**How should I take ATEBRIOZ?**

- Take ATEBRIOZ exactly as your healthcare provider tells you.
- **Do not** change your dose or stop taking ATEBRIOZ without first talking to your healthcare provider.
- Take ATEBRIOZ 1 time each day with or without food.
- For people who are unable to swallow whole tablets, ATEBRIOZ may be crushed and mixed in 4 tablespoons of water, orange juice, apple sauce, or plain yogurt. **Do not** take ATEBRIOZ with grapefruit, pomelo, or juices containing these fruits.

**What should I avoid while taking ATEBRIOZ?**

- Avoid becoming pregnant while taking ATEBRIOZ. (See "**What is the most important information I should know about ATEBRIOZ?**")
- **Do not** breastfeed while taking ATEBRIOZ. (See "**Before you take ATEBRIOZ, tell your healthcare provider about all of your medical conditions, including if you:**")

**What are the possible side effects of ATEBRIOZ?**

**ATEBRIOZ may cause serious side effects, including:**

- See "**What is the most important information I should know about ATEBRIOZ?**"

**The most common side effects of ATEBRIOZ include:**

- headache
- joint pain (arthralgia)
- common cold, sinus infections, or sore throat (upper respiratory tract infections)
- nosebleed (epistaxis)
- nausea

These are not all the possible side effects of ATEBRIOZ.

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 ATEBRIOZ?**

- Store ATEBRIOZ tablets between 68°F to 77°F (20°C to 25°C) in the original container.
- **Keep ATEBRIOZ and all medicines out of reach from children.**

**General information about the safe and effective use of ATEBRIOZ.**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use ATEBRIOZ for a condition for which it was not prescribed. Do not give ATEBRIOZ to other people, even if they have the same symptoms that you have. It may harm them. If you would like more information about ATEBRIOZ, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about ATEBRIOZ that is written for health professionals.

**What are the ingredients in ATEBRIOZ?**

**Active ingredient:** zilurgisertib

**Inactive ingredients:** colloidal silicon dioxide, crospovidone, magnesium stearate, mannitol, and microcrystalline cellulose. The tablet coating contains polyethylene glycol, polyvinyl alcohol, talc, and titanium dioxide.

Manufactured for: Mirum Pharmaceuticals, Inc., Foster City, CA 94404
Licensed from: Incyte Corporation, Wilmington, DE 19803

For more information, call 1-855-MRM-4YOU.

This Medication Guide has been approved by the U.S. Food and Drug Administration. Issued: 09/2026