PDL DRUG REVIEW

Proprietary Name: Lazcluze®
Common Name: lazertinib
PDL Category: Antineoplastics

Comparable Products	Preferred Drug List Status
Rybrevant (amivantamab)	Medical
Tagrisso (osimertinib)	Non-Recommended with Conditions

Pharmacology/Usage: Lazertinib, the active ingredient of Lazcluze®, is a kinase inhibitor of epidermal growth factor receptor (EGFR) that inhibits EGFR exon 19 deletions and exon 21 L858R substitution mutations at lower concentrations than wild-type EGFR.

Indication: In combination with amivantamab, is indicated for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test.

There is no pregnancy category for this medication; however, the risk summary indicates that based on findings from animal studies and its mechanism of action, Lazcluze® can cause fetal harm when administered to a pregnant woman. There are no available data on use in pregnant women to inform a drug-associated risk. Advise pregnant women of the potential risk to a fetus. Verify the pregnancy status of females of reproductive potential prior to starting Lazcluze®. In addition, advise females of reproductive potential to use effective contraception during treatment and for 3 weeks after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 weeks after the last dose. The safety and efficacy of use have not been established in the pediatric population.

Dosage Form: Film-Coated Tablets: 80mg and 240mg.

Swallow tablets whole; do not crush, split or chew.

Recommended Dosage: Select patients for the first-line treatment of NSCLC with Lazcluze®, in combination with amivantamab, based on the presence of EGFR exon 19 deletions or exon 21 L858R substitution mutations in tumor or plasma specimens. If these mutations are not detected in a plasma specimen, test tumor tissue. Information on FDA-approved tests is available at http://www.fda.gov/CompanionDiagnostics.

The recommended dosage is 240mg PO QD in combination with amivantamab with or without food. Continue until disease progression or unacceptable toxicity.

If a patient misses a dose of Lazcluze® within 12 hours, instruct patients to take the missed dose. If more than 12 hours has passed since the dose was to be given, instruct the patient to take the next dose at its scheduled time. If vomiting occurs any time after taking Lazcluze®, instruct the patient to take the next dose at its next regularly scheduled time.

Dose adjustments are not recommended in patients with mild or moderate renal impairment; however, use has not been studied in patients with severe renal impairment or end-stage renal disease. Dose

adjustments are not recommended in patients with mild or moderate hepatic impairment; however, use has not been studied in patients with severe hepatic impairment.

When starting Lazcluze® in combination with amivantamab, administer anticoagulant prophylaxis to prevent venous thromboembolic events (VTE) for the first four months of treatment. If there are no signs or symptoms of VTE during the first 4 months of treatment, consider discontinuation of anticoagulant prophylaxis at the discretion of the healthcare provider.

When starting Lazcluze® in combination with amivantamab, administer alcohol-free emollient cream and encourage patients to limit sun exposure during and for 2 months after treatment, to wear protective clothing and use broad-spectrum UVA/UVB sunscreen to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures to reduce the risk of dermatologic adverse reactions.

Refer to the prescribing information for information on dosage modifications for adverse reactions.

Drug Interactions: Lazertinib is a CYP3A4 substrate. Avoid concomitant use of Lazcluze® with strong and moderate CYP3A4 inducers. Consider an alternate concomitant medication with no potential to induce CYP3A4.

Lazertinib is a weak CYP3A4 inhibitor. Monitor for adverse reactions associated with a CYP3A4 substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the CYP3A4 substrate.

Lazertinib is a BCRP inhibitor. Monitor for adverse reactions associated with a BCRP substrate where minimal concentration changes may lead to serious adverse reactions, as recommended in the approved product labeling for the BCRP substrate, if use in combination with Lazcluze®.

Box Warning: There is no box warning listed with this product.

Common Adverse Drug Reactions: *Listed % incidence for adverse drug reactions= reported % incidence for drug (Lazcluze® in combination with amivantamab) minus reported % incidence for osimertinib for all grades. Please note that an incidence of 0% means the incidence was the same as or less than comparator.* The most frequently reported adverse events included rash (38%), nail toxicity (37%), dry skin (7%), pruritus (7%), infusion-related reaction (63%), musculoskeletal pain (8%), stomatitis (16%), diarrhea (0%), constipation (16%), nausea (7%), vomiting (7%), abdominal pain (1%), hemorrhoids (7.9%), edema (35%), fatigue (12%), pyrexia (3%), venous thromboembolism (28%), hemorrhage (12%), paresthesia (25%), dizziness (4%), headache (0%), COVID-19 (2%), conjunctivitis (9.4%), decreased appetite (6%), cough (0%), dyspnea (0%), ocular toxicity (9%), and insomnia (0%).

Laboratory abnormalities included decreased albumin (67%), increased ALT (36%), increased AST (16%), increased alkaline phosphatase (30%), decreased calcium, corrected (14%), increased GGT (15%), decreased sodium (3%), decreased potassium (15%), increased creatinine (0%), decreased magnesium (15%), increased magnesium (0%), decreased platelet count (0%), decreased hemoglobin (0%), decreased white blood cell (0%), and decreased neutrophils (0%).

Lazcluze® in combination with amivantamab can cause serious and fatal venous thromboembolic events (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE). The majority of these events occurred during the first four months of therapy. Administer prophylactic anticoagulation for the first four months of treatment. The use of vitamin K antagonists is not recommended. Monitor for signs and symptoms of VTE and treat as medically appropriate. Refer to the prescribing information for additional information.

Lazcluze® in combination with amivantamab can cause interstitial lung disease (ILD)/pneumonitis. Monitor patients for new or worsening symptoms indicative of ILD/pneumonitis. Immediately withhold Lazcluze® and amivantamab in patients with suspected ILD/pneumonitis and permanently discontinue if ILD/pneumonitis is confirmed.

Lazcluze® in combination with amivantamab can cause severe rash including dermatitis acneiform, pruritus, and dry skin. The median time to onset of rash was 14 days. When starting treatment with Lazcluze® in combination with amivantamab, administer alcohol-free emollient cream to reduce the risk of dermatologic adverse reactions. Consider prophylactic measures (e.g., use of oral antibiotics) to reduce the risk of dermatologic adverse reactions. If skin reactions develop, administer topical corticosteroids and topical and/or oral antibiotics. Promptly refer patients presenting with severe rash, atypical appearance or distribution, or lack of improvement within 2 weeks to a dermatologist. Withhold, reduce the dose or permanently discontinue Lazcluze® and amivantamab based on severity. Also refer to the recommended dosage section for further information.

Lazcluze® in combination with amivantamab, can cause ocular toxicity, including keratitis. Promptly refer patients presenting with new or worsening eye symptoms to an ophthalmologist. Withhold, reduce the dose, or permanently discontinue amivantamab and continue Lazcluze® based on severity.

Contraindications: There are no contraindications listed with this product.

Manufacturer: Janssen Biotech, Inc.

Analysis: The efficacy of Lazcluze® in combination with amivantamab, was assessed in MARIPOSA, a randomized, active-controlled, multicenter study that included patients required to have untreated locally advanced or metastatic NSCLC with either exon 19 deletions or exon 21 L858R substitution EGFR mutations identified by local testing, not amenable to curative therapy. Patients with asymptomatic or previously treated and stable intracranial metastases were eligible to enroll. Patients were randomized to receive Lazcluze® in combination with amivantamab (N=429), osimertinib monotherapy (N=429), or Lazcluze® monotherapy (an unapproved regimen for NSCLC) until disease progression or unacceptable toxicity.

The evaluation of efficacy for the treatment of untreated metastatic NSCLC relied upon comparison between:

- Lazcluze® 240mg PO QD in combination with amivantamab IV at 1050mg or 1400mg (per weight) QW for 4 weeks, then Q2W thereafter starting at week 5.
- Osimertinib 80mg PO QD.

Tumor assessments were performed every 8 weeks for 30 months, and then every 12 weeks until disease progression. The median age of included patients was 63 years (range 25-88), while 61% were female, 58% were Asian, 69% had never smoked, 41% had prior brain metastases, 34% had Eastern Cooperative Oncology Group (ECOG) performance status 0 and 66% had ECOG performance status of 1. In addition, 60% had tumors harboring exon 19 deletions and the remaining 40% had exon 21 L858R substitution mutations.

The main efficacy outcome measure was progression-free survival (PFS) as assessed by blinded independent central review (BICR). Additional efficacy outcome measures included overall survival (OS), overall response rate (ORR), and duration of response (DOR). Results suggested a statistically significant improvement in PFS by BICR assessment for Lazcluze® in combination with amivantamab as compared to osimertinib. Results are presented in the table below, which was adapted from the prescribing information.

	Lazcluze® in combination with amivantamab (N=429)	Osimertinib (N=429)
Progression-free survival (PFS)		
Number of events (%)	192 (45%)	252 (59%)
Median, months	23.7	16.6
HR; p-value	0.70; p=0.0002	
ORR		
ORR, %	78%	73%
Complete response, %	5%	3.5%
Partial response, %	73%	70%
DOR		
Median, months	25.8	16.7
Patients with DOR ≥6 months, %	86%	85%
Patients with DOR ≥12 months, %	68%	57%

While OS results were immature at the current analysis, with 55% of pre-specified deaths for the final analysis reported, no trend towards a detriment was observed.

Out of all randomized patients, 367 (43%) had baseline intracranial lesions assessed by BICR using modified RECIST. Results of pre-specified analyses of intracranial ORR and DOR by BICR in the subset of patients with intracranial lesions at baseline for the Lazcluze® in combination with amivantamab arm and the osimertinib arm are presented in the table below, which was adapted from the prescribing information.

	Lazcluze® in combination with amivantamab (N=180)	Osimertinib (N=187)
Intracranial Tumor Response Assessment		
Intracranial ORR, %	68%	69%
Complete response, %	55%	52%
Intracranial DOR		
Number of responders	122	129
Patients with DOR ≥12 months, %	66%	59%
Patients with DOR ≥18 months, %	35%	23%

Place in Therapy: Lazcluze® is a kinase inhibitor indicated in combination with amivantamab for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 L858R substitution mutations, as detected by an FDA-approved test. The efficacy of Lazcluze® in combination with amivantamab was

assessed in a randomized, active-controlled study that compared treatment with osimertinib monotherapy. Results suggested a statistically significant improvement in PFS (primary endpoint) by BICR assessment for Lazcluze® in combination with amivantamab as compared to osimertinib.

Summary

It is recommended that Lazcluze® should be non-recommended in order to confirm the appropriate diagnosis and clinical parameters for use.

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

References

[1] Lazcluze [package insert]. Horsham, PA: Janssen Biotech, Inc; 2024.

Prepared By: Iowa Medicaid Date: 09/23/2024