PDL DRUG REVIEW

Proprietary Name: Alecensa®
Common Name: alectinib
PDL Category: Antineoplastics Protein Tyrosine Kinase Inhibitors

Comparable Products	Preferred Drug List Status
Xalkori	Non-Recommended with Conditions
Zykadia	Non-Recommended with Conditions

Summary

Pharmacology/Usage: Alectinib, the active ingredient of Alecensa®, is a tyrosine kinase inhibitor that targets ALK and RET. The major active metabolite of alectinib, M4, showed similar in vitro potency and activity. Alectinib and M4 showed in vitro and in vivo activity against multiple mutant forms of the ALK enzyme, including some mutations identified in NSCLC tumors in patients who have progressed on crizotinib.

Indication: For the treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib. This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.

There is no pregnancy category for this product; however, the risk summary indicates that based on animal studies and its mechanism of action, Alecensa® may cause fetal harm when administered to a pregnant woman. There are no available data on use in pregnant women. It is recommended to advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 1 week after the final dose; males with female partners of reproductive potential should use contraception during treatment and for 3 months following the final dose. The safety and efficacy of use in the pediatric population have not been established.

Dosage Forms: Capsules: 150mg

Recommended Dosage: Take 600mg PO BID with food until disease progression or unacceptable toxicity. The capsules should not be opened or the contents dissolved. Dose modifications may be needed due to adverse reactions, and a specific dose reduction schedule should be followed. This includes a first dose reduction of 450mg PO BID and then a second dose reduction of 300mg BID. Treatment should be discontinued if patients are not able to tolerate the 300mg BID dose. Please refer to the prescribing information for specific dose modifications based on adverse reactions.

Dose adjustments are not required for patients with mild or moderate renal impairment or for patients with mild hepatic impairment (total bilirubin ≤ upper limit of normal [ULN] and aspartate transaminase [ST] > ULN or total

bilirubin > 1 to 1.5 times ULN and any AST). The safety in use with severe renal impairment or end-stage renal, as well as in patients with moderate or severe hepatic impairment disease, has not been studied.

Drug Interactions: No interactions with Alecensa® requiring dose adjustments have been identified.

Common Adverse Drug Reactions: *There was no placebo data available to compare with Alecensa®. The listed % incidence for adverse drug reactions= reported % incidence in ≥10% (all grades) of patients in 2 studies.* The most frequently reported adverse events included fatigue (41%), constipation (34%), edema (30%), myalgia (29%), cough (19%), rash (18%), nausea (18%), headache (17%), diarrhea (16%), dyspnea (16%), back pain (12%), vomiting (12%), increased weight (11%), and vision disorder (10%). Laboratory abnormalities (occurring in >20% of patients in 2 studies) included increased AST (51%), increased alkaline phosphatase (47%), increased creatine phosphokinase (43%), hyperbilirubinemia (39%), hyperglycemia (36%), increased ALT (34%), hypocalcemia (32%), hypokalemia (29%), increased creatinine (28%), hypophosphatemia (21%), and hyponatremia (20%). Anemia (56%) and lymphopenia (22%) were also reported.

Adverse reactions that could require dose modifications include elevations of hepatic enzymes, treatment-related interstitial lung disease/pneumonitis, symptomatic bradycardia, bradycardia with life-threatening consequences and urgent intervention, and elevations in blood creatine phosphokinase.

Contraindications: There are currently no contraindications listed with this product.

Manufacturer: Genentech

Analysis: The safety and efficacy of Alecensa® were established in 2 single-arm, multicenter trials (Study 1 and 2) that included patients with locally advanced or metastatic ALK-positive NSCLC who had progressed on crizotinib and had documented ALK positive NSCLC based on an FDA-approved test. Study 1 (N=87) was conducted in North America and Study 2 (N=138) was conducted internationally. The main efficacy outcome in both studies were objective response rate (ORR) as assessed per Independent Review Committee (IRC), as well as duration of response (DOR). The median duration of follow-up with Study 1 was 4.8 months for both IRC and Investigator assessments, while with Study 2 it was 10.9 months for IRC assessment and 7.0 months for Investigator Assessments. All responses were partial responses, and results can be seen in the table below.

Efficacy Outcome	Study 1 (N=87)		Study 2 (N=138)	
	IRC Assessment	Investigator Assessment	IRC Assessment	Investigator Assessment
ORR	38%	46%	44%	48%
Number of Responders	33	40	61	66
Duration of Responders, median in months	7.5	NE	11.2	7.8

A subgroup analysis (N=51) was also performed to assess ORR and duration of response for CNS metastases of patients in both studies with baseline measurable lesions in the CNS. There were 35 patients (69%) with measurable lesions who had received prior brain radiation, including 25 patients (49%) who completed radiation treatment ≥6 months before starting Alecensa®. Results are illustrated in the table below.

Efficacy Outcome	N=51
CNS ORR	61%
Complete Response	18%
Partial Response	43%
CNS Duration of Response, median in months	9.1

Place in Therapy: Alectinib is considered a second generation ALK inhibitor. One noted reference source recommends the initial use with crizotinib rather than chemotherapy for patients with advanced or metastatic NSCLC that have an ALK fusion oncogene.[2] While ceritinib is also available as an ALK inhibitor, alectinib (Alecensa®) is another treatment option available to patients whose disease has progressed while on crizotinib or who are intolerant to crizotinib.

It is recommended that Alecensa® require clinical prior authorization to verify diagnosis and that there has been an intolerance of crizotinib (Xalkori®) or a prior trial of it with subsequent progression.

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

References

[1] Alecensa [package insert]. South San Francisco, CA: Genentech USA, Inc, a member of the Roche Group; 2015.
[2] UpToDate desktop reference. Anaplastic lymphoma kinase (ALK) fusion oncogene positive non-small cell lung cancer. Accessed January 2016.