CENTENE PHARMACY AND THERAPEUTICS
DRUG REVIEW
1Q18 (January – February)

BRAND NAME
Alecensa®

GENERIC NAME
Alectinib

MANUFACTURER
Genentech, Inc.

DATE OF APPROVAL
November 06, 2017

PRODUCT LAUNCH DATE
Currently commercially available

REVIEW TYPE
☐ Review type 1 (RT1): New Drug Review
Full review of new chemical or biologic agents

☒ Review type 2 (RT2): New Indication Review
Abbreviated review of new dosage forms of existing agents that are approved for a new indication or use

☐ Review type 3 (RT3): Expedited CMS Protected Class Drug Review
Expedited abbreviated review of Centers for Medicare & Medicaid Services protected class drugs (anticonvulsants, antidepressants, antineoplastic, antipsychotics, antiretrovirals, and immunosuppressants)

☐ Review type 5 (RT5): Abbreviated Review for Intravenous Chemotherapy Agents
Abbreviated review for intravenous chemotherapy agents which are usually covered under the medical benefit

FDA APPROVED INDICATION(S)
New/Revised Indication(s)
Treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test.[1]

Current Indication(s)
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.

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OFF LABEL USES
Not applicable

CLINICAL EFFICACY

	Peters S, Camidge DR, Shaw AT, et al. Alectinib versus crizotinib in untreated ALK-positive NSCLC[2]
Study Design	Phase 3 international open-label, randomized, active-controlled, multicenter study (ALEX: NCT02075840) - patients with no prior systemic therapy for ALK-positive, metastatic NSCLC were randomized 1:1 to alectinib vs crizotinib.
N	303
Drug Regimen	Alectinib 600 mg PO BID vs crizotinib 250 mg PO BID
Primary Outcome(s)	Investigator-assessed progression-free survival after 12 months
Secondary Outcome(s)	Independent review committee–assessed progression-free survival, time to CNS progression, objective response rate, and overall survival.
Results	Compared with crizotinib, alectinib showed superior efficacy and lower toxicity in primary treatment of ALK-positive NSCLC. • The rate of investigator-assessed progression-free survival was significantly higher with alectinib than with crizotinib (12-month event-free survival rate, 68.4% [95% confidence interval (CI), 61.0 to 75.9] with alectinib vs. 48.7% [95% CI, 40.4 to 56.9] with crizotinib; hazard ratio for disease progression or death, 0.47 [95% CI, 0.34 to 0.65]; P<0.001); the median progression-free survival with alectinib was not reached (95% CI, 17.7 months to not estimable), as compared with 11.1 months (95% CI, 9.1 to 13.1) with crizotinib. o The results for independent review committee–assessed progression-free survival were consistent with those for the primary end point. • A total of 18 patients (12%) in the alectinib group had an event of CNS progression, as compared with 68 patients (45%) in the crizotinib group (cause-specific hazard ratio, 0.16; 95% CI, 0.10 to 0.28; P<0.001). A response occurred in 126 patients in the alectinib group (response rate, 82.9%; 95% CI, 76.0 to 88.5) and in 114 patients in the crizotinib group (response rate, 75.5%; 95% CI, 67.8 to 82.1) (P = 0.09).
# Withdrew due to Lack of Efficacy	Not reported
# Withdrew due to Adverse Effects	Grade 3 to 5 adverse events were less frequent with alectinib (41% vs. 50% with crizotinib). No patients withdrew from alectinib due to adverse events; 2 patients withdrew from crizotinib due to adverse events.

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CONTRAINDICATIONS
Not applicable

BLACK BOX WARNINGS
Not applicable

DRUG INTERACTIONS
Not applicable

ADVERSE REACTIONS
Incidence ≥20%: fatigue, constipation, edema, myalgia, and anemia.

DOSAGE AND ADMINISTRATION
600 mg PO BID

PRODUCT AVAILABILITY
Capsules: 150 mg

THERAPEUTIC ALTERNATIVES [3,4,5]

Drug Name	USAGE REGIMEN	COMMENTS
Xalkori® (crizotinib)*	ALK positive NSCLC: 250 mg PO BID	• Labeled for first- and second-line treatment. • NCCN: First-line treatment (1 if ALK rearrangement discovered prior to first-line chemotherapy; otherwise 2A); second-line treatment (2A).
Zykadia™ (ceritinib)*	ALK positive NSCLC: 750 mg PO QD	• Labeled for first- and second-line treatment. • NCCN: First-line treatment (1 if ALK rearrangement discovered prior to first-line chemotherapy; otherwise 2A); second-line treatment (2A).
Alunbrig™ (brigatinib)*	ALK positive NSCLC: 90 mg PO QDF for the first 7 days; if tolerated, increase to 180 mg PO QD	• Labeled for second-line treatment. • NCCN: Second-line treatment (2A).

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

**Requires Prior Authorization*

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Utilization Management Recommendation
1) There is significant potential for inappropriate use and utilization management should be maintained for the following reason(s): ☒ Opportunity exists to obtain clinically significant medical or laboratory information necessary to determine appropriate use of the medication. i) NSCLC is ALK-positive and either recurrent or metastatic; ii) Recommended utilization management tool(s): (check all that apply) (1) ☒ Prior authorization (2) ☐ Quantity limits (3) ☐ Provider newsletter (4) ☐ Hard block (plan exclusion) (5) ☐ Messaging (6) ☐ Electronic step therapy (7) ☐ Clinical program iii) Alecensa currently requires a PA; recommend to maintain PA status.
Product Comparison
• As first-line systemic therapy, it would be clinically appropriate to require a trial of Alecensa prior to Xalkori or Zykadia or to provide equal access to all three agents. • As subsequent systemic therapy, it would be clinically appropriate to provide equal access to Alecensa, Xalkori and Zykadia. • If subsequent specifically to ALK tyrosine kinase inhibitor therapy, it would be clinically appropriate to provide equal access to Alecensa, Xalkori, Zykadia, and Alunbrig.

REFERENCES

[1] Alecensa Prescribing Information. South San Francisco, CA: Genentech USA, Inc. November 2017. Available at https://www.gene.com/download/pdf/alecensa_prescribing.pdf. Accessed December 2017.
[2] Peters S, Camidge DR, Shaw AT, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer. New England Journal of Medicine. August 31, 2017; 377(9): 829-38. DOI: 10.1056/NEJMoa1704795
[3] Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2016. Available at: http://www.clinicalpharmacology-ip.com/. Accessed December 2017.
[4] National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. V1.2018. Available at http://www.nccn.org. Accessed December 2017.
[5] National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed December 2017.