Alectinib: Drug information

(For additional information see "Alectinib: Patient drug information")

For abbreviations and symbols that may be used in Lexicomp (show table)

Brand Names: US

Alecensa

Brand Names: Canada

Alecensaro

Pharmacologic Category

Antineoplastic Agent, Anaplastic Lymphoma Kinase Inhibitor; Antineoplastic Agent, Tyrosine Kinase Inhibitor

Dosing: Adult

Non-small cell lung cancer (NSCLC), metastatic (ALK-positive): Oral: 600 mg twice daily; continue until disease progression or unacceptable toxicity (Ou 2016)

Missed doses: If a dose is missed or if vomiting occurs, take the next dose at the regularly scheduled time.

Dosing: Geriatric

Refer to adult dosing.

Dosing: Renal Impairment

CrCl ≥30 mL/minute: No dosage adjustment is necessary.

CrCl <30 mL/minute or ESRD: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Dosing: Hepatic Impairment

Preexisting hepatic impairment:

Mild impairment (total bilirubin ≤ULN and AST >ULN **or** total bilirubin >1 to 1.5 times ULN and any AST): No dosage adjustment is necessary.

Moderate or severe impairment: There are no dosage adjustments provided in the manufacturer's labeling (has not been studied).

Hepatotoxicity during treatment:

ALT or AST >5 times ULN **and** total bilirubin ≤2 times ULN: Withhold alectinib; upon recovery to baseline or to ALT/AST ≤3 times ULN, may resume at a reduced dose.

ALT or AST >3 times ULN **and** total bilirubin >2 times ULN (in the absence of cholestasis or

hemolysis): Permanently discontinue.

Total bilirubin >3 times ULN: Withhold alectinib; upon recovery to baseline or to total bilirubin ≤1.5 times ULN, may resume at a reduced dose.

Dosing: Adjustment for Toxicity

Recommended alectinib dosage reductions for toxicity:

Initial starting dose: 600 mg twice daily

First dose reduction: 450 mg twice daily

Second dose reduction: 300 mg twice daily

If unable to tolerate 300 mg twice daily, discontinue alectinib

Cardiac toxicity:

Symptomatic bradycardia: Withhold alectinib until recovery to asymptomatic bradycardia or until the heart rate is ≥60 beats per minutes (bpm). If a contributing concomitant medication is identified and discontinued (or dose adjusted), resume alectinib at the previous dose upon recovery (to asymptomatic bradycardia or heart rate ≥60 bpm). If no contributing concomitant medication is identified (or cannot be discontinued or dose adjusted), resume alectinib at a reduced dose upon recovery (to asymptomatic bradycardia or heart rate ≥60 bpm).

Life-threatening bradycardia/heart rate <60 bpm (urgent intervention required): Permanently discontinue alectinib if no contributing concomitant medication is identified. If a contributing concomitant medication is identified and discontinued (or dose adjusted), resume alectinib (with frequent monitoring) at a reduced dose upon recovery to asymptomatic bradycardia or to a heart rate ≥60 bpm. Permanently discontinue for recurrent life-threatening bradycardia.

CPK elevation:

CPK >5 times ULN: Withhold alectinib; upon recovery to baseline or to ≤2.5 times ULN, may resume alectinib at the same dose.

CPK >10 times ULN or 2nd occurrence of CPK >5 times ULN: Withhold alectinib; upon recovery to baseline or to ≤2.5 times ULN, may resume alectinib at a reduced dose.

Pulmonary toxicity: Interstitial lung disease (ILD)/pneumonitis, any grade (treatment-related): Permanently discontinue

Dosage Forms

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, Oral:

Alecensa: 150 mg

Generic Equivalent Available (US)

No

Dosage Forms: Canada

Information with regard to form, strength, and availability of products

uniquely available in Canada but currently not available in the US. Refer also to Dosage forms.

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Capsule, Oral:

Alecensaro: 150 mg

Prescribing and Access Restrictions Available through specialty pharmacies and distributors. Further information may be obtained from the manufacturer, Genentech, at 1-888-249-4918 or at https://www.alecensa.com/.

Administration

Administer with food. Swallow capsule whole; do not open or dissolve the contents of the capsule. If vomiting occurs after taking the dose, do not administer an extra dose; administer the next dose at the regularly scheduled time.

Hazardous Drugs Handling Considerations

Hazardous agent (meets NIOSH 2016 criteria). This medication is not on the NIOSH (2016) list; however, it meets the criteria for a hazardous drug. Drugs are classified as hazardous based on their properties; the properties of a hazardous drug include one or more of the following characteristics: carcinogenic, teratogenic (or other developmental toxicity), reproductive toxicity, organotoxic at low doses, genotoxic, and/or new agents with structural or toxicity profiles similar to existing hazardous agents.

Use appropriate precautions for receiving, handling, administration, and disposal. Gloves (single) should be worn during receiving, unpacking, and placing in storage. NIOSH recommends single gloving for administration of intact tablets or capsules (NIOSH 2016).

Use **Non-small cell lung cancer, metastatic:** 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.

Medication Safety Issues

Sound-alike/look-alike issues:

Alectinib may be confused with afatinib, axitinib, brigatinib, ceritinib, crizotinib

Alecensa may be confused with Alesse

High alert medication:

This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes which have a heightened risk of causing significant patient harm when used in error.

Adverse Reactions

>10%:

Cardiovascular: Edema (30%), bradycardia (8% to 20%)

Central nervous system: Fatigue (≤41%), headache (17%)

Dermatologic: Skin rash (18%)

Endocrine & metabolic: Hyperglycemia (36%), hypocalcemia (32%), hypokalemia (29%), hypophosphatemia (21%), hyponatremia (20%), weight gain (11%)

Gastrointestinal: Constipation (34%), nausea (18%), diarrhea (16%), vomiting (12%)

Hematologic & oncologic: Anemia (56%, grades 3/4: 2%), lymphocytopenia (22%, grades 3/4: 5%)

Hepatic: Increased serum AST (51%, grades 3/4: 4%), increased serum alkaline phosphatase (47%), hyperbilirubinemia (39%, grades 3/4: 2% to 3%), increased serum ALT (34%, grades 3/4: 5%)

Neuromuscular & skeletal: Increased creatine phosphokinase (43%, grades 3/4: 5%), weakness (≤41%), musculoskeletal pain (≤29%), myalgia (≤29%), back pain (12%)

Renal: Increased serum creatinine (28%)

Respiratory: Cough (19%), dyspnea (16%)

1% to 10%:

Cardiovascular: Pulmonary embolism (1%)

Dermatologic: Photosensitivity dermatitis (10%)

Ophthalmic: Visual disturbances (10%)

<1%, postmarketing, and/or case reports: Interstitial pulmonary disease, pneumonitis

Contraindications

There are no contraindications listed in the manufacturer's US labeling.

Canadian labeling: Known hypersensitivity to alectinib or any component of the formulation.

Warnings/Precautions

Concerns related to adverse effects:

• Bradycardia: Symptomatic bradycardia may occur; heart rate <50 beats per minute has been reported in ~20% of patients treated with alectinib. Monitor heart rate and blood pressure regularly. If symptomatic bradycardia (non-life-threatening) occurs, withhold treatment until recovery to asymptomatic bradycardia or to a heart rate of ≥60 beats per minute, evaluate concurrent medications, and potentially reduce alectinib dose. Permanently discontinue for life-threatening bradycardia due to alectinib if no contributing concomitant medication is identified and for recurrent bradycardia. If life-threatening bradycardia occurs and concurrent medications associated with bradycardia can be discontinued or dose adjusted, restart alectinib at a reduced dose (with frequent

monitoring).

• Hepatotoxicity: Liver function test abnormalities have been reported, including elevations of AST/ALT >5 times ULN and bilirubin >3 times ULN; most abnormalities occurred during the first 3 months of therapy. Concurrent ALT/AST elevations ≥3 times ULN and total bilirubin ≥2 times ULN with normal alkaline phosphatase occurred rarely. Liver biopsy demonstrated drug induced liver injury in some patients with grade 3 to 4 AST or ALT elevations. Monitor liver function tests (ALT, AST, and total bilirubin) every 2 weeks during the first 3 months of therapy and then once a month and as clinically necessary; monitor more frequently in patients who develop transaminase and bilirubin elevations. May require therapy interruption, dose reduction, or permanent discontinuation.

• Myalgia: Myalgia or musculoskeletal pain occurred in over one-quarter of patients treated with alectinib (including grade 3 toxicity). Elevations of creatine phosphokinase (CPK) were reported in close to half of patients in clinical trials. The median time to grade 3 CPK elevations was 14 days. Monitor; advise patients to report unexplained muscle pain, tenderness, or weakness. Assess CPK every 2 weeks for the first month of therapy and then as clinically necessary. May require therapy interruption and/or dose reduction.

• Photosensitivity: Photosensitivity occurred in some patients. Patients should avoid sun exposure (during treatment and for 7 days after the final dose) and use a broad spectrum sunscreen and lip balm (SPF ≥50).

• Pulmonary toxicity: Severe interstitial lung disease (ILD) has been reported rarely. Monitor for ILD/pneumonitis; evaluate promptly in patients who present with worsening of respiratory symptoms or who have signs/symptoms suggestive of ILD/pneumonitis (eg, cough, dyspnea, fever). Immediately interrupt therapy for confirmed ILD/pneumonitis; permanently discontinue if alectinib is determined to be the causative factor.

Concurrent drug therapy issues:

• Drug-drug interactions: Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Other warnings/precautions:

• Anaplastic lymphoma kinase testing: Approved for use only in patients with metastatic non-small cell lung cancer (NSCLC) who test positive for the abnormal anaplastic lymphoma kinase (ALK) gene.

Metabolism/Transport Effects

Substrate of CYP3A4 (minor); **Note:** Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Drug Interactions

(For additional information: Launch drug interactions program) Lexicomp®

Bradycardia-Causing Agents: May enhance the bradycardic effect of other Bradycardia-Causing Agents. *Risk C: Monitor therapy*

Bretylium: May enhance the bradycardic effect of Bradycardia-Causing Agents. Bretylium may also enhance atrioventricular (AV) blockade in patients receiving AV blocking agents. *Risk C: Monitor therapy*

Ceritinib: Bradycardia-Causing Agents may enhance the bradycardic effect of Ceritinib. Management: If this combination cannot be avoided, monitor patients for evidence of symptomatic bradycardia, and closely monitor blood pressure and heart rate during therapy. *Risk X: Avoid combination*

Ivabradine: Bradycardia-Causing Agents may enhance the bradycardic effect of Ivabradine. *Risk C: Monitor therapy*

Lacosamide: Bradycardia-Causing Agents may enhance the AV-blocking effect of Lacosamide. *Risk C: Monitor therapy*

Ruxolitinib: May enhance the bradycardic effect of Bradycardia-Causing Agents. Management: Ruxolitinib Canadian product labeling recommends avoiding use with bradycardia-causing agents to the extent possible. *Risk C: Monitor therapy*

Tofacitinib: May enhance the bradycardic effect of Bradycardia-Causing Agents. *Risk C: Monitor therapy*

Pregnancy Implications Based on data from animal reproduction studies and its mechanism of action, alectinib may be expected to cause fetal harm if administered during pregnancy. Women of reproductive potential should use effective contraception during therapy and for 1 week after the final dose. Males with female partners of reproductive potential should use effective contraception during therapy and for 3 months after the last dose.

Breast-Feeding Considerations It is not known if alectinib is excreted in breast milk. Due to the potential for serious adverse reactions in the nursing infant, the manufacturer does not recommend breast-feeding during therapy or for 1 week after the final dose.

Monitoring Parameters Test for ALK positivity. Liver function tests (ALT, AST, total bilirubin) every 2 weeks during the first 3 months of therapy, then monthly and as clinically necessary (monitor more frequently in patients who develop transaminase and bilirubin elevations; CPK levels every 2 weeks for the first month of therapy, then as clinically necessary; monitor heart rate and blood pressure regularly; monitor for signs/symptoms of interstitial lung disease/pneumonitis and myalgia.

Mechanism of Action Alectinib is a tyrosine kinase receptor inhibitor which inhibits anaplastic lymphoma kinase (ALK) and RET (with similar potency to ALK; Ou 2016). ALK gene abnormalities due to mutations or translocations may result in expression of oncogenic fusion proteins (eg, ALK fusion protein) which alter signaling and expression and result in increased cellular proliferation and survival in tumors which express these fusion proteins. Inhibition of ALK phosphorylation and ALK-mediated activation of downstream signaling results in decreased tumor cell viability. Alectinib is more potent than crizotinib against ALK, and can inhibit most of the clinically observed acquired ALK resistance mutations to crizotinib (Ou 2016).

Pharmacodynamics/Kinetics

Absorption: A high-fat, high-calorie meal increased the combined exposure of alectinib plus its active metabolite M4 by 3.1-fold

Distribution: Parent drug: 4,016 L; M4 (active metabolite): 10,093 L; distributes in the CSF at approximately the free concentrations in plasma

Protein binding: >99% to plasma proteins

Metabolism: Hepatic via CYP3A4 to major active metabolite M4; M4 is also metabolized by CYP3A4

Bioavailability: 37% (under fed conditions)

Half-life elimination: Parent drug: 33 hours; M4: 31 hours

Time to peak: 4 hours

Excretion: Feces (98%; 84% as unchanged parent drug and 6% as M4); urine (<0.5%)

Pricing: US

Capsules (Alecensa Oral)

150 mg (240): $15976.33

Disclaimer: The pricing data provide a representative AWP and/or AAWP price from a single manufacturer of the brand and/or generic product, respectively. The pricing data should be used for benchmarking purposes only, and as such should not be used to set or adjudicate any prices for reimbursement or purchasing functions. Pricing data is updated monthly.

International Brand Names

Alecensa (HK, JP)

REFERENCES

1. *Alecensa (alectinib) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; November 2016.*
2. *Alecensaro (alectinib) [product monograph]. Mississauga, Ontario, Canada: Hoffmann-La Roche Limited; September 2016.*
3. *Ou SI, Ahn JS, De Petris L, et al. Alectinib in crizotinib-refractory ALK-rearranged non-small-cell lung cancer: a phase II global study. J Clin Oncol. 2016;34(7):661-668. [PubMed 26598747]*
4. *US Department of Health and Human Services; Centers for Disease Control and Prevention; National Institute for Occupational Safety and Health. NIOSH list of antineoplastic and other hazardous drugs in healthcare settings 2016. http://www.cdc.gov/niosh/topics/antineoplastic/pdf/hazardous-drugs-list_2016-161.pdf. Updated September 2016. Accessed October 26, 2016.*

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