Indication
ALECENSA® is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (mNSCLC) as detected by an FDA-approved test.

Please see Important Safety Information on pages 6-7 and in accompanying full Prescribing Information.
Dosing Schedule for ALECENSA

**4**

**150 mg capsules**

**ALE**

**ALE**

**ALE**

**ALE**

**Twice daily W I T H F O O D**

**4**

**150 mg capsules**

**ALE**

**ALE**

**ALE**

**ALE**

Pills shown at actual size.

Administer ALECENSA until disease progression or unacceptable toxicity.

- The recommended dose of ALECENSA is 600 mg orally twice daily with food
- The recommended dose of ALECENSA in patients with severe hepatic impairment (Child-Pugh C) is 450 mg orally twice daily
- Do not open or dissolve the contents of the capsule
- If a dose of ALECENSA is missed or vomiting occurs after taking a dose of ALECENSA, take the next dose at the scheduled time

**Dose Reduction Schedule**

<table>
<thead>
<tr>
<th>Dose Reduction Schedule</th>
<th>Dose Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Starting dose</td>
<td>ALECENSA 600 mg taken orally twice daily</td>
</tr>
<tr>
<td>First dose reduction</td>
<td>ALECENSA 450 mg taken orally twice daily</td>
</tr>
<tr>
<td>Second dose reduction</td>
<td>ALECENSA 300 mg taken orally twice daily</td>
</tr>
<tr>
<td>Discontinue if patients are unable to tolerate the 300 mg twice daily dose.</td>
<td></td>
</tr>
</tbody>
</table>

**Dose Modifications for Adverse Reactions**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>ALECENSA Dose Modification</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT or AST elevation of &gt;5X ULN with total bilirubin ≤2X ULN</td>
<td>Temporarily withhold until recovery to baseline or to ≤3X ULN, then resume at reduced dose. See table on page 2 for dose reduction schedule.</td>
</tr>
<tr>
<td>ALT or AST elevation &gt;3X ULN with total bilirubin elevation &gt;2X ULN in the absence of cholestasis or hemolysis</td>
<td>Permanently discontinue ALECENSA.</td>
</tr>
<tr>
<td>Total bilirubin elevation &gt;3X ULN</td>
<td>Temporarily withhold until recovery to baseline or to ≤1.5X ULN, then resume at reduced dose. See table on page 2 for dose reduction schedule.</td>
</tr>
<tr>
<td>Any Grade treatment-related ILD/pneumonitis</td>
<td>Permanently discontinue ALECENSA.</td>
</tr>
<tr>
<td>Grade 3 renal impairment</td>
<td>Temporarily withhold until serum creatinine recovers to ≤1.5X ULN, then resume at reduced dose.</td>
</tr>
<tr>
<td>Grade 4 renal impairment</td>
<td>Permanently discontinue ALECENSA.</td>
</tr>
<tr>
<td>Symptomatic bradycardia</td>
<td>Withhold ALECENSA until recovery to asymptomatic bradycardia or to a heart rate of ≥60 bpm. If contributing concomitant medication is identified and discontinued, or its dose is adjusted, resume ALECENSA at previous dose upon recovery to asymptomatic bradycardia or to a heart rate of ≥60 bpm. If no contributing concomitant medication is identified, or if contributing concomitant medications are not discontinued or dose modified, resume ALECENSA at reduced dose upon recovery to asymptomatic bradycardia or to a heart rate of ≥60 bpm. See table on page 2 for dose reduction schedule.</td>
</tr>
<tr>
<td>CPK elevation &gt;5X ULN</td>
<td>Temporarily withhold until recovery to baseline or to ≤2.5X ULN, then resume at same dose.</td>
</tr>
<tr>
<td>CPK elevation &gt;10X ULN or second occurrence of CPK elevation of &gt;5X ULN</td>
<td>Temporarily withhold until recovery to baseline or to ≤2.5X ULN, then resume at reduced dose. See table on page 2 for dose reduction schedule.</td>
</tr>
</tbody>
</table>

*Heart rate <60 bpm.
ALT=alanine transaminase; AST=aspartate transaminase; BPM=beats per minute;
CPK=creatine phosphokinase; ILD=interstitial lung disease; ULN=upper limit of normal.

Please see additional Important Safety Information on pages 6-7 and in accompanying full Prescribing Information.
Monitoring Patients on ALECENSA

Liver Monitoring:
- Monitor liver function tests including ALT, AST, and total bilirubin every 2 weeks during the first 3 months of treatment, then once a month and as clinically indicated, with more frequent testing in patients who develop transaminase and bilirubin elevations

Lung Monitoring:
- Promptly investigate for ILD/pneumonitis in any patient who presents with worsening of respiratory symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, and fever)

Kidney Monitoring:
- Withhold ALECENSA for severe renal impairment, then resume ALECENSA at reduced dose upon recovery or permanently discontinue

Heart Monitoring:
- Monitor heart rate and blood pressure regularly

CPK Monitoring:
- Assess CPK levels every 2 weeks for the first month of treatment and as clinically indicated in patients reporting any unexplained muscle pain, tenderness, or weakness

Embryo-Fetal Toxicity:
- ALECENSA can cause fetal harm. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment

Based on the severity of the adverse drug reaction, temporary interruption, dose reduction, or discontinuation of treatment with ALECENSA may be required. The dose reduction schedule and recommendations for dose modifications of ALECENSA in the event of adverse reactions are provided on pages 2-3.

Patient Resource Center for ALECENSA
Phone services from live representatives who will guide patients and their care partners to the resources they need.

(800) ALECENSA (253-2367)
- Translation services for a number of languages

How to Store ALECENSA

Do not store above 30°C (86°F). Store in the original container to protect from light and moisture.

Patient Counseling Information

Advise Patients
- To read the FDA-approved Patient Information
- To contact their healthcare provider immediately for signs or symptoms of bilirubin and hepatic transaminase elevations
- To contact their healthcare provider immediately to report new or worsening respiratory symptoms
- To contact their healthcare provider to report change in urine color, reduced urine output, or swelling in the legs and feet
- To contact their healthcare provider to report symptoms of bradycardia, including dizziness, lightheadedness, and syncope, as well as the use of any heart or blood pressure medications
- To contact their healthcare provider immediately to report new or worsening symptoms of muscle pain or weakness
- To avoid prolonged sun exposure while taking ALECENSA, and for at least 7 days after discontinuation, and to use proper protection from the sun. Advise patients to use a broad spectrum ultraviolet A/ultraviolet B sunscreen and lip balm (SPF ≥50) to help protect against potential sunburn
- To use effective contraception during treatment with ALECENSA and for at least 1 week after the last dose of ALECENSA. This applies to female patients of reproductive potential. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ALECENSA and for 3 months after the last dose of ALECENSA
- That women should not breastfeed during treatment with ALECENSA and for 1 week after the last dose
- To take ALECENSA twice a day with food and to swallow ALECENSA capsules whole
- To take the next dose at the regular time if a dose of ALECENSA is missed or if the patient vomits after taking a dose of ALECENSA. Advise patients not to take an extra dose

Inform Patients
- About the signs and symptoms of bilirubin and hepatic transaminase elevations
- About the signs and symptoms of ILD/pneumonitis
- About the signs and symptoms of myalgia, including unexplained and/or persistent muscle pain, tenderness, or weakness
- About the signs and symptoms of photosensitivity
- ALECENSA can cause fetal harm if taken during pregnancy. Advise a pregnant woman of the potential risk to a fetus

Please see additional Important Safety Information on pages 6-7 and in accompanying full Prescribing Information.
Important Safety Information

Warnings and Precautions

Hepatotoxicity
• Of 405 patients, elevations of AST >5X the upper limit of normal (ULN) occurred in 4.6% of patients, and elevations of ALT >5X the ULN occurred in 5.3% of patients. Elevations of bilirubin >3X the ULN occurred in 3.7% of patients. The majority (69% of the patients with hepatic transaminase elevations and 68% of the patients with bilirubin elevations) of these events occurred during the first 3 months of treatment. Six patients discontinued ALECENSA for Grades 3-4 AST and/or ALT elevations, and 4 patients discontinued ALECENSA for Grade 3 bilirubin elevations. Concurrent elevations in ALT or AST ≥3X the ULN and total bilirubin ≥2X the ULN, with normal alkaline phosphatase, occurred in <1% of patients treated with ALECENSA across clinical trials. Three patients with Grades 3-4 AST/ALT elevations had drug-induced liver injury.
• Monitor liver function tests including ALT, AST, and total bilirubin every 2 weeks during the first 3 months of treatment, then once a month and as clinically indicated, with more frequent testing in patients who develop transaminase and bilirubin elevations. Based on the severity of the adverse drug reaction, withhold ALECENSA and resume at a reduced dose, or permanently discontinue ALECENSA.

Interstitial Lung Disease (ILD)/Pneumonitis
• ILD/pneumonitis occurred in 3 (0.7%) patients treated with ALECENSA. One (0.2%) of these events was severe (Grade 3).
• Promptly investigate for ILD/pneumonitis in any patient who presents with worsening of respiratory symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, and fever).
• Immediately withhold ALECENSA treatment in patients diagnosed with ILD/pneumonitis and permanently discontinue ALECENSA if no other potential causes of ILD/pneumonitis have been identified.

Renal Impairment
• Renal impairment occurred in 8% of patients. The incidence of Grade ≥3 renal impairment was 1.7%, of which 0.5% were fatal events.
• Dose modifications for renal impairment were required in 3.2% of patients. Median time to Grade ≥3 renal impairment was 3.7 months (range 0.5 to 14.7 months).
• Permanently discontinue ALECENSA for Grade 4 renal toxicity. Withhold ALECENSA for Grade 3 renal toxicity, then resume at reduced dose.

Bradycardia
• Cases of bradycardia (8.6%) have been reported in patients treated with ALECENSA. Eighteen percent of 365 patients treated with ALECENSA for whom serial ECGs were available had heart rates of <50 beats per minute (bpm).
• Monitor heart rate and blood pressure regularly.
• In cases of symptomatic bradycardia that are not life-threatening, withhold ALECENSA until recovery to asymptomatic bradycardia or to a heart rate of ≥60 bpm and evaluate concomitant medications known to cause bradycardia, as well as anti-hypertensive medications.
• If attributable to a concomitant medication, resume ALECENSA at a reduced dose upon recovery to asymptomatic bradycardia or to a heart rate of ≥60 bpm, with frequent monitoring as clinically indicated.
• Permanently discontinue ALECENSA in case of recurrence or in cases of life-threatening bradycardia if no contributing concomitant medication is identified.

Severe Myalgia and Creatine Phosphokinase (CPK) Elevation
• Myalgia or musculoskeletal pain occurred in 26% of patients. The incidence of Grade 3 myalgia/musculoskeletal pain was 0.7%. Dose modifications for myalgia/musculoskeletal pain were required in 0.5% of patients.
• Elevations of CPK occurred in 41% of 347 patients with CPK laboratory data. The incidence of Grade 3 elevations of CPK was 4.0%. Median time to Grade 3 CPK elevation was 14 days (interquartile range 13-28 days). Dose modifications for elevation of CPK occurred in 3.2% of patients.
• Advise patients to report any unexplained muscle pain, tenderness, or weakness. Assess CPK levels every 2 weeks for the first month of treatment and as clinically indicated in patients reporting symptoms. Based on the severity of the CPK elevation, withhold, then resume or dose reduce ALECENSA.

Embryo-Fetal Toxicity
• ALECENSA can cause fetal harm when administered to pregnant women. Administration of ALECENSA to pregnant rats and rabbits during the period of organogenesis resulted in embryo-fetal toxicity and abortion at maternally toxic doses with exposures approximately 2.7X those observed in humans with ALECENSA 600 mg twice daily. Advise pregnant women of the potential risk to a fetus.
• Advise females of reproductive potential to use effective contraception during treatment with ALECENSA and for 1 week following the final dose.
• Advise males with female partners of reproductive potential to use effective contraception during treatment with ALECENSA and for 3 months following the final dose.

Most Common Adverse Reactions
• The most common adverse reactions (incidence ≥20%) were constipation (34%), fatigue (26%), edema (22%), myalgia (23%), and anemia (20%).

Use in Specific Populations

Lactation Risk Summary
• Because of the potential for serious adverse reactions in breastfed infants from ALECENSA, advise a lactating woman not to breastfeed during treatment with ALECENSA and for 1 week after the final dose. You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-835-2555.


Please see additional Important Safety Information in accompanying full Prescribing Information.
**Dosing and Administration Guide**

**Dosing Schedule for ALECENSA**

![Pills shown at actual size.](image)

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- Do not open or dissolve the contents of the capsule
- If a dose of ALECENSA is missed or vomiting occurs after taking a dose of ALECENSA, take the next dose at the scheduled time

Visit alecensa.com/hcp to learn more or contact your local Genentech representative

**Select Important Safety Information**

**Hepatotoxicity**

- Of 405 patients, elevations of AST >5X the upper limit of normal (ULN) occurred in 4.6% of patients, and elevations of ALT >5X the ULN occurred in 5.3% of patients. Elevations of bilirubin >3X the ULN occurred in 3.7% of patients. Six patients discontinued ALECENSA for Grades 3-4 AST and/or ALT elevations, and 4 patients discontinued ALECENSA for Grade 3 bilirubin elevations. Three patients with Grades 3-4 AST/ALT elevations had drug-induced liver injury
- Monitor liver function tests every 2 weeks during the first 3 months of treatment, then once a month and as clinically indicated, with more frequent testing in patients who develop transaminase and bilirubin elevations. Based on the severity of the adverse drug reaction, withhold then dose reduce, or permanently discontinue ALECENSA

Please see additional Important Safety Information on pages 6-7 and in accompanying full Prescribing Information.