

Getting
started with
ALECENSA®
(alectinib)

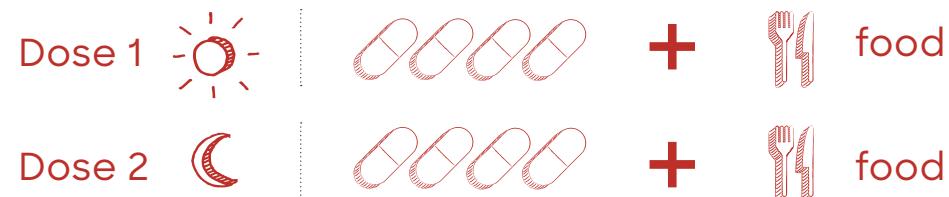
ALECENSA®
alectinib 150 mg capsules

ALECENSA

Your quick start guide

Now that you've received your prescription for ALECENSA, you can use this brochure—filled with helpful and important information—to help you on your journey.

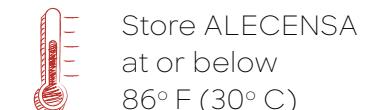
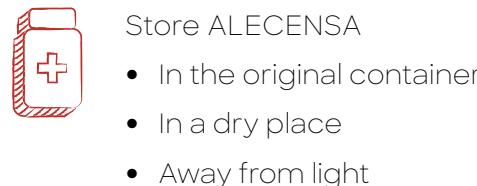
Dosage information



- ALECENSA is taken twice daily
- The standard dose of ALECENSA has 4 capsules—150 mg per capsule x 4 = 600 mg

Your doctor may change your dose of ALECENSA or tell you to stop taking ALECENSA depending on how your treatment is going.

Storage information



For more information on dosing and storage see pages 6, 7, and 9.

Who is ALECENSA for?

ALECENSA is a prescription medicine used to treat people with non-small cell lung cancer (**NSCLC**) that has spread to other parts of the body (**metastatic NSCLC or mNSCLC**) and is caused by an abnormal anaplastic lymphoma kinase (**ALK**) gene. Your healthcare provider will perform a test to make sure that ALECENSA is right for you.

It is not known if ALECENSA is safe and effective in children.

Important Contacts



As always, your doctor is the best resource for any questions you may have. Here is some additional contact information that may be helpful.

To speak with one of our live representatives, who will guide you to the resources you need

ALECENSA Patient Resource Center:
(800) ALECENSA (253-2367)
(Translation services available)

Monday–Friday,
9 AM–8 PM ET

To ask a nurse specific medical questions related to your Genentech medicine

Genentech: (800) 821-8590

Monday–Friday,
8 AM–8 PM ET

To report side effects

FDA: (800) FDA-1088
www.fda.gov/medwatch
Genentech: (888) 835-2555

7 days/week,
24 hrs/day

For more important contact information, see page 28.

ALECENSA may cause serious side effects, including:

- Liver problems (hepatotoxicity)
- Lung problems
- Kidney problems
- Slow heartbeat (bradycardia)
- Muscle pain, tenderness, and weakness (myalgia)

The most common side effects of ALECENSA include:

- Tiredness
- Constipation
- Swelling in your hands, feet, ankles, face, and eyelids
- Muscle pain, tenderness, and weakness (myalgia)
- Low red blood cell count (anemia)

These are not all of the possible side effects of ALECENSA. For more information, see pages 10–11 of this brochure. For medical advice about side effects ask your doctor or pharmacist.





THE ALK-POSITIVITY PROJECT

The photos in this brochure are from the ALK Positivity Project—a collection of personalized artwork created by people with **ALK+ metastatic** non-small cell lung cancer (**mNSCLC**) who took ALECENSA and whose outlook isn't defined by their diagnosis. See more at www.alecensa.com/patient/alk-positivity-project/the-alk-positivity-gallery.html

What's inside

Dosing & Storage

More information about taking ALECENSA	6
Specialty pharmacy overview	8
Storage information	9
What Are The Possible Side Effects?	10
What Should I Tell My Doctor Before Taking ALECENSA?	13
Some Things You Can Do About The Most Common Side Effects	14
Treatment Journey Support	16
Financial Resources	18
How ALECENSA Works	23
Clinical Trial Results	24
Important Contact Information	28
Glossary	30

The definitions of **gray highlighted words** in this brochure can be found in the Glossary on pages 30-31.

Please see additional side effects on pages 10-11 and for additional information, please see the **Patient Information** in the accompanying Prescribing Information.



More information about taking ALECENSA

Dose 1 + food

Dose 2 + food

- ALECENSA is taken twice daily
- The standard dose of ALECENSA has 4 capsules—150 mg per capsule \times 4 = 600 mg
- You will take 8 capsules a day for a total of 1200 mg a day
- Take ALECENSA exactly as your doctor tells you to take it
- If you have severe liver disease, your doctor may start you on a different dose.

Your doctor may change your dose of ALECENSA or tell you to stop taking ALECENSA depending on how your treatment is going.



Tip: Set an alarm or use a phone app to help remind you to take your medication.

What to do if you miss a dose

- If you miss a dose of ALECENSA, do not take the missed dose
- Take your next dose at your regular time

What to do if you vomit after a dose

- If you vomit after taking a dose of ALECENSA, do not take an extra dose
- Take your next dose at your regular time

Things to remember

- Take ALECENSA exactly as your doctor tells you to
- Do not change your dose or stop taking ALECENSA unless your doctor tells you to
- Your doctor may change your dose, temporarily stop, or permanently stop treatment with ALECENSA
- Swallow ALECENSA capsules whole. Do not open or dissolve the capsule contents

Please see additional side effects on pages 10–11 and for additional information, please see the **Patient Information** in the accompanying Prescribing Information.





Your ALECENSA may be delivered by a specialty pharmacy

Your specialty pharmacy is different from your regular mail-order pharmacy. It handles drugs like ALECENSA. You may not be able to get your ALECENSA right away. First, your doctor's office or specialty pharmacy will have to check to make sure your health insurance plan covers your medicine.

The specialty pharmacy may call you to find out:



How to have your ALECENSA sent to your home



How you will pay for your medicine and what type of insurance you have



If you need help paying for your medicine



If you have any questions about your medicine

Storage information



Store ALECENSA

- In the original container
- In a dry place
- Away from light



Store ALECENSA at or below 86° F (30° C)



Tip: Contact the specialty pharmacy if you have questions about storing or shipping ALECENSA.



Tip: Make sure you take and return all calls from the specialty pharmacy. Add their phone number to your contacts so that you can recognize and answer their calls promptly.

Tip: If you're not home to receive packages, your specialty pharmacy may be able to deliver your medication to your local retail pharmacy for you to pick up at your convenience.

If you think your medication has been exposed to extreme temperatures, please contact your pharmacy.

Please see additional side effects on pages 10–11 and for additional information, please see the [Patient Information](#) in the accompanying Prescribing Information.



What are possible side effects?

ALECENSA may cause serious side effects. Tell your doctor right away if you have any new or worsening symptoms such as those described below.

Liver problems (hepatotoxicity)



ALECENSA may cause liver injury. Your doctor will do blood tests at least every 2 weeks for the first 3 months, and then 1 time each month and as needed during treatment with ALECENSA.

Symptoms to look out for include:

- Feeling tired
- Feeling less hungry than usual
- Yellowing of your skin or the whites of your eyes
- Dark urine
- Itchy skin
- Nausea or vomiting
- Pain on the right side of your stomach area
- Bleeding or bruising more easily than normal

Lung problems



ALECENSA may cause severe or life-threatening swelling (inflammation) of the lungs during treatment. Symptoms may be similar to those symptoms from lung cancer.

Symptoms to look out for include:

- Trouble breathing
- Shortness of breath
- Cough
- Fever

Kidney problems



ALECENSA may cause severe or life-threatening kidney problems

Symptoms to look out for include:

- A change in the amount or color of your urine
- New or worsening swelling in your legs or feet

Slow heartbeat (bradycardia)



ALECENSA may cause very slow heartbeats that can be severe. Your doctor will check your heart rate and blood pressure during treatment with ALECENSA.

Symptoms to look out for include:

- Feeling dizzy
- Feeling lightheaded
- If you faint during treatment with ALECENSA

Tell your doctor if you take any heart or blood pressure medications.

Muscle pain, tenderness, and weakness (myalgia)



Muscle problems are common with ALECENSA and can be severe. Your doctor will do blood tests at least every 2 weeks for the first month and as needed during treatment with ALECENSA.

Symptoms to look out for include:

- Unexplained muscle pain
- Muscle pain that does not go away
- Tenderness
- Weakness

**These are not all of the possible side effects of ALECENSA.
For medical advice about side effects, ask your doctor or pharmacist.**

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

“It's very important to have a positive frame of mind. It's not always easy to do, but I think that positivity does have an impact on how you get through the difficult days. **”**

—Colleen



Colleen is a real person who received ALECENSA.

What should I tell my doctor before taking ALECENSA?

Before you take ALECENSA, tell your doctor about all of your medical conditions, including if you:

- Have liver problems
- Have lung or breathing problems
- Have a slow heartbeat
- Are pregnant or plan to become pregnant. ALECENSA can harm your unborn baby. Tell your doctor right away if you become pregnant during treatment with ALECENSA or think you may be pregnant
 - **Women** who are able to become pregnant should use effective birth control during treatment with ALECENSA and for 1 week after the final dose of ALECENSA
 - **Men** who have female partners that are able to become pregnant should use effective birth control during treatment with ALECENSA and for 3 months after the final dose of ALECENSA
- Are breastfeeding or plan to breastfeed. It is not known if ALECENSA passes into your breast milk. Do not breastfeed during treatment with ALECENSA and for 1 week after the final dose of ALECENSA. Talk to your doctor about the best way to feed your baby during this time

Tell your doctor about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.





Some things you can do about the most common side effects

What if side effects occur while taking ALECENSA?
We've provided some guidance that may help.

As always, your doctor is the best resource for any questions you may have.



Should I avoid being in the sunlight while taking ALECENSA?

- You may burn more easily and get severe sunburns, so avoid spending time in the sunlight during treatment with ALECENSA and for 7 days after the final dose of ALECENSA

- Use sunscreen and lip balm with SPF 50 or greater to help protect against sunburn
- Wear a long-sleeved shirt, long pants and/or skirts, and a wide-brimmed hat to help protect your skin from UV rays



How can I combat my tiredness or fatigue?¹

- Talk to your doctor about how to stay active
- Practice mind-body strategies, like meditation
- Work with a physical therapist
- Talk with a counselor



How should I deal with constipation?²

- Drink more liquids (water is your friend)
- Eat more fiber (think whole grains, vegetables, fruit, and nuts)
- Increase physical activity
- Talk to your doctor about taking fiber supplements or laxatives



What if I get swelling in my hands, feet, ankles, face, or eyelids (edema)?³

- Limit sodium in your diet (another good reason to avoid junk food)
- Do light exercise
- Raise your feet (Ah, feels nice)
- Wear loose clothing around swollen areas
- Wear special socks, sleeves, or gloves that help with circulation and may help severe swelling



What can I do if I have muscle pain, tenderness, or weakness (myalgia)?⁴

- Get a massage or physical therapy
- Do light exercise
- Apply heat or cold
- Try relaxation techniques (*It can be as easy as taking a few deep breaths*)
- Talk to your doctor about medications to treat muscle aches and reduce the pain



Is there something I can do if I have a low red blood cell count (anemia)?⁵

- Eat foods that are good sources of iron
- Talk to your doctor about treatment options like medication or supplements



Tip: For managing any side effects, it's important to talk to your healthcare team before taking any action.

Adapted with permission. © 2020 American Society of Clinical Oncology. All rights reserved. See the full reference list on the back cover of this brochure for more information.

Treatment journey support

Many organizations offer helpful information about lung cancer and support for patients and their loved ones. If you would like to learn more about cancer care, how to talk to loved ones about your diagnosis, or how to seek support in living with your type of lung cancer, these organizations may be able to help.



alkpositive.org

ALK Positive is a community of patients and caregivers, family, and friends affected by ALK+ lung cancer. Its Facebook support group has several thousand members in 50+ countries worldwide. They share experiences, knowledge, and emotional support with the hope of improving quality of life and extending life expectancies. It is a patient-driven voice and advocacy group securing research and awareness for **ALK+ lung cancer**.



Lung Cancer HELPLINE
(844) 360-5864
lungevity.org

The LUNGevity Foundation is firmly committed to making an immediate impact on increasing quality of life and survivorship of people with lung cancer by accelerating research into early detection and more effective treatments, as well as by providing community, support, and education for all those affected by the disease.



(800) 298-2436
go2foundation.org

GO₂ Foundation for Lung Cancer transforms survivorship as the world's leading organization dedicated to saving, extending, and improving the lives of those vulnerable, at risk, and diagnosed with lung cancer. They work to change the reality of living with lung cancer by ending stigma, increasing public and private research funding, and ensuring access to care.

Genentech does not control or endorse the content of the third-party websites listed above, and Genentech makes no representation as to the accuracy of the information contained on these websites. The information provided by these organizations is meant for informational purposes only and is not meant to replace a doctor's medical advice. Your use of third-party websites is at your own risk and subject to the terms and conditions of use for such sites.



Looking for support from Genentech, the manufacturer of ALECENSA?

Join **Staying Positive**, an ALECENSA Support Program, which includes:

- Advice, tailored for people with **ALK+ mNSCLC** like you, from real people on the same journey, sent through a series of emails and videos. Advice about topics such as sharing your diagnosis with loved ones, coping with scan anxiety, practicing self care, and more will be emailed to you
- Information on financial assistance programs that may be available after you have been prescribed ALECENSA

Find out more at alecensa.com/stayingpositive.

Please see additional side effects on pages 10-11 and for additional information, please see the **Patient Information** in the accompanying Prescribing Information.





Financial resources

Committed to helping you find assistance options for ALECENSA

ALECENSA®
alectinib

ACCESS ► SOLUTIONS®

Genentech Access Solutions is a program that helps people who are taking a Genentech medicine.

We work to connect you to the ALECENSA medicine you have been prescribed in 3 ways:



Checking your coverage and costs—we can find out if your health insurance plan covers your medicine and how much your out-of-pocket costs will be



Helping you find ways to pay for your medicine—we can refer you to financial assistance options to help you pay for your medicine



Working to get your medicine to you—we work with your doctor's office and/or your specialty pharmacy to help you get your medicine

To learn more about how Genentech Access Solutions can help,



Call (866) 422-2377 if you have questions or to see if you qualify for assistance

or

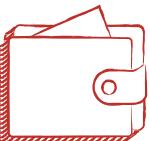


Visit [Genentech-Access.com/
ALECENSA/patients](http://Genentech-Access.com/ALECENSA/patients)



How can we help you?

Get help understanding your insurance coverage and assistance options from Genentech Access Solutions. We are here to help you get the medicine your doctor prescribed.



Genentech Co-pay Assistance Program^a

- Helps people with commercial (also known as private) health insurance
- This might be a plan you get through your employer or one you purchased through a Health Insurance Marketplace like HealthCare.gov
- Has zero income requirements
- To qualify, you must also meet other criteria

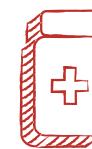
To find out if you qualify, call (855) MYCOPAY (692-6729) or visit copayassistance.com.



Independent Co-pay Assistance Foundations^b

- Help patients with public health insurance or commercial health insurance
- If you need help with your co-pay for your Genentech medicine, Genentech Access Solutions for ALECENSA can refer you to an independent co-pay assistance foundation

You can visit Genentech-Access.com to view a list of independent co-pay assistance foundations or call (888) 249-4918 to get help.



Genentech Patient Foundation^c

The Genentech Patient Foundation is a program that gives free Genentech medicine to people who don't have insurance coverage or who have financial concerns and meet certain eligibility criteria.

To learn more and to apply for help, visit genentechpatientfoundation.com.

^aThis Genentech Co-pay Assistance Program is valid ONLY for patients with commercial insurance who have a valid prescription for a Food and Drug Administration (FDA)-approved indication of a Genentech medication. Patients using Medicare, Medicaid, or any other federal or state government program to pay for their medications are not eligible. Under the Program, the patient will pay a co-pay. After reaching the maximum Program benefit, the patient will be responsible for all out-of-pocket costs. All participants are responsible for reporting the receipt of all Program benefits as required by any insurer or by law. No party may seek reimbursement for all or any part of the benefit received through this Program. This Program is void where prohibited by law. Genentech reserves the right to rescind, revoke, or amend the Program without notice at any time. Additional eligibility criteria apply. See full terms and conditions at copayassistance.com.

^bIndependent co-pay assistance foundations have their own rules for eligibility. We cannot guarantee a foundation will help you. We can only refer you to a foundation that supports your disease state. We do not endorse or show financial preference for any particular foundation. The foundations we refer you to are not the only ones that might be able to help you.

^cIf you have health insurance, you must have already tried other types of patient assistance. You also need to meet income requirements. If you do not have insurance, or if your insurance does not cover your Genentech medicine, you must meet different income requirements.

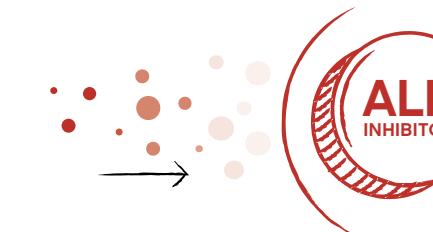




Please see additional side effects on pages 10-11 and for additional information, please see the **Patient Information** in the accompanying Prescribing Information.

How ALECENSA works

Treatment options for people with ALK+ mNSCLC include therapies called **ALK inhibitors** that target abnormal ALK proteins.



ALK inhibitors work by blocking the abnormal ALK protein responsible for the growth and spread of ALK+ mNSCLC. ALECENSA is an ALK inhibitor that helps treat ALK+ mNSCLC.

- To be eligible to take ALECENSA, a biomarker test must confirm that your lung cancer is caused by abnormal ALK proteins
- It is not known if ALECENSA is safe and effective in children



The definitions of **gray highlighted words** in this brochure can be found in the Glossary on pages 30-31.

What are the most serious side effects of ALECENSA?

ALECENSA may cause serious side effects, including:

- Liver problems (hepatotoxicity)
- Lung problems
- Kidney problems
- Slow heartbeat (bradycardia)
- Muscle pain, tenderness, and weakness (myalgia)



Newly diagnosed

Clinical trial results

ALECENSA was compared against crizotinib (also known as XALKORI®) in a large study of newly diagnosed people with ALK+ mNSCLC who hadn't been previously treated with an ALK inhibitor. These people were evaluated at 2 different time points.

First assessment (main results used to support the approval of ALECENSA)



Independent Review Committee (IRC)

These experts do not treat the people in a study but evaluate and verify the results objectively



- The Independent Review Committee (IRC) found that, on average, people taking ALECENSA lived more than twice as long without their ALK+ mNSCLC growing or spreading (called progression-free survival, or PFS) compared to people taking crizotinib.

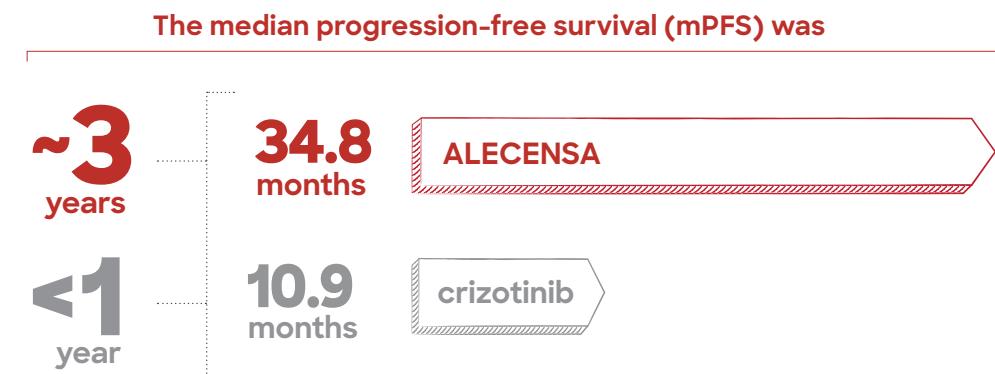
ALECENSA extended the median length of time people lived without ALK+ mNSCLC growing or spreading, which is called progression-free survival, or PFS.

Follow-up assessment (exploratory analysis 10 months later)



Investigators (INV)

These are the doctors who treat and evaluate people in a study.



- The Investigators (INV) found that the median time people taking ALECENSA lived without their disease spreading or growing (PFS) was 34.8 months. The results from this assessment are from an exploratory analysis and were not used to support ALECENSA's approval. This exploratory analysis was not specifically designed to find differences between ALECENSA and crizotinib.

What should I tell my doctor before taking ALECENSA?

Before you take ALECENSA, tell your doctor about all of your medical conditions, including if you:

- Have liver problems
- Have a slow heartbeat
- Have lung or breathing problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed

Tell your doctor about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, and herbal supplements.

XALKORI® is a registered trademark of Pfizer Inc.

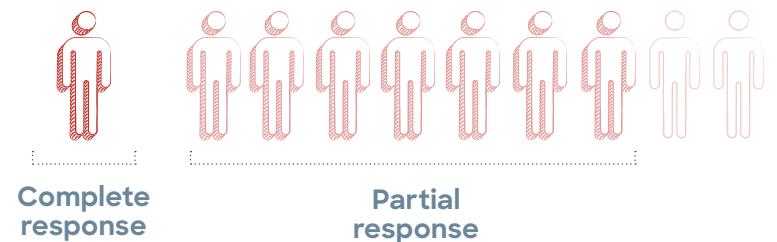
Please see additional side effects on pages 10-11 and for additional information, please see the [Patient Information](#) in the accompanying Prescribing Information.

Newly diagnosed

First assessment (main results used to support the approval of ALECENSA)

ALECENSA was able to shrink the size of tumors in nearly 80% of people with ALK+ mNSCLC

Nearly **8** out of **10** people taking ALECENSA had their tumors shrink



The results seen with **crizotinib** were similar to those seen with ALECENSA.

Of the people with ALK+ mNSCLC who had a reduction in tumor size, a response to treatment for 12 months or longer was seen in:

- 64% of people taking ALECENSA
- 36% of people taking crizotinib

People in the **study** were also evaluated to see how long they lived (**overall survival**) after receiving either ALECENSA or crizotinib. However, there were not enough data to determine overall survival at that time.

Fewer people who took ALECENSA experienced their ALK+ mNSCLC spreading to or growing in the brain

In the first assessment, the IRC found that fewer people who took ALECENSA experienced their ALK+ mNSCLC growing in or spreading to the brain as the first place their cancer spread. This included 122 people with and 181 people without ALK+ mNSCLC tumors that had spread to the brain at the start of the study.

12% who took ALECENSA had ALK+ mNSCLC tumors grow in or spread to the brain

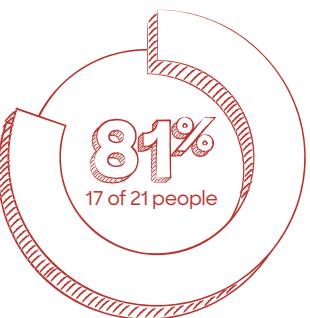
vs

45% who took crizotinib had ALK+ mNSCLC tumors grow in or spread to the brain

People in this study who did not have ALK+ mNSCLC grow or spread to the brain first may still have had their cancer spread to other parts of the body.

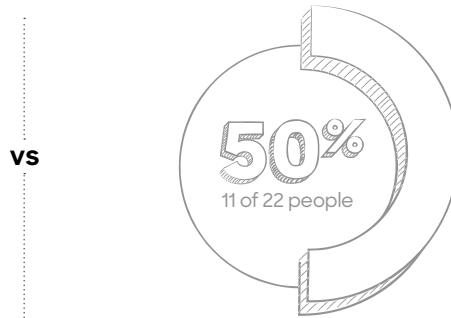
Some people had tumors that had spread to the brain at the start of the study and some did not. In an **exploratory analysis** of people whose tumors were visible on a brain scan at the start of the study:

ALECENSA was able to shrink the size of ALK+ mNSCLC tumors that had spread to the brain



who took ALECENSA had the size of their ALK+ mNSCLC-related brain tumors shrink

- 38% had a complete response
- 59% had their response last for more than a year



who took crizotinib had the size of their ALK+ mNSCLC-related brain tumors shrink

- 5% had a complete response
- 36% had their response last for more than a year

It is important to know that a **complete response** does not mean that the cancer has been cured.

What are the possible side effects of ALECENSA?

The most common side effects of ALECENSA include:

- Tiredness
- Constipation
- Swelling in your hands, feet, ankles, face, and eyelids
- Muscle pain, tenderness, and weakness (myalgia)
- Low red blood cell count (anemia)

For more information and full study information and results, visit alecensa.com.

Please see additional side effects on pages 10-11 and for additional information, please see the **Patient Information** in the accompanying Prescribing Information.



Important contact information

As always, your doctor is the best resource for any questions you may have.

Here is some additional contact information that may be helpful.

For more information on your treatment

alecensa.com

To enroll in Staying Positive, an ALECENSA Support Program

alecensa.com/stayingpositive

To speak with one of our live representatives, who will guide you to the resources you need

ALECENSA Patient Resource Center:
(800) ALECENSA (253-2367)
(Translation services available)

Monday–Friday,
9 AM–8 PM ET

To ask a nurse specific medical questions related to your Genentech medicine

FDA: (800) FDA-1088
Genentech: (888) 835-2555
www.fda.gov/medwatch

7 days/week,
24 hr/day

To report a product complaint

Genentech: (800) 334-0290

Monday-Friday,
8 AM-8 PM ET

xtra phone numbers, questions, and notes can go here



Tip: You may be able to maintain your normal routine, or you may need to do less and rest more often. Talk to your doctor about your priorities and goals for ALECENSA treatment.





Glossary

ALK (anaplastic lymphoma kinase) gene: The ALK gene makes an ALK protein, which may be involved in cell growth. Mutations of the ALK gene and protein have been found in certain types of cancer, including non-small cell lung cancer.

ALK inhibitors: ALK inhibitors are medicines that bind to and stop the ALK fusion protein. This may help prevent the growth and spread of tumor cells.

ALK+ mNSCLC: ALK (anaplastic lymphoma kinase) metastatic non-small cell lung cancer is a type of lung cancer that has spread to other places in the body, involving the ALK gene.

Complete response: The disappearance of all signs of cancer, such as tumors, in response to treatment. This does not mean the cancer has been cured.

Co-pay: An amount you have to pay for healthcare services or medicines. You pay this amount after you pay your deductible. A co-pay is usually a set amount, such as \$10.

Crizotinib: The drug that was used as a comparator to ALECENSA in clinical trials. Also known as XALKORI®. XALKORI® is a registered trademark of Pfizer Inc.

Exploratory analysis: An assessment of study results that was not specifically designed to find differences between 2 treatments in a study.

Genentech Patient Foundation: A program that gives free Genentech medicine to people who don't have insurance coverage or who have financial concerns and meet certain eligibility criteria.

Median: The median is the middle value, or number, in a set of measurements when arranged from least to greatest.

Metastatic: The spread of cancer from where it originated to other places in the body

NSCLC (non-small cell lung cancer): A group of different lung cancers that are named for the types of cells found in the cancer and how they look under a microscope.

Overall survival: The length of time from the date of diagnosis or the start of treatment for a disease that people diagnosed with the disease are still alive.

Partial response: The decrease in the size and spread of tumors in response to a given treatment.

Patient information: A document included in the package of a medication that provides information about that drug and its use.

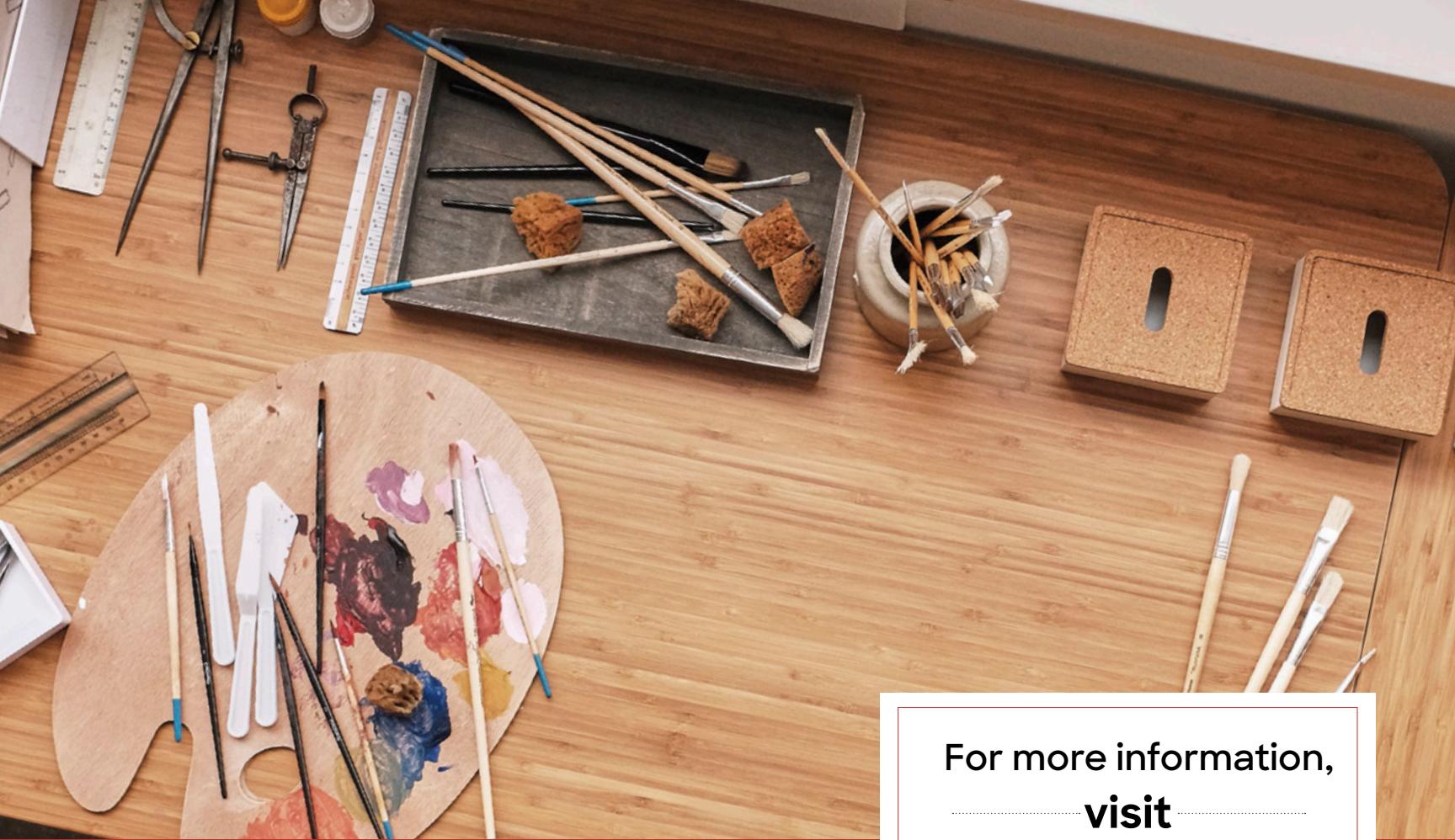
PFS (progression-free survival): The length of time during and after cancer treatment when a patient lives with the disease without it getting worse.

Prescribing information: Also known as "package insert," this is a document written for healthcare professionals that contains a summary of essential scientific information needed for safe and effective use of a prescription drug.

Protein: A molecule that is needed for your body to function properly. Proteins are the basis of cells in your body, including ALK.

Study: A type of research that tests how well a new medicine works in people. Studies can test new methods of screening, prevention, diagnosis, or treatment of a disease.





Scan the QR code using your phone camera to download a digital version (PDF) of this brochure.

For more information,
visit

ALECENSA.COM

References: **1.** Fatigue. Cancer.net Doctor-Approved Patient Information from ASCO®. Approved August 2018. Accessed April 24, 2020. <https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/fatigue>. **2.** Constipation. Cancer.net Doctor-Approved Patient Information from ASCO®. Approved December 2019. Accessed April 24, 2020. <https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/constipation>. **3.** Edema (Swelling) and Cancer Treatment. NIH National Cancer Institute <https://www.cancer.gov/about-cancer/treatment/side-effects/edema>. Accessed April 24, 2020. **4.** Muscle Aches. Cancer.net Doctor-Approved Patient Information from ASCO®. Approved December 2018. Accessed April 24, 2020. <https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/muscle-aches>. **5.** Anemia. Cancer.net. Doctor-Approved Patient Information from ASCO®. Approved April 2019. Accessed April 24, 2020. <https://www.cancer.net/coping-with-cancer/physical-emotional-and-social-effects-cancer/managing-physical-side-effects/anemia>.

Genentech

A Member of the Roche Group

ALECENSA® and its logo are registered trademarks of Chugai Pharmaceutical Co., Ltd., Tokyo, Japan. The Genentech logo is a registered trademark of Genentech, Inc. The Access Solutions logo is a registered trademark of Genentech, Inc. © 2020 Genentech USA, Inc. All rights reserved. M-US-00002509(v1.0) Printed in USA.

ALECENSA®
alectinib 150 mg capsules

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ALECENSA safely and effectively. See full prescribing information for ALECENSA.

ALECENSA® (alectinib) capsules, for oral use

Initial U.S. Approval: 2015

RECENT MAJOR CHANGES

Dosage and Administration (2.1)

1/2021

INDICATIONS AND USAGE

ALECENSA is a kinase inhibitor indicated for the treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer (NSCLC) as detected by an FDA-approved test. (1)

DOSAGE AND ADMINISTRATION

600 mg orally twice daily. Administer ALECENSA with food. (2.2)

DOSAGE FORMS AND STRENGTHS

Capsules: 150 mg (3)

CONTRAINDICATIONS

None. (4)

WARNINGS AND PRECAUTIONS

- Hepatotoxicity: Monitor liver laboratory 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. In case of severe ALT, AST, or bilirubin elevations, withhold, then reduce dose, or permanently discontinue ALECENSA. (2.3, 5.1)

- Interstitial Lung Disease (ILD)/Pneumonitis: Immediately withhold ALECENSA in patients diagnosed with ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis have been identified. (2.3, 5.2)
- Renal Impairment: Withhold ALECENSA for severe renal impairment, then resume ALECENSA at reduced dose upon recovery or permanently discontinue. (2.3, 5.3).
- Bradycardia: Monitor heart rate and blood pressure regularly. If symptomatic, withhold ALECENSA then reduce dose, or permanently discontinue. (2.3, 5.4)
- Severe Myalgia and Creatine Phosphokinase (CPK) Elevation: Assess CPK every 2 weeks during the first month of treatment and in patients reporting unexplained muscle pain, tenderness, or weakness. In case of severe CPK elevations, withhold, then resume or reduce dose. (2.3, 5.5)
- Embryo-Fetal Toxicity: ALECENSA can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception. (5.6, 8.1, 8.3)

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥20%) were fatigue, constipation, edema, myalgia, and anemia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS

Lactation: Do not breastfeed. (8.2)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 1/2021

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE

2 DOSAGE AND ADMINISTRATION

- 2.1 Patient Selection
- 2.2 Dosing and Administration
- 2.3 Dose Modifications for Adverse Reactions

3 DOSAGE FORMS AND STRENGTHS

4 CONTRAINDICATIONS

5 WARNINGS AND PRECAUTIONS

- 5.1 Hepatotoxicity
- 5.2 Interstitial Lung Disease (ILD)/Pneumonitis
- 5.3 Renal Impairment
- 5.4 Bradycardia
- 5.5 Severe Myalgia and Creatine Phosphokinase (CPK) Elevation
- 5.6 Embryo-Fetal Toxicity

6 ADVERSE REACTIONS

- 6.1 Clinical Trials Experience

8 USE IN SPECIFIC POPULATIONS

- 8.1 Pregnancy

8.2 Lactation

8.3 Females and Males of Reproductive Potential

- 8.4 Pediatric Use
- 8.5 Geriatric Use
- 8.6 Renal Impairment
- 8.7 Hepatic Impairment

10 OVERDOSAGE

11 DESCRIPTION

12 CLINICAL PHARMACOLOGY

- 12.1 Mechanism of Action
- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

13 NONCLINICAL TOXICOLOGY

- 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

14 CLINICAL STUDIES

16 HOW SUPPLIED/STORAGE AND HANDLING

17 PATIENT COUNSELING INFORMATION

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for the treatment of metastatic NSCLC with ALECENSA based on the presence of ALK positivity in tumor tissue or plasma specimens [*see Indications and Usage (1) and Clinical Studies (14)*]. If ALK rearrangements are not detected in a plasma specimen, test tumor tissue if feasible.

Information on FDA-approved tests for the detection of ALK rearrangements in NSCLC is available at <http://www.fda.gov/CompanionDiagnostics>

2.2 Dosing and Administration

The recommended dose of ALECENSA is 600 mg orally twice daily [*see Clinical Pharmacology (12.3)*]. Administer ALECENSA until disease progression or unacceptable toxicity.

The recommended dose of ALECENSA in patients with severe hepatic impairment (Child-Pugh C) is 450 mg orally twice daily [*see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)*].

ALECENSA should be taken with food. 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.

2.3 Dose Modifications for Adverse Reactions

The dose reduction schedule for ALECENSA is provided in Table 1.

Table 1: ALECENSA Dose Reduction Schedule

Dose reduction schedule	Dose level
Starting dose	600 mg taken orally twice daily
First dose reduction	450 mg taken orally twice daily
Second dose reduction	300 mg taken orally twice daily

Discontinue if patients are unable to tolerate the 300 mg twice daily dose.

Recommendations for dose modifications of ALECENSA in case of adverse reactions are provided in Table 2.

Table 2: ALECENSA Dose Modifications for Adverse Reactions

Criteria ^a	ALECENSA Dose Modification
ALT or AST elevation of greater than 5 times upper limit of normal (ULN) <u>with</u> total bilirubin less than or equal to 2 times ULN	Temporarily withhold until recovery to baseline or to less than or equal to 3 times ULN, then resume at reduced dose as per Table 1.
ALT or AST elevation greater than 3 times ULN <u>with</u> total bilirubin elevation greater than 2 times ULN in the absence of cholestasis or hemolysis	Permanently discontinue ALECENSA.
Total bilirubin elevation of greater than 3 times ULN	Temporarily withhold until recovery to baseline or to less than or equal to 1.5 times ULN, then resume at reduced dose as per Table 1.
Any grade treatment-related interstitial lung disease (ILD)/pneumonitis	Permanently discontinue ALECENSA.
Grade 3 renal impairment	Temporarily withhold until serum creatinine recovers to less than or equal to 1.5 times ULN, then resume at reduced dose.
Grade 4 renal impairment	Permanently discontinue ALECENSA.
Symptomatic bradycardia	Withhold ALECENSA until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above. 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 or above. If no contributing concomitant medication is identified, or if contributing concomitant medications are not discontinued or dose modified, resume ALECENSA at reduced dose (see Table 1) upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above.
Bradycardia ^b (life-threatening consequences, urgent intervention indicated)	Permanently discontinue ALECENSA if no contributing concomitant medication is identified. If contributing concomitant medication is identified and discontinued, or its dose is adjusted, resume ALECENSA at reduced dose (see Table 1) upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, with frequent monitoring as clinically indicated. Permanently discontinue ALECENSA in case of recurrence.
CPK elevation greater than 5 times ULN	Temporarily withhold until recovery to baseline or to less than or equal to 2.5 times ULN, then resume at same dose.
CPK elevation greater than 10 times ULN or second occurrence of CPK elevation of greater than 5 times ULN	Temporarily withhold until recovery to baseline or to less than or equal to 2.5 times ULN, then resume at reduced dose as per Table 1.

^a ALT = alanine transaminase; AST = aspartate transaminase; ULN = upper limit of normal; ILD = interstitial lung disease; CPK = blood creatine phosphokinase

^b Heart rate less than 60 beats per minute (bpm)

3 DOSAGE FORMS AND STRENGTHS

150 mg hard capsules, white, with “ALE” printed in black ink on the cap and “150 mg” printed in black ink on the body.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Elevations of AST greater than 5 times the upper limit of normal (ULN) occurred in 4.6% of patients, and elevations of ALT greater than 5 times the ULN occurred in 5.3% of the 405 patients in Studies NP28761, NP28673 and ALEX who received ALECENSA at a dose of 600 mg BID. Elevations of bilirubin greater than 3 times 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 greater than or equal to 3 times the ULN and total bilirubin greater than or equal to 2 times the ULN, with normal alkaline phosphatase, occurred in less than 1% of patients treated with ALECENSA across clinical trials. Three patients with Grades 3–4 AST/ALT elevations had drug-induced liver injury (documented by liver biopsy in two cases).

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 as described in Table 2 [*see Dosage and Administration (2.3)*].

5.2 Interstitial Lung Disease (ILD)/Pneumonitis

ILD/pneumonitis occurred in three (0.7%) patients treated with ALECENSA in Studies NP28761, NP28673 and ALEX. 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 (e.g., 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 [*see Dosage and Administration (2.3) and Adverse Reactions (6)*].

5.3 Renal Impairment

Renal impairment occurred in 8% of patients in Studies NP28761, NP28673, and ALEX. 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 until recovery to less than or equal to 1.5 times ULN, then resume at reduced dose [*see Dosage and Administration (2.3)*].

5.4 Bradycardia

Symptomatic bradycardia can occur with ALECENSA. Cases of bradycardia (8.6%) have been reported in patients treated with ALECENSA in Studies NP28761, NP28673 and ALEX. Eighteen percent of 365 patients treated with ALECENSA for whom serial ECGs were available had heart rates of less than 50 beats per minute (bpm).

Monitor heart rate and blood pressure regularly. Dose modification is not required in cases of asymptomatic bradycardia. In cases of symptomatic bradycardia that is not life-threatening, withhold ALECENSA until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above 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 (see Table 1) upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, with frequent monitoring as clinically indicated. Permanently discontinue ALECENSA in case of recurrence. Permanently discontinue ALECENSA in cases of life-threatening bradycardia if no contributing concomitant medication is identified [see *Dosage and Administration* (2.3)].

5.5 Severe Myalgia and Creatine Phosphokinase (CPK) Elevation

Myalgia or musculoskeletal pain occurred in 26% of patients in Studies NP28761, NP28673 and ALEX. 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 available in Studies NP28761, NP28673 and ALEX. 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 ALECENSA, then resume or reduce dose [see *Dosage and Administration* (2.3)].

5.6 Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, ALECENSA can cause fetal harm when administered to pregnant women. Administration of alectinib to pregnant rats and rabbits during the period of organogenesis resulted in embryo-fetal toxicity and abortion at maternally toxic doses with exposures approximately 2.7 times those observed in humans with alectinib 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 [see *Use in Specific Populations* (8.1 and 8.3) and *Clinical Pharmacology* (12.1)].

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Hepatotoxicity [see *Warnings and Precautions* (5.1)]
- Interstitial Lung Disease (ILD)/Pneumonitis [see *Warnings and Precautions* (5.2)]
- Renal Impairment [see *Warnings and Precautions* (5.3)]
- Bradycardia [see *Warnings and Precautions* (5.4)]
- Severe Myalgia and Creatine Phosphokinase (CPK) Elevation [see *Warnings and Precautions* (5.5)]
- Embryo-Fetal Toxicity [see *Warnings and Precautions* (5.6)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Previously Untreated ALK-Positive Metastatic NSCLC

The safety of ALECENSA was evaluated in 152 patients with ALK-positive NSCLC in the ALEX study. The median duration of exposure to ALECENSA was 17.9 months. Patient characteristics of the ALEX study population (n=303) were: median age 56 years, age less than 65 (77%), female (56%), Caucasian (50%), Asian (46%), adenocarcinoma histology (92%), never smoker (63%), and ECOG PS 0 or 1 (93%).

Serious adverse reactions occurred in 28% of patients treated with ALECENSA; serious adverse reactions reported in 2% or more of patients treated with ALECENSA were pneumonia (4.6%), and renal impairment (3.9%). Grade \geq 3 adverse events were reported for 41% of patients in the ALECENSA arm. Fatal adverse reactions occurred in 3.3% of patients treated with ALECENSA; these were renal impairment (2 patients), sudden death, cardiac arrest, and pneumonia (1 patient each). Permanent discontinuation of ALECENSA for adverse reactions occurred in 11% of patients. Adverse drug reactions that led to discontinuation of ALECENSA in 1% or more of patients were renal impairment (2.0%), hyperbilirubinemia (1.3%), increased ALT (1.3%), and increased AST (1.3%). Dose reductions and drug interruption due to adverse reactions occurred in 16% and 19% of patients, respectively, in the ALECENSA arm. The most frequent adverse reactions that led to dose modifications in the ALECENSA arm were hyperbilirubinemia (6%), increased AST (5%), increased ALT (4.6%), and pneumonia (3.3%).

Tables 3 and 4 summarize the common adverse reactions and laboratory abnormalities observed in ALEX.

Table 3: Adverse Drug Reactions (>10% for all NCI CTCAE Grades or ≥2% for Grades 3-4) in Patients Treated with ALECENSA in ALEX

	Aleensa N=152		Crizotinib N=151	
	All Grades (%)	Grades 3-4 (%)	All Grades (%)	Grades 3-4 (%)
Adverse Reaction				
Gastrointestinal				
Constipation	34	0	33	0
Nausea	14	0.7	48	3.3
Diarrhea	12	0	45	2.0
Vomiting	7	0	38	3.3
General				
Fatigue ^a	26	1.3	23	0.7
Edema ^b	22	0.7	34	0.7
Musculoskeletal				
Myalgia ^c	23	0	4.0	0
Skin				
Rash ^d	15	0.7	13	0
Nervous system				
Dysgeusia ^e	3.3	0.7	19	0
Eye				
Vision disorders ^f	4.6	0	23	0
Cardiac				
Bradycardia ^g	11	0	15	0
Renal				
Renal impairment ^h	12	3.9*	0	0

NCI CTCAE= National Cancer Institute Common Terminology Criteria for Adverse Events; MedDRA=Medical Dictionary for Regulatory Activities; SOC=System Organ Class.

^a Includes fatigue and asthenia.

^b Includes peripheral edema, edema, eyelid edema, localized edema, and face edema.

^c Includes myalgia and musculoskeletal pain.

^d Includes rash, rash maculo-papular, dermatitis acneiform, erythema, generalized rash, rash macular, rash papular, exfoliative rash, and pruritic rash.

^e Includes dysgeusia and hypogeusia.

^f Includes blurred vision, visual impairment, vitreous floaters, reduced visual acuity, and diplopia.

^g Includes reported cases of bradycardia and sinus bradycardia but is not based on serial ECG assessment.

^h Includes increased blood creatinine, creatinine renal clearance decreased, glomerular filtration rate decreased, and acute kidney injury.

* Includes two Grade 5 events.

The following additional clinically significant adverse drug reactions were observed in patients treated with ALECENSA: weight gain (9.9%), photosensitivity reaction (5.3%), stomatitis (3.3%), interstitial lung disease (1.3%), and drug-induced liver injury (1.3%).

Table 4: Treatment-Emergent Worsening in Laboratory Values Occurring in >10% of Patients in ALEX

Parameter	ALECENSA N= 152		Crizotinib N=151	
	All Grades (%)	Grades 3–4 (%)	All Grades (%)	Grades 3–4 (%)
Chemistry				
Hyperbilirubinemia ^a	54	5	4.7	0
Increased AST ^b	50	6	56	11
Increased alkaline phosphatase ^c	50	0	44	0
Increased ALT ^c	40	6	62	16
Increased creatinine ^{c,d}	38	4.1	23	0.7
Increased CPK ^e	37	2.8	52	1.4
Hypocalcemia ^a	29	0	61	1.4
Hyperglycemia ^f	22	2.2	19	2.3
Hyponatremia ^g	18	6	20	4.1
Hypokalemia ^c	17	2	12	0.7
Hypoalbuminemia ^h	14	0	57	3.4
Hyperkalemia ^c	12	1.4	16	1.4
Hypophosphatemia ⁱ	9	1.4	25	2.7
Increased gamma glutamyl transferase ^j	7	0.7	39	4.1
Hematology				
Anemia ^c	62	7	36	0.7
Lymphopenia ^a	14	1.4	34	4.1
Neutropenia ^c	14	0	36	7

Note: Based on National Cancer Institute Common Terminology Criteria for Adverse Events v4.03.

Excludes patients with no post-baseline lab assessments.

^a n=147 for alectinib (with baseline values missing for 1 of these patients), n=148 for crizotinib.

^b n=147 for alectinib (with baseline values missing for 2 of these patients), n=148 for crizotinib.

^c n=147 for alectinib, n=148 for crizotinib.

^d Only patients with creatinine increases based on ULN definition.

^e n=143 for alectinib (with baseline values missing for 14 of these patients), n=143 for crizotinib (with baseline values missing for 13 of these patients).

^f n=134 for alectinib (with baseline values missing for 18 of these patients), n=131 for crizotinib (with baseline values missing for 8 of these patients).

^g n=147 for alectinib, n=148 for crizotinib (with baseline values missing for 1 of these patients).

^h n=146 for alectinib (with baseline values missing for 1 of these patients), n=148 for crizotinib (with baseline values missing for 1 of these patients).

ⁱ n=145 for alectinib (with baseline values missing for 2 of these patients), n=148 for crizotinib (with baseline values missing for 4 of these patients).

^j n=143 for alectinib (with baseline values missing for 4 of these patients), n=148 (with baseline values missing for 5 of these patients).

ALK-Positive Metastatic NSCLC Previously Treated with Crizotinib

The safety of ALECENSA was evaluated in 253 patients with ALK-positive non-small cell lung cancer (NSCLC) treated with ALECENSA in two clinical trials, Studies NP28761 and NP28673. The median duration of exposure to ALECENSA was 9.3 months. One hundred sixty-nine patients (67%) were exposed to ALECENSA for more than 6 months, and 100 patients (40%) for more than one year. The population characteristics were: median age 53 years, age less than 65 (86%), female (55%), White (74%), Asian (18%), NSCLC adenocarcinoma histology (96%), never or former smoker (98%), ECOG Performance Status (PS) 0 or 1 (91%), and prior chemotherapy treatment (78%).

Serious adverse reactions occurred in 19% of patients; the most frequently reported serious adverse reactions were pulmonary embolism (1.2%), dyspnea (1.2%), and hyperbilirubinemia (1.2%). Fatal adverse reactions occurred in 2.8% of patients and included hemorrhage (0.8%), intestinal perforation (0.4%), dyspnea (0.4%), pulmonary embolism (0.4%), and endocarditis (0.4%). Permanent discontinuation of ALECENSA for adverse reactions occurred in 6% of patients. The most frequent adverse reactions that led to permanent discontinuation were hyperbilirubinemia (1.6%), increased ALT levels (1.6%), and increased AST levels (1.2%). Overall, 23% of patients initiating treatment at the recommended dose required at least one dose reduction. The median time to first dose reduction was 48 days. The most frequent adverse reactions that led to dose reductions or interruptions were elevations in bilirubin (6%), CPK (4.3%), ALT (4.0%), and AST (2.8%), and vomiting (2.8%).

Tables 5 and 6 summarize the common adverse reactions and laboratory abnormalities observed in Studies NP28761 and NP28673.

Table 5: Adverse Reactions in ≥ 10% (All Grades) or ≥ 2% (Grade 3–4) of Patients in Studies NP28761 and NP28673

Adverse Reactions	ALECENSA N=253	
	All Grades (%)	Grades 3–4 (%)*
Fatigue ^a	41	1.2
Constipation	34	0
Edema ^b	30	0.8
Myalgia ^c	29	1.2
Cough	19	0
Rash ^d	18	0.4
Nausea	18	0
Headache	17	0.8
Diarrhea	16	1.2
Dyspnea	16	3.6 ^e
Back pain	12	0
Vomiting	12	0.4
Increased weight	11	0.4
Vision disorder ^f	10	0

* Per Common Terminology Criteria for Adverse Events (CTCAE) version 4.0

^a Includes fatigue and asthenia.

^b Includes peripheral edema, edema, generalized edema, eyelid edema, and periorbital edema.

^c Includes myalgia and musculoskeletal pain.

^d Includes rash, maculopapular rash, acneiform dermatitis, erythema, generalized rash, papular rash, pruritic rash, and macular rash.

^e Includes one Grade 5 event.

^f Includes blurred vision, vitreous floaters, visual impairment, reduced visual acuity, asthenopia, and diplopia.

An additional clinically significant adverse drug reaction was photosensitivity, which occurred in 9.9% of patients exposed to ALECENSA in Studies NP28761 and NP28673. Patients were advised to avoid sun exposure and to use broad-spectrum sunscreen. The incidence of Grade 2 photosensitivity was 0.4%; the remaining events were Grade 1 in severity.

Table 6: Treatment-Emergent Worsening in Laboratory Values Occurring in > 20% of Patients in Studies NP28761 and NP28673

Parameter	ALECENSA N=250	
	All Grades (%)	Grades 3–4 (%)*
Chemistry		
Increased AST	51	3.6
Increased Alkaline Phosphatase	47	1.2
Increased CPK ^a	43	4.6
Hyperbilirubinemia	39	2.4
Hyperglycemia ^b	36	2.0
Increased ALT	34	4.8
Hypocalcemia	32	0.4
Hypokalemia	29	4.0
Increased Creatinine ^c	28	0
Hypophosphatemia	21	2.8
Hyponatremia	20	2.0
Hematology		
Anemia	56	2.0
Lymphopenia ^d	22	4.6

* Per CTCAE version 4.0.

^a n=218 for CPK (with baseline values missing for 91 of these patients).

^b n=152 for fasting blood glucose (with baseline values missing for 5 of these patients).

^c Only patients with creatinine increases based on ULN definition.

^d n=217 for lymphocytes (with baseline values missing for 5 of these patients).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on animal studies and its mechanism of action, ALECENSA can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology (12.1)*]. There are no available data on ALECENSA use in pregnant women.

Administration of alectinib to pregnant rats and rabbits by oral gavage during the period of organogenesis resulted in embryo-fetal toxicity and abortion at maternally toxic doses with exposures approximately 2.7 times those observed in humans treated with alectinib at 600 mg twice daily (see *Data*). Advise pregnant women of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data

In a preliminary rabbit embryo-fetal study, administration of alectinib by oral gavage during the period of organogenesis resulted in abortion or complete embryo-fetal mortality at a maternally toxic dose of 27 mg/kg/day (approximately 2.9-fold the estimated area under the curve (AUC_{0-24h,ss}) in humans treated with alectinib 600 mg BID) in three of six pregnant rabbits. The remaining three pregnant rabbits in this group had few live fetuses, decreased fetal and placental weights, and retroesophageal subclavian artery. In a rat preliminary embryo-fetal development study, administration of alectinib during organogenesis resulted in complete litter loss in all pregnant rats at 27 mg/kg/day (approximately 4.5-fold the estimated AUC_{0-24h,ss} in humans treated with alectinib 600 mg BID). Doses greater than or equal to 9 mg/kg/day (approximately 2.7-fold the estimated human AUC_{0-24h,ss} in humans treated with alectinib 600 mg BID), resulted in maternal toxicity as well as developmental toxicities including decreased fetal weight, dilated ureter, thymic cord, small ventricle and thin ventricle wall, and reduced number of sacral and caudal vertebrae.

8.2 Lactation

Risk Summary

There are no data on the presence of alectinib or its metabolites in human milk, the effects of alectinib on the breastfed infant, or its effects on milk production. Because of the potential for serious adverse reactions in breastfed infants from alectinib, advise a lactating woman not to breastfeed during treatment with ALECENSA and for 1 week after the final dose.

8.3 Females and Males of Reproductive Potential

Contraception

Females

ALECENSA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with ALECENSA and for 1 week after the final dose [*see Use in Specific Populations (8.1)*].

Males

Based on genotoxicity findings, advise males with female partners of reproductive potential to use effective contraception during treatment with ALECENSA and for 3 months following the final dose [*see Nonclinical Toxicology (13.1)*].

8.4 Pediatric Use

The safety and effectiveness of ALECENSA in pediatric patients have not been established.

Animal Data

Juvenile animal studies have not been conducted using alectinib. In general toxicology studies, treatment of rats with doses of alectinib resulting in exposures greater than or equal to approximately 4.5 times those in humans treated with alectinib at 600 mg twice daily resulted in changes in the growing teeth and bones. Findings in teeth included discoloration and changes in tooth size along with histopathological disarrangement of the ameloblast and odontoblast layers. There were also decreases in the trabecular bone and increased osteoclast activity in the femur and sternum.

8.5 Geriatric Use

Clinical studies of ALECENSA did not include sufficient number of subjects aged 65 and older to determine whether they respond differently from younger subjects.

8.6 Renal Impairment

No dose adjustment is recommended for patients with mild or moderate renal impairment. The safety of ALECENSA in patients with severe renal impairment (creatinine clearance less than 30 mL/min) or end-stage renal disease has not been studied [*see Clinical Pharmacology (12.3)*].

8.7 Hepatic Impairment

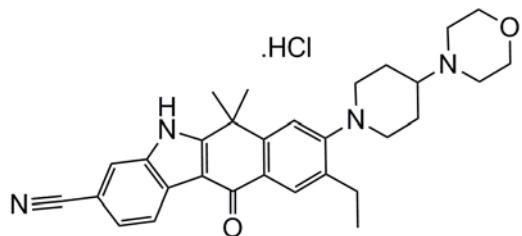
No dose adjustment is recommended for patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment. Increased exposure of alectinib occurred in patients with severe hepatic impairment (Child-Pugh C). The recommended dose of ALECENSA in patients with severe hepatic impairment (Child-Pugh C) is 450 mg orally twice daily [*see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)*].

10 OVERDOSAGE

No experience with overdose is available. There is no specific antidote for overdose with ALECENSA. Alectinib and its major active metabolite M4 are > 99% bound to plasma proteins; therefore, hemodialysis is likely to be ineffective in the treatment of overdose.

11 DESCRIPTION

ALECENSA (alectinib) is a kinase inhibitor for oral administration. The molecular formula for alectinib is $C_{30}H_{34}N_4O_2 \cdot HCl$. The molecular weight is 482.62 g/mol (free base form) and 519.08 g/mol (hydrochloride salt). Alectinib is described chemically as 9-ethyl-6, 6-dimethyl-8-[4-(morpholin-4-yl)piperidin-1-yl]-11-oxo-6, 11-dihydro-5H-benzo[b]carbazole-3-carbonitrile hydrochloride. The chemical structure of alectinib is shown below:



Alectinib HCl is a white to yellow white powder or powder with lumps with a pKa of 7.05 (base).

ALECENSA is supplied as hard capsules containing 150 mg of alectinib (equivalent to 161.33 mg alectinib HCl) and the following inactive ingredients: lactose monohydrate, hydroxypropylcellulose, sodium lauryl sulfate, magnesium stearate, and carboxymethylcellulose calcium. The capsule shell contains hypromellose, carrageenan, potassium chloride, titanium dioxide, corn starch, and carnauba wax. The printing ink contains red iron oxide (E172), yellow iron oxide (E172), FD&C Blue No. 2 aluminum lake (E132), carnauba wax, white shellac, and glyceryl monooleate.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Alectinib is a tyrosine kinase inhibitor that targets ALK and RET. In nonclinical studies, alectinib inhibited ALK phosphorylation and ALK-mediated activation of the downstream signaling proteins STAT3 and AKT, and decreased tumor cell viability in multiple cell lines harboring ALK fusions, amplifications, or activating mutations. The major active metabolite of alectinib, M4, showed similar in vitro potency and activity.

Alectinib and M4 demonstrated 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.

In mouse models implanted with tumors carrying ALK fusions, administration of alectinib resulted in antitumor activity and prolonged survival, including in mouse models implanted intracranially with ALK-driven tumor cell lines.

12.2 Pharmacodynamics

Cardiac Electrophysiology

The ability of alectinib to prolong the QT interval was assessed in 221 patients administered ALECENSA 600 mg twice daily in clinical studies. ALECENSA did not prolong the QTc (QT corrected for heart rate) interval to any clinically relevant extent. One patient had a maximum post-baseline QTcF value of greater than 500 msec, and one patient had a maximum QTcF change from baseline of greater than 60 msec.

12.3 Pharmacokinetics

The pharmacokinetics of alectinib and its major active metabolite M4 have been characterized in patients with ALK-positive NSCLC and healthy subjects.

In patients with ALK-positive NSCLC, the geometric mean (coefficient of variation %) steady-state maximal concentration ($C_{\max,ss}$) for alectinib was 665 ng/mL (44%) and for M4 was 246 ng/mL (45%) with peak to trough concentration ratio of 1.2. The geometric mean steady-state area under the curve from 0 to 12 hours ($AUC_{0-12h,ss}$) for alectinib was 7,430 ng*h/mL (46%) and for M4 was 2,810 ng*h/mL (46%). Alectinib exposure is dose proportional across the dose range of 460 mg to 900 mg (i.e., 0.75 to 1.5 times the approved recommended dosage) under fed conditions. Alectinib and M4 reached steady-state concentrations by day 7. The geometric mean accumulation was approximately 6-fold for both alectinib and M4.

Absorption

Alectinib reached maximal concentrations at 4 hours following administration of ALECENSA 600 mg twice daily under fed conditions in patients with ALK-positive NSCLC.

The absolute bioavailability of alectinib was 37% (90% CI: 34%, 40%) under fed conditions.

A high-fat, high-calorie meal increased the combined exposure ($AUC_{0-\infty}$) of alectinib plus M4 by 3.1-fold (90% CI: 2.7, 3.6) following oral administration of a single 600 mg dose of ALECENSA.

Distribution

The apparent volume of distribution is 4,016 L for alectinib and 10,093 L for M4.

Alectinib and M4 are bound to human plasma proteins greater than 99%, independent of drug concentration.

Alectinib concentrations in the cerebrospinal fluid in patients with ALK-positive NSCLC approximate estimated alectinib free concentrations in the plasma.

In vitro studies suggest that alectinib is not a substrate of P-glycoprotein (P-gp), but M4 is a substrate of P-gp. Alectinib and M4 are not substrates of breast cancer resistance protein (BCRP), organic anion-transporting polypeptide (OATP) 1B1, or OATP1B3.

Elimination

The apparent clearance (CL/F) is 81.9 L/hour for alectinib and 217 L/hour for M4. The geometric mean elimination half-life is 33 hours for alectinib and 31 hours for M4 in patients with ALK-positive NSCLC.

Metabolism

Alectinib is metabolized by CYP3A4 to its major active metabolite M4. The geometric mean metabolite/parent exposure ratio at steady-state is 0.40. M4 is subsequently metabolized by CYP3A4. Alectinib and M4 were the main circulating moieties in plasma, constituting 76% of the total radioactivity.

Excretion

Ninety-eight percent of the radioactivity was excreted in feces following oral administration of a single radiolabeled dose of alectinib under fed conditions. Eighty-four percent of the dose was excreted in the feces as unchanged alectinib, and 6% of the dose was excreted as M4. Excretion of radioactivity in urine was less than 0.5% of administered radiolabeled dose of alectinib.

Specific Populations

Age (21 to 83 years), body weight (38 to 128 kg), mild hepatic impairment (total bilirubin \leq ULN and AST $>$ ULN or total bilirubin 1 to \leq 1.5 \times ULN and AST any value), mild to moderate renal impairment (creatinine clearance 30 to 89 mL/min), race (White, Asian, and Other), and sex had no clinically meaningful effect on the systemic exposure of alectinib and M4. The pharmacokinetics of alectinib have not been studied in patients with severe renal impairment (creatinine clearance $<$ 30 mL/min), or end-stage renal disease.

Hepatic Impairment: Following administration of a single oral dose of 300 mg ALECENSA, the geometric mean ratio [90% confidence interval] for the combined AUC_{inf} of alectinib and M4 in subjects with moderate hepatic impairment (Child-Pugh B) was 1.36 [0.947, 1.96] and in subjects with severe hepatic impairment (Child-Pugh C) was 1.76 [0.984, 3.15] as compared to that in subjects with normal hepatic function. The combined C_{max} of alectinib and M4 was comparable among the three groups. No dose adjustment is recommended for patients with mild or moderate hepatic impairment. The recommended dose of ALECENSA in patients with severe hepatic impairment is 450 mg orally twice daily [*see Dosage and Administration (2.2) and Use in Specific Populations (8.7)*].

Drug Interactions

Effect of Other Drugs on Alectinib

No clinically meaningful effect on the combined exposure of alectinib plus M4 was observed in clinical studies following co-administration of ALECENSA with a strong CYP3A inhibitor (posaconazole), a strong CYP3A inducer (rifampin), or an acid-reducing agent (esomeprazole).

Effect of Alectinib on Other Drugs

No clinically meaningful effect on the exposure of midazolam (sensitive CYP3A substrate) or repaglinide (sensitive CYP2C8 substrate) is expected following co-administration with ALECENSA.

In vitro studies suggest that alectinib and M4 do not inhibit CYP1A2, 2B6, 2C9, 2C19 or 2D6.

In vitro studies suggest that alectinib and M4 inhibit P-gp and BCRP. Alectinib did not inhibit OATP1B1, OATP1B3, OAT1, OAT3, or OCT2 transport activity in vitro.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies with alectinib have not been conducted.

Alectinib was not mutagenic in vitro in the bacterial reverse mutation (Ames) assay, but was positive with an increased number of micronuclei in a rat bone marrow micronucleus test. The mechanism of micronucleus induction was abnormal chromosome segregation (aneugenicity) and not a clastogenic effect on chromosomes.

No studies in animals have been performed to evaluate the effect of alectinib on fertility. No adverse effects on male and female reproductive organs were observed in general toxicology studies conducted in rats and monkeys.

14 CLINICAL STUDIES

Previously Untreated ALK-Positive Metastatic NSCLC

The efficacy of ALECENSA for the treatment of patients with ALK-positive NSCLC who had not received prior systemic therapy for metastatic disease was established in an open-label, randomized, active-controlled,

multicenter study (ALEX: NCT02075840). Patients were required to have an ECOG performance status of 0-2 and ALK-positive NSCLC as identified by the VENTANA ALK (D5F3) CDx assay. Neurologically stable patients with treated or untreated central nervous system (CNS) metastases, including leptomeningeal metastases, were eligible; patients with neurologic signs and symptoms due to CNS metastases were required to have completed whole brain radiation or gamma knife irradiation at least 14 days prior to enrollment and be clinically stable. Patients with a baseline QTc > 470 ms were ineligible.

Patients were randomized 1:1 to receive ALECENSA 600 mg orally twice daily or crizotinib 250 mg orally twice daily. Randomization was stratified by ECOG performance status (0/1 vs. 2), race (Asian vs. non-Asian), and the presence or absence of CNS metastases at baseline. Treatment on both arms was continued until disease progression or unacceptable toxicity. The major efficacy outcome measure was progression-free survival (PFS) as determined by investigator assessment according to RECIST v1.1. Additional efficacy outcome measures were PFS as determined by independent review committee (IRC), time to CNS progression by IRC based on RECIST v1.1, objective response rate (ORR) and duration of response (DOR), and overall survival (OS). Additional exploratory outcome measures were CNS objective response rate (CNS-ORR) and CNS duration of response (CNS-DOR) by IRC in patients with CNS metastases at baseline.

A total of 303 patients were randomized to ALECENSA (n=152) or crizotinib (n=151). The demographic characteristics of the study population were 56% female, median age 56 years (range: 18 to 91 years), 50% White, 46% Asian, 1% Black, and 3% other races. The majority of patients had adenocarcinoma (92%) and never smoked (63%). CNS metastases were present in 40% (n=122) of patients: of these, 43 patients had measurable CNS lesions as determined by an IRC. The ALEX study demonstrated a significant improvement in PFS. The time to cause-specific CNS progression as assessed by IRC was also significantly improved; there was a lower incidence of progression in the CNS as the first site of disease progression, alone or with concurrent systemic progression, in the ALECENSA arm (12%) as compared to the crizotinib arm (45%). Efficacy results from ALEX are summarized in Table 7 and Figure 1.

Table 7: Efficacy Results in ALEX per IRC Assessment

	ALECENSA N=152	Crizotinib N=151
Progression-Free Survival		
Number of events (%)	63 (41%)	92 (61%)
Progressive disease (%)	51 (34%)	82 (54%)
Death (%)	12 (8%)	10 (7%)
Median in months (95% CI)	25.7 (19.9, NE)	10.4 (7.7, 14.6)
Hazard ratio (95% CI) ^a	0.53 (0.38, 0.73)	
P-value ^b	< 0.0001	
Overall Response Rate		
Overall response rate, % (95% CI) ^c	79% (72, 85)	72% (64, 79)
P-value ^d	0.1652	
Complete response, %	13%	6%
Partial response, %	66%	66%
Duration of Response		

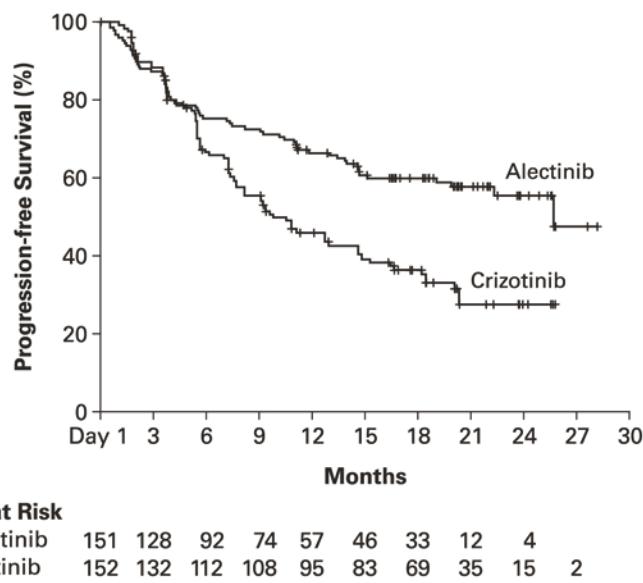
Number of responders	n=120	n=109
Response duration \geq 6 months	82%	57%
Response duration \geq 12 months	64%	36%
Response duration \geq 18 months	37%	14%

CNS: central nervous system, ORR: overall response rate, IRC: independent review committee, CI: confidence interval, NE: not estimable.

a, b, d Stratified by race (Asian vs. non-Asian) and CNS metastases at baseline (yes vs. no) for Cox model, log-rank test and Cochran Mantel-Haenszel test, respectively

c Clopper and Pearson exact binomial 95% confidence interval.

Figure 1: Kaplan Meier Plot of Progression-Free Survival (IRC) in ALEX



Results for PFS as determined by investigator assessment (HR=0.48 [95% CI: 0.35-0.66], stratified log-rank p<0.0001) were similar to that observed by IRC. At the data cutoff point overall survival data was not mature.

The results of prespecified exploratory analyses of CNS response rate in patients with measurable CNS lesions at baseline are summarized in Table 8.

Table 8: IRC-Assessed CNS Responses in Patients with Measurable CNS Lesions at Baseline in ALEX

	ALECENSA	Crizotinib
CNS Tumor Response Assessment	N = 21	N = 22
CNS Objective Response Rate, % (95% CI ^a)	81% (58, 95)	50% (28,72)
Complete Response	38%	5%
Duration of CNS Response		
Number of responders	17	11
CNS response duration \geq 12 months	59%	36%

IRC: Independent Review Committee; CI: Confidence Interval; NE: Not Estimable

^a Clopper and Pearson exact binomial 95% confidence interval

ALK-Positive Metastatic NSCLC Previously Treated with Crizotinib

The safety and efficacy of ALECENSA were established in two single-arm, multicenter clinical trials: NP28761 (NCT01588028) and NP28673 (NCT01801111). Patients with locally advanced or metastatic ALK-positive NSCLC, who have progressed on crizotinib, with documented ALK-positive NSCLC based on an FDA-approved test, and ECOG PS of 0-2 were enrolled in both studies. Eligibility criteria permitted enrollment of patients with prior chemotherapy and prior CNS radiotherapy provided that CNS metastases were stable for at least two weeks. All patients received ALECENSA 600 mg orally twice daily. The major efficacy outcome measure in both studies was objective response rate (ORR) according to Response Evaluation Criteria in Solid Tumours (RECIST v1.1) as evaluated per Independent Review Committee (IRC). Additional outcome measures as evaluated by the IRC included duration of response (DOR), CNS ORR, and CNS DOR.

NP28761 was conducted in North America and enrolled 87 patients. Baseline demographic and disease characteristics in NP28761 were median age 54 years old (range 29 to 79, 18% 65 and over), 84% White and 8% Asian, 55% female, 35% ECOG PS 0 and 55% ECOG PS 1, 100% never or former smokers, 99% Stage IV, 94% adenocarcinoma, and 74% prior chemotherapy. The most common sites of extra-thoracic metastasis included 60% CNS (of whom 65% had received CNS radiation), 43% lymph nodes, 36% bone, and 34% liver.

NP28673 was conducted internationally and enrolled 138 patients. Baseline demographic and disease characteristics in NP28673 were median age 52 years old (range 22 to 79, 10% 65 and over), 67% White and 26% Asian, 56% female, 32% ECOG PS 0 and 59% ECOG PS 1, 98% never or former smokers, 99% Stage IV, 96% adenocarcinoma, and 80% prior chemotherapy. The most common sites of extra-thoracic metastasis included 61% CNS (of whom 73% had received CNS radiation), 51% bone, 38% lymph nodes, and 30% liver.

Efficacy results from NP28761 and NP28673 in all treated patients are summarized in Table 9. The median duration of follow-up on Study NP28761 was 4.8 months for both IRC and Investigator assessments and on Study NP28673, 10.9 months for IRC assessment and 7.0 months for Investigator assessment. All responses were partial responses.

Table 9: Efficacy Results in Studies NP28761 and NP28673

Efficacy Parameter	NP28761 (N=87)		NP28673 (N=138)	
	IRC* Assessment	Investigator Assessment	IRC* Assessment	Investigator Assessment
Objective Response Rate (95% CI)	38% (28; 49)	46% (35; 57)	44% (36; 53)	48% (39; 57)
Number of Responders	33	40	61	66
Duration of Response, median in months (95% CI)	7.5 (4.9, Not Estimable)	NE (4.9, Not Estimable)	11.2 (9.6, Not Estimable)	7.8 (7.4, 9.2)

* 18 patients in NP28761 and 16 patients in NP28673 did not have measurable disease at baseline as per IRC assessment and were classified as non-responders in the IRC analysis.

An assessment of ORR and duration of response for CNS metastases in the subgroup of 51 patients in NP28761 and NP28673 with baseline measurable lesions in the CNS according to RECIST v1.1 are summarized in Table 10. Thirty-five (69%) patients with measurable CNS lesions had received prior brain radiation, including 25 (49%) who completed radiation treatment at least 6 months before starting treatment with ALECENSA. Responses were observed irrespective of prior brain radiation status.

Table 10: CNS Objective Response in Patients with Measurable CNS Lesions in Studies NP28761 and NP28673

Efficacy Parameter	N=51
CNS Objective Response Rate (95% CI)	61% (46, 74)
Complete Response	18%
Partial Response	43%
CNS Duration of Response, median in months (95% CI)	9.1 (5.8, Not Estimable)

16 HOW SUPPLIED/STORAGE AND HANDLING

Hard capsules, white 150 mg capsules with “ALE” printed in black ink on the cap and “150 mg” printed in black ink on the body, available in:

240 capsules per bottle: NDC 50242-130-01

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

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Patient Information).

Inform patients of the following:

Hepatotoxicity

Inform patients of the signs and symptoms of bilirubin and hepatic transaminase elevations. Advise patients to contact their healthcare provider immediately for signs or symptoms of bilirubin and hepatic transaminase elevations [*see Warnings and Precautions (5.1)*].

Interstitial Lung Disease (ILD)/Pneumonitis

Inform patients of the risks of severe ILD/pneumonitis. Advise patients to contact their healthcare provider immediately to report new or worsening respiratory symptoms [*see Warnings and Precautions (5.2)*].

Renal Impairment

Inform patients of the risk of severe and potentially fatal renal impairment. Advise patients to contact their health care provider for change in urine color, reduced urine output, or swelling in the legs and feet [*see Warnings and Precautions (5.3)*].

Bradycardia

Inform patients that symptoms of bradycardia including dizziness, lightheadedness, and syncope can occur while taking ALECENSA. Advise patients to contact their healthcare provider to report these symptoms and to inform their healthcare provider about the use of any heart or blood pressure medications [*see Warnings and Precautions (5.4)*].

Severe Myalgia/CPK elevation

Inform patients of signs and symptoms of myalgia, including unexplained and/or persistent muscle pain, tenderness, or weakness. Advise patients to contact their healthcare provider immediately to report new or worsening symptoms of muscle pain or weakness [*see Warnings and Precautions (5.5)*].

Photosensitivity

Inform patients of the signs and symptoms of photosensitivity. Advise patients to avoid prolonged sun exposure while taking ALECENSA and for at least 7 days after study drug discontinuation and to use proper protection

from the sun. Advise patients to use a broad spectrum ultraviolet A (UVA)/ultraviolet B (UVB) sunscreen and lip balm (SPF ≥ 50) to help protect against potential sunburn [*see Adverse Reactions (6.1)*].

Embryo-Fetal Toxicity

ALECENSA can cause fetal harm if taken during pregnancy. Advise a pregnant woman of the potential risk to a fetus [*see Warnings and Precautions (5.6) and Use in Specific Populations (8.1, 8.3)*].

Advise females of reproductive potential to use effective contraception during treatment with ALECENSA and for at least 1 week after the last dose of ALECENSA. Advise patients to inform their healthcare provider of a known or suspected pregnancy [*see Warnings and Precautions (5.6) and Use in Specific Populations (8.1, 8.3)*].

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 [*see Use in Specific Populations (8.3) and Nonclinical Toxicology (13.1)*].

Lactation

Advise women not to breastfeed during treatment with ALECENSA and for one week after the last dose [*see Use in Specific Populations (8.2)*].

Administration

Instruct patients to take ALECENSA twice a day. Advise patients to take ALECENSA with food and to swallow ALECENSA capsules whole [*see Dosage and Administration (2.2)*].

Missed Dose

Advise patients that if a dose of ALECENSA is missed or if the patient vomits after taking a dose of ALECENSA, patients should be advised not to take an extra dose, but to take the next dose at the regular time [*see Dosage and Administration (2.2)*].

Distributed by:

Genentech USA, Inc.

A Member of the Roche Group
1 DNA Way
South San Francisco, CA 94080-4990

ALECENSA® is a registered trademark of
Chugai Pharmaceutical Co., Ltd., Tokyo, Japan
©2021 Genentech, Inc. All rights reserved.

PATIENT INFORMATION

ALECENSA® (a-le-sen-sah)
(alectinib)
capsules

What is the most important information I should know about ALECENSA?

ALECENSA may cause serious side effects, including:

- **Liver problems (hepatotoxicity).** ALECENSA may cause liver injury. Your healthcare provider will do blood tests at least every 2 weeks for the first 3 months, and then 1 time each month and as needed during treatment with ALECENSA. **Tell your healthcare provider right away if you get any of the following signs and symptoms:**
 - feeling tired
 - feeling less hungry than usual
 - yellowing of your skin or the whites of your eyes
 - dark urine
 - itchy skin
 - nausea or vomiting
 - pain on the right side of your stomach area
 - bleeding or bruising more easily than normal
- **Lung problems.** ALECENSA may cause severe or life-threatening swelling (inflammation) of the lungs during treatment. Symptoms may be similar to those symptoms from lung cancer. Tell your healthcare provider right away if you have any new or worsening symptoms, including trouble breathing, shortness of breath, cough, or fever.
- **Kidney problems.** ALECENSA may cause severe or life-threatening kidney problems. Tell your healthcare provider right away if you have a change in the amount or color of your urine, or if you get new or worsening swelling in your legs or feet.
- **Slow heartbeat (bradycardia).** ALECENSA may cause very slow heartbeats that can be severe. Your healthcare provider will check your heart rate and blood pressure during treatment with ALECENSA. Tell your healthcare provider right away if you feel dizzy, lightheaded, or if you faint during treatment with ALECENSA. Tell your healthcare provider if you take any heart or blood pressure medicines.
- **Muscle pain, tenderness, and weakness (myalgia).** Muscle problems are common with ALECENSA and can be severe. Your healthcare provider will do blood tests at least every 2 weeks for the first month and as needed during treatment with ALECENSA. Tell your healthcare provider right away if you get new or worsening signs and symptoms of muscle problems, including unexplained muscle pain or muscle pain that does not go away, tenderness, or weakness.

See "What are the possible side effects of ALECENSA?" for more information about side effects.

What is ALECENSA?

ALECENSA is a prescription medicine used to treat people with non-small cell lung cancer (NSCLC):

- that is caused by an abnormal anaplastic lymphoma kinase (ALK) gene, **and**
- that has spread to other parts of your body

It is not known if ALECENSA is safe and effective in children.

Before you take ALECENSA, tell your healthcare provider about all of your medical conditions, including if you:

- have liver problems
- have lung or breathing problems
- have a slow heartbeat
- are pregnant or plan to become pregnant. ALECENSA can harm your unborn baby. Tell your healthcare provider right away if you become pregnant during treatment with ALECENSA or think you may be pregnant.
 - **Females** who are able to become pregnant should use effective birth control during treatment with ALECENSA and for 1 week after the final dose of ALECENSA.
 - **Males** who have female partners that are able to become pregnant should use effective birth control during treatment with ALECENSA and for 3 months after the final dose of ALECENSA.
- are breastfeeding or plan to breastfeed. It is not known if ALECENSA passes into your breast milk. Do not breastfeed during treatment with ALECENSA and for 1 week after the final dose of ALECENSA. Talk to your healthcare provider about the best way to feed your baby during this time.

Tell your healthcare provider about all the medicines you take, including prescription medicines, over-the-counter medicines, vitamins, or herbal supplements.

How should I take ALECENSA?

- Take ALECENSA exactly as your healthcare provider tells you to take it. Do not change your dose or stop taking ALECENSA unless your healthcare provider tells you to.
- Your healthcare provider may change your dose, temporarily stop, or permanently stop treatment with ALECENSA if you have side effects.
- Take ALECENSA 2 times a day.
- Take ALECENSA with food.

- Swallow ALECENSA capsules whole. Do not open or dissolve the capsule contents.
- If you miss a dose of ALECENSA, do not take the missed dose. Take your next dose at your regular time.
- If you vomit after taking a dose of ALECENSA, do not take an extra dose. Take your next dose at your regular time.

What should I avoid while taking ALECENSA?

- Avoid spending time in the sunlight during treatment with ALECENSA and for 7 days after the final dose of ALECENSA. You may burn more easily and get severe sunburns. Use sunscreen and lip balm with a SPF 50 or greater to help protect against sunburn.

What are the possible side effects of ALECENSA?

ALECENSA may cause serious side effects, including:

- See “What is the most important information I should know about ALECENSA?”

The most common side effects of ALECENSA include:

- | | |
|---|---|
| <ul style="list-style-type: none"> • tiredness • constipation • swelling in your hands, feet, ankles, face and eyelids | <ul style="list-style-type: none"> • muscle pain, tenderness, and weakness (myalgia). See “What is the most important information I should know about ALECENSA?” • anemia |
|---|---|

These are not all of the possible side effects of ALECENSA. For more information, ask your healthcare provider or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store ALECENSA?

- Do not store ALECENSA at temperatures above 86°F (30°C).
- Store ALECENSA capsules in the original container.
- Keep ALECENSA capsules dry and away from light.

Keep ALECENSA and all medicines out of the reach of children.

General information about the safe and effective use of ALECENSA.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use ALECENSA for a condition for which it was not prescribed. Do not give ALECENSA to other people, even if they have the same symptoms that you have. It may harm them. You can ask your healthcare provider or pharmacist for information about ALECENSA that is written for health professionals.

What are the ingredients in ALECENSA?

Active ingredient: alectinib

Inactive ingredients: lactose monohydrate, hydroxypropylcellulose, sodium lauryl sulfate, magnesium stearate and carboxymethylcellulose calcium. Capsule shell contains: hypromellose, carrageenan, potassium chloride, titanium dioxide, corn starch, and carnauba wax. Printing ink contains: red iron oxide (E172), yellow iron oxide (E172), FD&C Blue No. 2 aluminum lake (E132), carnauba wax, white shellac, and glyceryl monooleate.

Distributed by: Genentech, Inc., A Member of the Roche Group, 1 DNA Way, South San Francisco, CA 94080-4990

ALECENSA® is a registered trademark of Chugai Pharmaceutical Co., Ltd., Tokyo, Japan

©2017 Genentech, Inc.

For more information, go to www.ALECENSA.com or call 1-800-253-2367.

This Patient Information has been approved by the U.S. Food and Drug Administration

Revised: 11/2017