ALECENSA® (alectinib) Fact Sheet

ALECENSA is a kinase inhibitor approved for the treatment of people with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

This indication is approved under accelerated approval based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.[1]

What is NSCLC?

There are many types of lung cancer. NSCLC is the most common type and accounts for 85 to 90 percent of lung cancer cases.[2] According to the American Cancer Society, **more than 222,000 Americans** will be **diagnosed with lung cancer in 2017**.[3] It is estimated that **approximately 60 percent of lung cancer diagnoses in the United States are made when the disease is in the advanced stages.**[4]

Approximately 5 percent of people with NSCLC in the United States are ALK-positive, meaning their tumors contain ALK fusion genes.[5] ALK-positive NSCLC is often found in younger people who have a light or non-smoking history.[6]

ALECENSA Efficacy and Safety Profile[1]

The FDA's accelerated approval of ALECENSA was based on results of two Phase II studies of ALECENSA in people with ALK-positive, metastatic NSCLC who have progressed on or are intolerant to crizotinib.

Study 1 is a Phase I/II North American, single-arm, open-label, multicenter trial evaluating the safety and efficacy of ALECENSA (600 mg orally twice daily) in 87 people with ALK-positive, metastatic NSCLC whose disease progressed on crizotinib. Study 2 is a Phase II global, single-arm, open-label, multicenter trial evaluating the safety and efficacy of ALECENSA (600 mg orally twice daily) in 138 people with ALK-positive, metastatic NSCLC whose disease progressed on crizotinib.

A summary of the efficacy and safety data from both studies is included on the following page.

Important Safety Information

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

Everyone reacts differently to treatment with ALECENSA. It's important to know the most serious and most common side effects with ALECENSA.

Your doctor may lower the dose or stop treatment with ALECENSA if any side effects occur. **Contact your doctor right away if you have any of the following side effects.**

ALECENSA may cause serious side effects, including:

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 once a month and as needed during treatment with ALECENSA. Tell your doctor 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

Please see the following pages and ALECENSA full Prescribing Information including Most Serious Side Effects for Important Safety Information.

Efficacy Parameter	Study 1 (North American) n=87		Study 2 (Global) n=138	
	IRC* Assessment	Investigator Assessment	IRC* Assessment	Investigator Assessment
Objective Response Rate (ORR, primary endpoint)				
ORR (%) (95% CI)	38 (28, 49)	46 (35, 57)	44 (36, 53)	48 (39, 57)
Number of Responders				
Number of responders	33	40	61	66
Duration of Response (DOR, secondary endpoint)				
DOR (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)

CNS Efficacy (secondary endpoints, based on a pooled analysis of 51 people in Studies 1 and 2 with measurable CNS lesions at baseline according to RECIST v1.1)	
ORR (%) (95% CI)	61 (46, 74)
CNS complete response rate (%)	18
CNS partial response rate (%)	43
CNS DOR (median in months) (95% CI)	9.1 (5.8, Not Evaluable)

* 18 patients in Study 1 and 16 patients in Study 2 did not have measurable disease at baseline as per IRC assessment and were classified as non-responders in the IRC analysis.

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.

Adverse Reactions

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%)
- 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%), AST (2.8%), and vomiting (2.8%).

ALT=alanine transaminase; AST=aspartate transaminase; CPK=creatine phosphokinase.

Please see the following pages and ALECENSA full Prescribing Information including Most Serious Side Effects for Important Safety Information.

Adverse Reactions (continued)

The following table summarizes selected adverse reactions in Studies 1 and 2.

Adverse Reactions in ≥10% (All Grades) or ≥2% (Grade 3-4) of Patients in Studies 1 and 2

Adverse Reactions	ALECENSA=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
Back pain	12	0
Vomiting	12	0.4
Increased weight	11	0.4
Vision disorder[e]	10	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 blurred vision, vitreous floaters, visual impairment, reduced visual acuity, asthenopia, and diplopia.

Additional Safety Information From Clinical Trial Experience

Photosensitivity occurred in 9.9% of patients exposed to ALECENSA in Studies 1 and 2. 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.

Adverse Reactions (continued)

Laboratory Abnormalities Occurring in >20% of Patients in Studies 1 and 2

Parameter	ALECENSA=250[a]	
	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

[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).

ULN=upper limit of normal.

Important Safety Information (continued)

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 doctor right away if you have any new or worsening symptoms, including:

- Trouble breathing
- Shortness of breath
- Cough
- Fever

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. Tell your doctor right away if you feel dizzy, lightheaded, or faint during treatment with ALECENSA. Tell your doctor if you take any heart or blood pressure medicines.

Important Safety Information (continued)

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. Tell your doctor right away if you have any new or worsening signs and symptoms of muscle problems, including unexplained muscle pain or muscle pain that does not go away, tenderness, or weakness.

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.

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?

The most common side effects of ALECENSA include:

- Tiredness
- Constipation
- Swelling in your hands, feet, ankles, and eyelids

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

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.

Please see additional Important Safety Information in full Prescribing Information, including Patient Information.

References

1. ALECENSA (alectinib) Prescribing Information. Genentech, Inc. 2016.
2. American Cancer Society. Lung cancer (Non-Small Cell). http://www.cancer.org/acs/groups/cid/documents/webcontent/003115-pdf.pdf. Accessed January 11, 2017.
3. American Cancer Society. Cancer Facts & Figures 2017. Atlanta: American Cancer Society, 2017.
4. National Cancer Institute. Surveillance Epidemiology and End Results Stat Fact Sheets: Lung and Bronchus. http://seer.cancer.gov/statfacts/html/lungb.html.
5. Solomon B, Wilner KD, & Shaw AT (2014). Current status of targeted therapy for anaplastic lymphoma kinase-rearranged non-small cell lung cancer. *Clin Pharmacol Ther,* 95(1), 15-23. doi:10.1038/clpt.2013.200.
6. Paik JH, Choi CM, Kim H, … Chung JH (2012). Clinicopathologic implication of ALK rearrangement in surgically resected lung cancer. *Lung Cancer*, 76(3), 403-409. doi:10.1016/j.lungcan.2011.11.008.