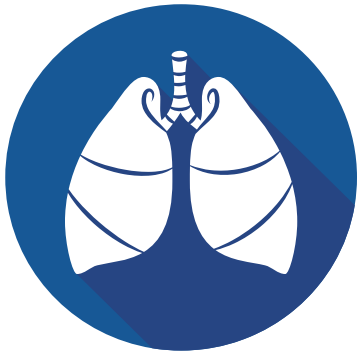
ALECENSA® (alectinib) Fact Sheet

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

What is NSCLC?

There are many types of lung cancer. NSCLC is the most common type and accounts for 80 to 85 percent of lung cancer cases.[2] According to the American Cancer Society, **more than 228,000 Americans** will be **diagnosed with lung cancer in 2019**.[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 approval of ALECENSA was based on the results of the Phase III ALEX study of ALECENSA in people with ALK-positive metastatic NSCLC who had not received prior treatment and the results of two Phase II studies, NP28761 and NP28673, of ALECENSA in people with ALK-positive, metastatic NSCLC who have progressed on or are intolerant to crizotinib.

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.

ALECENSA Efficacy and Safety Profile[1] (continued)

ALEX (NCT02075840/B028984) is an open-label, randomized, active-controlled, multicenter, Phase III study evaluating the efficacy and safety of ALECENSA versus crizotinib in people with ALK-positive NSCLC who had not received prior systemic therapy for metastatic disease and whose tumors were characterized as ALK-positive by the VENTANA ALK (D5F3) CDx Assay, a companion immunohistochemistry (IHC) test developed by Roche Tissue Diagnostics. People were randomized (one-to-one ratio) to receive either ALECENSA or crizotinib. The multicenter study was conducted in 303 people across 161 sites in 31 countries.

Summary of Efficacy and Safety Results from ALEX as Assessed by Independent Review Committee (IRC):

Efficacy Parameter	ALECENSA n=152	Crizotinib n=151
Progression-Free Survival (PFS)		
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)	0.53 (0.38, 0.73)	
P-value	< 0.0001	
Overall Response Rate (ORR)		
Overall response rate, % (95% CI)	79% (72, 85)	72% (64, 79)
P-value	0.1652	
Complete response, %	13%	6%
Partial response, %	66%	66%
Duration of Response (DOR)		
Number of responders	n=120	n=109
Response duration ≥6 months	82%	57%
Response duration ≥12 months	64%	36%
Response duration ≥18 months	37%	14%

IRC-Assessed CNS Responses in Patients with measurable CNS Lesions at Baseline in ALEX:

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

ALT=alanine transaminase; AST=aspartate transaminase.

* Based on a time to CNS progression analysis in which there was a lower risk of progression in the CNS as the first site of disease progression for people who received ALECENSA (12%) compared to people who received crizotinib (45%).

**At the data cutoff point overall survival data was not mature.

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

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.

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

Grade ≥ 3 adverse reactions were reported for 41% of people treated with ALECENSA. Serious adverse reactions occurred in 28% of patients treated with ALECENSA; serious adverse reactions reported in ≥ 2% of patients treated with ALECENSA were pneumonia (4.6%), and renal impairment (3.9%). Fatal adverse reactions occurred in 3.3% of patients treated with ALECENSA; these were renal impairment (2 patients), sudden cardiac arrest, and pneumonia (1 patient each). Permanent discontinuation of ALECENSA for adverse reactions occurred in 11% of patients.

NP28761 is a Phase I/II North American, single-arm, open-label, multicenter trial evaluating the safety and efficacy of ALECENSA in 87 people with ALK-positive, metastatic NSCLC whose disease progressed on crizotinib.

NP28673 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.

Summary of Efficacy and Safety Results from NP28761 and NP28673:

Efficacy Parameter	NP28761 (North American) n=87		NP28673 (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 NP28761 and NP28673 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 Estimable)			

* 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.

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.

The most common Grade 3-4 AEs (≥3 percent) occurring in patients treated with ALECENSA were dyspnea (3.6%), elevated CPK (4.6%), elevated ALT (4.8%), elevated AST levels (3.6%), hypokalemia (4.0%) and lymphopenia (4.6%). 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%).

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

Important Safety Information (continued)

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.

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

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
- Muscle pain, tenderness, and weakness (myalgia)
- Low red blood cell count

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. 2018.
2. American Cancer Society. About Non-Small Cell Lung Cancer. https://www.cancer.org/content/dam/CRC/PDF/Public/8703.00.pdf. Accessed January 2019.
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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. Accessed January 2019.

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