HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use XALKORI® safely and effectively. See full prescribing information for XALKORI.

XALKORI® (crizotinib) Capsules, oral
Initial U.S. Approval: 2011

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

----------DOSAGE AND ADMINISTRATION----------
- Recommended dose: 250 mg orally, twice daily (2.2)
- Renal Impairment: 250 mg orally, once daily in patients with severe renal impairment (creatinine clearance <30 mL/min) not requiring dialysis. (2.2)
- Dosing interruption and/or dose reductions may be required based on adverse drug reactions. (2.3)

----------DOSAGE FORMS AND STRENGTHS----------
- Capsules: 250 mg and 200 mg (3)

----------CONTRAINDICATIONS----------
- None (4)

----------WARNINGS AND PRECAUTIONS----------
- Hepatotoxicity: Fatal hepatotoxicity occurred in 0.2% of patients. Monitor with periodic liver testing. Temporarily suspend, dose reduce, or permanently discontinue XALKORI. (5.1)
- Interstitial Lung Disease (ILD)/Pneumonitis: Occurred in 2% of patients. Permanently discontinue in patients with ILD/pneumonitis. (5.2)
- QT Interval Prolongation: Occurred in 2.7% of patients. Monitor with electrocardiograms and electrolytes in patients who have a history of or predisposition for QTc prolongation, or who are taking medications that prolong QT. Temporarily suspend, dose reduce, or permanently discontinue XALKORI. (5.3)
- Bradycardia: XALKORI can cause bradycardia. Monitor heart rate and blood pressure regularly. Temporarily suspend, dose reduce, or permanently discontinue XALKORI. (5.4)
- Embryofetal Toxicity: XALKORI can cause fetal harm when administered to a pregnant woman. (5.5, 8.1)

----------ADVERSE REACTIONS----------
The most common adverse reactions (≥25%) are vision disorders, nausea, diarrhea, vomiting, constipation, edema, elevated transaminases, and fatigue. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Pfizer Inc. at 1-800-438-1985 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------
- CYP3A Inhibitors: Avoid concurrent use of XALKORI with strong CYP3A inhibitors. (7.1)
- CYP3A Inducers: Avoid concurrent use of XALKORI with strong CYP3A inducers. (7.2)
- CYP3A Substrates: Avoid concurrent use of XALKORI with CYP3A substrates with narrow therapeutic indices. (7.3)

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

Revised: 03/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the Full Prescribing Information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

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

2 DOSAGE AND ADMINISTRATION

2.1 Patient Selection

Select patients for the treatment of metastatic NSCLC with XALKORI based on the presence of ALK positivity in tumor specimens [see Indications and Usage (1) and Clinical Studies (14)]. Information on FDA-approved tests for the detection of ALK rearrangements in NSCLC is available at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm301431.htm.

2.2 Recommended Dosing

The recommended dose of XALKORI is 250 mg orally, twice daily until disease progression or no longer tolerated by the patient. The recommended dose of XALKORI in patients with severe renal impairment (creatinine clearance <30 mL/min) not requiring dialysis is 250 mg orally, once daily [*see Use in Specific Populations (8.7) and Clinical Pharmacology (12.3)*].

XALKORI may be taken with or without food. Swallow capsules whole. If a dose of XALKORI is missed, make up that dose unless the next dose is due within 6 hours. If vomiting occurs after taking a dose of XALKORI, take the next dose at the regular time.

2.3 Dose Modification

Reduce dose as below, if one or more dose reductions are necessary due to adverse reactions of Grade 3 or 4 severity, as defined by NCI Common Terminology Criteria for Adverse Events (CTCAE) version 4.0:

- First dose reduction: XALKORI 200 mg taken orally twice daily
- Second dose reduction: XALKORI 250 mg taken orally once daily
- Permanently discontinue if unable to tolerate XALKORI 250 mg taken once daily

Dose reduction guidelines are provided in Tables 1 and 2.

Table 1. XALKORI Dose Modification – Hematologic Toxicities[a]

CTCAE Grade	XALKORI Dosing
Grade 3	Withhold until recovery to Grade 2 or less, then resume at the same dose schedule
Grade 4	Withhold until recovery to Grade 2 or less, then resume at next lower dose

[a] Except lymphopenia (unless associated with clinical events, e.g., opportunistic infections).

Table 2. XALKORI Dose Modification – Non-Hematologic Toxicities

Criteria	XALKORI Dosing
Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevation greater than 5 times upper limit of normal (ULN) with total bilirubin less than or equal to 1.5 times ULN	Withhold until recovery to baseline or less than or equal to 3 times ULN, then resume at reduced dose
ALT or AST elevation greater than 3 times ULN with concurrent total bilirubin elevation greater than 1.5 times ULN (in the absence of cholestasis or hemolysis)	Permanently discontinue
Any Grade drug-related interstitial lung disease/pneumonitis	Permanently discontinue
QTc greater than 500 ms on at least 2 separate ECGs	Withhold until recovery to baseline or to a QTc less than 481 ms, then resume at reduced dose
QTc greater than 500 ms or greater than or equal to 60 ms change from baseline with Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia	Permanently discontinue
Bradycardia[a] (symptomatic, may be severe and medically significant, medical intervention indicated)	Withhold until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above Evaluate concomitant medications known to cause bradycardia, as well as anti-hypertensive medications If contributing concomitant medication is identified and discontinued, or its dose is adjusted, resume 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 at reduced dose upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above
Bradycardia[a,b] (life-threatening consequences, urgent intervention indicated)	Permanently discontinue if no contributing concomitant medication is identified If contributing concomitant medication is identified and discontinued, or its dose is adjusted, resume at 250 mg once daily upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, with frequent monitoring

[a] Heart rate less than 60 beats per minute (bpm).
[b] Permanently discontinue for recurrence.

Monitor complete blood counts including differential white blood cell counts monthly and as clinically indicated, with more frequent repeat testing if Grade 3 or 4 abnormalities are observed, or if fever or infection occurs.

3 DOSAGE FORMS AND STRENGTHS

250 mg capsules

Hard gelatin capsule, size 0, pink opaque cap and body, with “Pfizer” on the cap and “CRZ 250” on the body.

200 mg capsules

Hard gelatin capsule, size 1, white opaque body and pink opaque cap, with “Pfizer” on the cap and “CRZ 200” on the body.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Hepatotoxicity

Drug-induced hepatotoxicity with fatal outcome occurred in 2 (0.2%) of the 1225 patients treated with XALKORI across three main clinical trials. Concurrent elevations in alanine aminotransferase (ALT) greater than three times the upper limit of normal and total bilirubin greater than two times the upper limit of normal, with normal alkaline phosphatase, occurred in 7 patients (0.6%). Additionally, elevations in ALT greater than five times the upper limit of normal occurred in 109 patients (9.2%). Eight patients (0.7%) required permanent discontinuation due to elevated transaminases. These laboratory findings were generally reversible upon dosing interruption. Transaminase elevations generally occurred within the first 2 months of treatment.

Monitor with liver function tests including ALT and total bilirubin every 2 weeks during the first 2 months of treatment, then once a month and as clinically indicated, with more frequent repeat testing for increased liver transaminases, alkaline phosphatase, or total bilirubin in patients who develop transaminase elevations. Temporarily suspend, dose reduce, or permanently discontinue XALKORI as described in Table 2 *[see Dosage and Administration (2.3) and Adverse Reactions (6)]*.

5.2 Interstitial Lung Disease (Pneumonitis)

Severe, life-threatening, or fatal interstitial lung disease (ILD)/pneumonitis can occur in patients treated with XALKORI. Across clinical trials (n=1225), 31 XALKORI-treated patients (2.5%) had any grade ILD, 11 patients (0.9%) had Grade 3 or 4, and 6 patients (0.5%) had fatal cases. These cases generally occurred within 2 months after the initiation of treatment.

Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis. Exclude other potential causes of ILD/pneumonitis, and permanently discontinue XALKORI in patients diagnosed with drug-related ILD/pneumonitis *[see Dosage and Administration (2.3) and Adverse Reactions (6)]*.

5.3 QT Interval Prolongation

QTc prolongation can occur in patients treated with XALKORI. Across clinical trials (n=1225), QTc prolongation (all grades) was observed in 34 (2.7%) patients and QTc greater than 500 ms on at least 2 separate ECGs occurred in 17 (1.4%) patients.

Avoid use of XALKORI in patients with congenital long QT syndrome. Consider periodic monitoring with electrocardiograms (ECGs) and electrolytes in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities, or who are taking medications that are known to prolong the QT interval. Permanently discontinue XALKORI in patients who develop QTc greater than 500 ms or greater than or equal to 60 ms change from baseline with Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia. Withhold XALKORI in patients who develop QTc greater than 500 ms on at least 2 separate ECGs until recovery to a QTc less than or equal to 480 ms, then resume XALKORI at a reduced dose as described in Table 2 *[see Dosage and Administration (2.3)* and *Clinical Pharmacology (12.2)]*.

5.4 Bradycardia

Symptomatic bradycardia can occur in patients receiving XALKORI. Across clinical trials, bradycardia with a heart rate less than 50 beats per minute occurred in 11% of 1174 patients treated with XALKORI. In Study 1, Grade 3 syncope occurred in 2.9% of XALKORI-treated patients and in none of the chemotherapy-treated patients.

Avoid using XALKORI in combination with other agents known to cause bradycardia (e.g., beta-blockers, non-dihydropyridine calcium channel blockers, clonidine and digoxin) to the extent possible. Monitor heart rate and blood pressure regularly. In cases of symptomatic bradycardia that is not life-threatening, hold XALKORI until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, re-evaluate the use of concomitant medications, and adjust the dose of XALKORI. Permanently discontinue for life-threatening bradycardia due to XALKORI; however, if associated with concomitant medications known to cause bradycardia or hypotension, hold XALKORI until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, and if concomitant medications can be adjusted or discontinued, restart XALKORI at 250 mg once daily with frequent monitoring *[see Dosage and Administration (2.3) and Adverse Reactions (6)]*.

5.5 Embryofetal Toxicity

XALKORI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. In nonclinical studies in rats, crizotinib was embryotoxic and fetotoxic at exposures similar to those observed in humans at the recommended clinical dose of 250 mg twice daily. There are no adequate and well-controlled studies in pregnant women using XALKORI. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to a fetus *[see Use in Specific Populations (8.1)]*.

6 ADVERSE REACTIONS

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

- Hepatotoxicity *[see Warnings and Precautions (5.1)]*
- Interstitial Lung Disease/Pneumonitis *[see Warnings and Precautions (5.2)]*
- QT Interval Prolongation *[see Warnings and Precautions (5.3)]*
- Bradycardia *[see Warnings and Precautions (5.4)]*

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 clinical practice.

Safety evaluation of XALKORI is based on more than 1200 patients with ALK-positive metastatic NSCLC who received XALKORI as monotherapy at a starting oral dose of 250 mg twice daily continuously.

The most common adverse reactions (≥25%) of XALKORI are vision disorder, nausea, diarrhea, vomiting, constipation, edema, elevated transaminases, and fatigue.

ALK-positive metastatic NSCLC-Study 1

The data in Table 3 are derived from 343 patients with ALK-positive metastatic NSCLC enrolled in a randomized, multicenter, active-controlled, open-label trial (Study 1). Patients in the XALKORI arm (n=172) received XALKORI 250 mg orally twice daily until documented disease progression, intolerance to therapy, or the investigator determined that the patient was no longer experiencing clinical benefit. A total of 171 patients in the chemotherapy arm received pemetrexed 500 mg/m^2 (n=99) or docetaxel 75 mg/m^2 (n=72) by intravenous infusion every three weeks until documented disease progression, intolerance to therapy, or the investigator determined that the patient was no longer experiencing clinical benefit. Patients in the chemotherapy arm received pemetrexed unless they had received pemetrexed as part of first-line or maintenance treatment.

The median duration of study treatment was 7.1 months for patients who received XALKORI and 2.8 months for patients who received chemotherapy. Across the 347 patients who were randomized to study treatment (343 received at least one dose of study treatment), the median age was 50 years; 84% of patients in the XALKORI arm and 87% of patients in the chemotherapy arm were younger than 65 years. A total of 57% of patients on XALKORI and 55% of chemotherapy patients were female. Forty-six percent (46%) of XALKORI-treated and 45% of chemotherapy-treated patients were from Asia.

Serious adverse reactions were reported in 64 patients (37.2%) treated with XALKORI and 40 patients (23.4%) in the chemotherapy arm. The most frequent serious adverse reactions reported in patients treated with XALKORI were pneumonia (4.1%), pulmonary embolism (3.5%), dyspnea (2.3%), and interstitial lung disease (ILD; 2.9%). Fatal adverse reactions in XALKORI-treated patients in Study 1 occurred in 9 (5%) patients, consisting of: acute respiratory distress syndrome, arrhythmia, dyspnea, pneumonia, pneumonitis, pulmonary embolism, ILD, respiratory failure, and sepsis.

Dose reductions due to adverse reactions were required in 16% of XALKORI-treated patients. The most frequent adverse reactions that led to dose reduction in the patients treated with XALKORI were alanine aminotransferase (ALT) elevation (7.6%) including some patients with concurrent aspartate aminotransferase (AST) elevation, QTc prolongation (2.9%), and neutropenia (2.3%).

Discontinuation of therapy in XALKORI-treated patients for adverse reactions was 17.0%. The most frequent adverse reactions that led to discontinuation in XALKORI-treated patients were ILD (1.7%), ALT and AST elevation (1.2%), dyspnea (1.2%), and pulmonary embolism (1.2%). Tables 3 and 4 summarize common Adverse Reactions and Laboratory Abnormalities in XALKORI-treated patients.

Table 3. Adverse Reactions Reported at a Higher Incidence (≥5% Higher for All Grades or ≥2% Higher for Grades 3/4) with XALKORI than Chemotherapy in Study 1

Adverse Reaction	XALKORI (N=172)		Chemotherapy (Pemetrexed or Docetaxel) (N=171)	
	All Grades (%)	Grade 3/4 (%)	All Grades (%)	Grade 3/4 (%)
Nervous System Disorder				
Dizziness[a]	22	1	8	0
Dysgeusia	26	0	9	0
Syncope	3	3	0	0
Eye Disorders				
Vision disorder[b]	60	0	9	0
Cardiac Disorders				
Electrocardiogram QT prolonged	5	3	0	0
Bradycardia[c]	5	0	0	0
Investigations				
Weight decreased	10	1	4	0
Gastrointestinal Disorders				
Vomiting	47	1	18	0
Nausea	55	1	37	1
Diarrhea	60	0	19	1
Constipation	42	2	23	0
Dyspepsia	8	0	3	0
Infections and Infestations				
Upper respiratory infection[d]	26	0	13	1
Respiratory, Thoracic and Mediastinal Disorders				
Pulmonary embolism[e]	6	5	2	2
General Disorders and Administration Site Conditions				
Edema[f]	31	0	16	0

Includes cases reported within the clustered terms:
[a] Dizziness (Balance disorder, Dizziness, Dizziness postural)
[b] Vision Disorder (Diplopia, Photophobia, Photopsia, Vision blurred, Visual acuity reduced, Visual impairment, Vitreous floaters)
[c] Bradycardia (Bradycardia, Sinus bradycardia)
[d] Upper respiratory infection (Laryngitis, Nasopharyngitis, Pharyngitis, Rhinitis, Upper respiratory tract infection)
[e] Pulmonary embolism (Pulmonary artery thrombosis, Pulmonary embolism)
[f] Edema (Face edema, Generalized edema, Local swelling, Localized edema, Edema, Edema peripheral, Periorbital edema)

Additional adverse reactions occurring at an overall incidence between 1% and 30% in patients treated with XALKORI included decreased appetite (27%), fatigue (27%), neuropathy (19%; dysesthesia, gait disturbance, hypoesthesia, muscular weakness, neuralgia, peripheral neuropathy, parasthesia, peripheral sensory neuropathy, polyneuropathy, burning sensation in skin), rash (9%), ILD (4%; acute respiratory distress syndrome, ILD, pneumonitis), renal cyst (4%), and hepatic failure (1%).

Table 4. Summary of Treatment-Emergent Laboratory Abnormalities with Grade 3 or 4 Incidence of ≥4% in XALKORI-Treated Patients

Laboratory Abnormality	Crizotinib		Chemotherapy	
	Any Grade	Grade 3/4	Any Grade	Grade 3/4
Hematology				
Neutropenia	49%	12%	28%	12%
Lymphopenia	51%	9%	60%	25%
Chemistry				
ALT elevation	76%	17%	38%	4%
AST elevation	61%	9%	33%	0%
Hypokalemia	18%	4%	10%	1%
Hypophosphatemia	28%	5%	25%	6%

ALK-positive metastatic NSCLC- Study 2

The safety analysis population in Study 2 included 934 patients with ALK-positive metastatic NSCLC who received XALKORI in a clinical trial. The median duration of treatment was 23 weeks. Dosing interruptions and reductions due to treatment-related adverse events occurred in 23% and 12% of patients, respectively. The rate of treatment-related adverse events resulting in permanent discontinuation was 5%. The most common adverse reactions (≥25%) included vision disorder (55%), nausea (51%), vomiting (46%), diarrhea (46%), edema (39%), constipation (38%), and fatigue (26%).

Description of selected adverse drug reactions

Vision disorders
Vision disorders, most commonly visual impairment, photopsia, blurred vision, or vitreous floaters, occurred in 691 (56%) patients across clinical trials (n=1225). The majority (99%) of these patients had Grade 1 or 2 visual adverse reactions. Across clinical studies, one patient had a treatment-related grade 3 vision abnormality.

Based on the Visual Symptom Assessment Questionnaire (VSAQ-ALK), patients treated with XALKORI in Study 1 reported a higher incidence of visual disturbances compared to patients treated with chemotherapy. The onset of vision disorders generally started within the first week of drug administration. The majority of patients on the XALKORI arm in Study 1 (> 50%) reported visual disturbances; these visual disturbances occurred at a frequency of 4-7 days each week, lasted up to 1 minute, and had mild or no impact (scores 0 to 3 out of a maximum score of 10) on daily activities as captured in a patient questionnaire.

Neuropathy
Neuropathy, most commonly sensory in nature, occurred in 235 (19%) of 1225 patients. Most events (95%) were Grade 1 or Grade 2 in severity.

Renal Cysts
Renal cysts occurred in 7 (4%) patients treated with XALKORI and 1 (1%) patient treated with chemotherapy in Study 1. The majority of renal cysts in XALKORI-treated patients were complex. Local cystic invasion beyond the kidney occurred, in some cases with imaging characteristics suggestive of abscess formation. However, across clinical trials no renal abscesses were confirmed by microbiology tests.

7 DRUG INTERACTIONS

7.1 Drugs That May Increase Crizotinib Plasma Concentrations

Coadministration of crizotinib with strong CYP3A inhibitors increases crizotinib plasma concentrations *[see Clinical Pharmacology (12.3)]*. Avoid concomitant use of strong CYP3A inhibitors, including but not limited to

atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin, and voriconazole. Avoid grapefruit or grapefruit juice which may also increase plasma concentrations of crizotinib. Exercise caution with concomitant use of moderate CYP3A inhibitors.

7.2 Drugs That May Decrease Crizotinib Plasma Concentrations

Coadministration of crizotinib with strong CYP3A inducers decreases crizotinib plasma concentrations *[see Clinical Pharmacology (12.3)]*. Avoid concomitant use of strong CYP3A inducers, including but not limited to carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, and St. John's Wort.

7.3 Drugs Whose Plasma Concentrations May Be Altered By Crizotinib

Crizotinib inhibits CYP3A both *in vitro* and *in vivo [see Clinical Pharmacology (12.3)]*. Avoid concomitant use of CYP3A substrates with narrow therapeutic range, including but not limited to alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus in patients taking XALKORI. If concomitant use of these CYP3A substrates with narrow therapeutic range is required in patients taking XALKORI, dose reductions of the CYP3A substrates may be required due to adverse reactions.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category D *[see Warnings and Precautions (5.5)]*

XALKORI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. There are no adequate and well-controlled studies of XALKORI in pregnant women. In nonclinical studies in rats, crizotinib was embryotoxic and fetotoxic at exposures similar to those observed in humans at the recommended clinical dose of 250 mg twice daily. Crizotinib was administered to pregnant rats and rabbits during organogenesis to study the effects on embryo-fetal development. Postimplantation loss was increased at doses ≥ 50 mg/kg/day (approximately 0.6 times the AUC at the recommended human dose) in rats. No teratogenic effects were observed in rats at doses up to the maternally toxic dose of 200 mg/kg/day (approximately 2.7 times the AUC at the recommended human dose) or in rabbits at doses of up to 60 mg/kg/day (approximately 1.6 times the AUC at the recommended human dose), though fetal body weights were reduced at these doses.

Advise women of childbearing potential to avoid becoming pregnant while receiving XALKORI. Women of childbearing potential who are receiving this drug, or partners of women of childbearing potential receiving this drug, should use adequate contraceptive methods during therapy and for at least 90 days after completing therapy. If this drug is used during pregnancy, or if the patient or their partner becomes pregnant while taking this drug, apprise the patient of the potential hazard to a fetus.

8.3 Nursing Mothers

It is not known whether XALKORI is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from XALKORI, consider whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.4 Pediatric Use

The safety and efficacy of XALKORI in pediatric patients has not been established. Decreased bone formation in growing long bones was observed in immature rats at 150 mg/kg/day following once daily dosing for 28 days

(approximately 5.4 times the AUC in adult patients at the recommended human dose). Other toxicities of potential concern to pediatric patients have not been evaluated in juvenile animals.

8.5 Geriatric Use

Of XALKORI treated patients in Study 1, 27 (16%) were 65 years or older, in Study 2, 152 (16%) were 65 years or older, and in Study 3, 16 (13%) were 65 years or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

8.6 Hepatic Impairment

XALKORI has not been studied in patients with hepatic impairment. As crizotinib is extensively metabolized in the liver, hepatic impairment is likely to increase plasma crizotinib concentrations. Clinical studies excluded patients with AST or ALT greater than 2.5 x ULN, or greater than 5 x ULN, if due to liver metastases. Patients with total bilirubin greater than 1.5 x ULN were also excluded. Therefore, use caution in patients with hepatic impairment *[see Clinical Pharmacology (12.3)]*.

8.7 Renal Impairment

No starting dose adjustment is needed for patients with mild (creatinine clearance [CLcr] 60-89 mL/min) or moderate (CLcr 30-59 mL/min) renal impairment based on a population pharmacokinetic analysis.

Increased exposure to crizotinib occurred in patients with severe renal impairment (CLcr <30 mL/min) not requiring dialysis. Administer XALKORI at a dose of 250 mg taken orally once daily in patients with severe renal impairment not requiring dialysis *[see Dosage and Administration (2.2) and Clinical Pharmacology (12.3)]*.

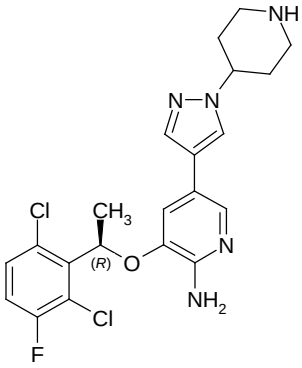
10 OVERDOSAGE

There have been no known cases of XALKORI overdose. There is no antidote for XALKORI.

11 DESCRIPTION

XALKORI (crizotinib) is an oral receptor tyrosine kinase inhibitor. The molecular formula for crizotinib is $C_{21}H_{22}Cl_2FN_5O$. The molecular weight is 450.34 Daltons. Crizotinib is described chemically as (*R*)-3-[1-(2,6-Dichloro-3-fluorophenyl)ethoxy]-5-[1-(piperidin-4-yl)-1*H*-pyrazol-4-yl]pyridin-2-amine.

The chemical structure of crizotinib is shown below:



Crizotinib is a white to pale-yellow powder with a pKa of 9.4 (piperidinium cation) and 5.6 (pyridinium cation). The solubility of crizotinib in aqueous media decreases over the range pH 1.6 to pH 8.2 from greater than 10 mg/mL to less than 0.1 mg/mL. The log of the distribution coefficient (octanol/water) at pH 7.4 is 1.65.

XALKORI capsules are supplied as printed hard-shell capsules containing 250 mg or 200 mg of crizotinib together with colloidal silicon dioxide, microcrystalline cellulose, anhydrous dibasic calcium phosphate, sodium starch glycolate, magnesium stearate, and hard gelatin capsule shells as inactive ingredients.

The pink opaque capsule shell components contain gelatin, titanium dioxide, and red iron oxide. The white opaque capsule shell components contain gelatin, and titanium dioxide. The printing ink contains shellac, propylene glycol, strong ammonia solution, potassium hydroxide, and black iron oxide.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Crizotinib is an inhibitor of receptor tyrosine kinases including ALK, Hepatocyte Growth Factor Receptor (HGFR, c-Met), ROS1 (c-ros), and Recepteur d'Origine Nantais (RON). Translocations can affect the ALK gene resulting in the expression of oncogenic fusion proteins. The formation of ALK fusion proteins results in activation and dysregulation of the gene's expression and signaling which can contribute to increased cell proliferation and survival in tumors expressing these proteins. Crizotinib demonstrated concentration-dependent inhibition of ALK, ROS1, and c-Met phosphorylation in cell-based assays using tumor cell lines and demonstrated antitumor activity in mice bearing tumor xenografts that expressed EML4- or NPM-ALK fusion proteins or c-Met.

12.2 Pharmacodynamics

Cardiac Electrophysiology

The QT interval prolongation potential of crizotinib was assessed in all patients who received XALKORI 250 mg twice daily. Serial ECGs in triplicate were collected following a single dose and at steady state to evaluate the effect of crizotinib on QT intervals. Sixteen of 1167 patients (1.4%) were found to have QTcF (corrected QT by the Fridericia method) greater than or equal to 500 msec and 51 of 1136 patients (4.4%) had an increase from baseline QTcF greater than or equal to 60 msec by automated machine-read evaluation of ECG.

In an ECG sub-study conducted in 52 patients with ALK-positive NSCLC who received crizotinib 250 mg twice daily, the maximum mean QTcF change from baseline was 12.3 msec (two-sided 90% upper CI: 19.5 msec). An exposure-QT analysis suggested a crizotinib plasma concentration dependent increase in QTcF *[see Warnings and Precautions (5.3)]*.

12.3 Pharmacokinetics

Absorption

Following a single oral dose, crizotinib was absorbed with median time to achieve peak concentration of 4 to 6 hours. Following crizotinib 250 mg twice daily, steady state was reached within 15 days and remained stable, with a median accumulation ratio of 4.8. Steady-state systemic exposure (C_{min} and AUC) appeared to increase in a greater than dose proportional manner over the dose range of 200-300 mg twice daily.

The mean absolute bioavailability of crizotinib was 43% (range: 32% to 66%) following a single 250 mg oral dose.

A high-fat meal reduced crizotinib AUC_{inf} and C_{max} by approximately 14%. XALKORI can be administered with or without food *[see Dosage and Administration (2.2)]*.

Distribution

The geometric mean volume of distribution (Vss) of crizotinib was 1,772 L following intravenous administration of a 50 mg dose, indicating extensive distribution into tissues from the plasma.

Binding of crizotinib to human plasma proteins *in vitro* is 91% and is independent of drug concentration. *In vitro* studies suggested that crizotinib is a substrate for P-glycoprotein (P-gp). The blood-to-plasma concentration ratio is approximately 1.

Metabolism

Crizotinib is predominantly metabolized by CYP3A4/5. The primary metabolic pathways in humans were oxidation of the piperidine ring to crizotinib lactam and *O*-dealkylation, with subsequent Phase 2 conjugation of *O*-dealkylated metabolites.

Elimination

Following single doses of crizotinib, the mean apparent plasma terminal half-life of crizotinib was 42 hours in patients.

Following the administration of a single 250 mg radiolabeled crizotinib dose to healthy subjects, 63% and 22% of the administered dose was recovered in feces and urine, respectively. Unchanged crizotinib represented approximately 53% and 2.3% of the administered dose in feces and urine, respectively.

The mean apparent clearance (CL/F) of crizotinib was lower at steady state (60 L/h) after 250 mg twice daily than that after a single 250 mg oral dose (100 L/h), which was likely due to autoinhibition of CYP3A by crizotinib after multiple dosing.

Drug interactions

CYP3A inhibitors: Coadministration of a single 150 mg oral dose of crizotinib with ketoconazole (200 mg twice daily), a strong CYP3A inhibitor, increased crizotinib AUC_{inf} and C_{max} values by approximately 3.2-fold and 1.4-fold, respectively, compared to crizotinib alone. However, the magnitude of effect of CYP3A inhibitors on steady-state crizotinib exposure has not been evaluated *[see Drug Interactions (7.1)]*.

CYP3A inducers: Coadministration of a single 250 mg oral dose of crizotinib with rifampin (600 mg once daily), a strong CYP3A inducer, decreased crizotinib AUC_{inf} and C_{max} by 82% and 69%, respectively, compared to crizotinib alone. However, the magnitude of effect of CYP3A inducers on steady-state crizotinib exposure has not been evaluated *[see Drug Interactions (7.2)]*.

Gastric pH elevating medications: In healthy subjects, coadministration of a single 250 mg oral dose of crizotinib following administration of esomeprazole 40 mg daily for 5 days did not result in a clinically relevant change in crizotinib exposure (AUC_{inf} decreased by 10% and no change in C_{max}).

CYP3A substrates: Coadministration of crizotinib (250 mg twice daily for 28 days) in patients increased the AUC_{inf} of oral midazolam 3.7-fold compared to midazolam alone, suggesting that crizotinib is a moderate inhibitor of CYP3A *[see Drug Interactions (7.3)]*.

Other CYP substrates: In vitro studies suggest that clinical drug-drug interactions as a result of crizotinib-mediated inhibition of the metabolism of substrates for CYP1A2, CYP2C8, CYP2C9, CYP2C19, or CYP2D6 are unlikely to occur.

Crizotinib is an inhibitor of CYP2B6 *in vitro*. Therefore, crizotinib may increase plasma concentrations of coadministered drugs that are predominantly metabolized by CYP2B6.

An *in vitro* study suggests that clinical drug-drug interactions as a result of crizotinib-mediated induction of the metabolism of substrates for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP3A are unlikely to occur.

UGT substrates: In vitro studies suggest that clinical drug-drug interactions as a result of crizotinib-mediated inhibition of the metabolism of drugs that are substrates for UGT1A1, UGT1A4, UGT1A6, UGT1A9 or UGT2B7 are unlikely to occur.

Substrates of transporters: Crizotinib inhibited P-glycoprotein (P-gp) *in vitro* at clinically relevant concentrations. Therefore, crizotinib has the potential to increase plasma concentrations of coadministered drugs that are substrates of P-gp.

Crizotinib inhibited the hepatic uptake transporter, organic cation transporter 1 (OCT1), and renal uptake transporter, organic cation transporter 2 (OCT2), *in vitro* at clinically relevant concentrations. Therefore, crizotinib has the potential to increase plasma concentrations of coadministered drugs that are substrates of OCT1 or OCT2.

Crizotinib did not inhibit the human hepatic uptake transport proteins OATP1B1 or OATP1B3, or the renal uptake transport proteins OAT1 or OAT3 *in vitro* at clinically relevant concentrations.

Effect on other transport proteins: Crizotinib did not inhibit the hepatic efflux bile salt export pump transporter (BSEP) *in vitro* at clinically relevant concentrations.

Specific populations

Hepatic Impairment: As crizotinib is extensively metabolized in the liver, hepatic impairment is likely to increase plasma crizotinib concentrations. However, XALKORI has not been studied in patients with hepatic impairment. Clinical studies excluded patients with ALT or AST greater than 2.5 x ULN or greater than 5 x ULN if due to liver metastases. Patients with total bilirubin greater than 1.5 x ULN were also excluded *[see Use in Specific Populations (8.6)]*. The population pharmacokinetic analysis using the data from Studies 1, 2 and 3 suggested that baseline total bilirubin (0.1 to 2.1 mg/dL) or AST levels (7 to 124 U/L) did not have a clinically relevant effect on the exposure of crizotinib.

Renal impairment: The pharmacokinetics of crizotinib were evaluated using a population pharmacokinetic analysis in patients with mild (CLcr 60-89 mL/min, N=433) and moderate (CLcr 30-59 mL/min, N=137) renal impairment enrolled in Studies 1, 2, and 3. Mild or moderate renal impairment has no clinically relevant effect on the exposure of crizotinib.

A study was conducted in 7 patients with severe renal impairment (CLcr <30 mL/min) who did not require dialysis and 8 patients with normal renal function (CLcr ≥ 90 mL/min). All patients received a single 250 mg oral dose of XALKORI. The mean AUC_{inf} for crizotinib increased by 79% and the mean C_{max} increased by 34% in patients with severe renal impairment compared to those with normal renal function. Similar changes in AUC_{inf} and C_{max} were observed for the active metabolite of crizotinib *[see Dosage and Administration (2.2) and Use in Specific Populations (8.7)]*.

Ethnicity: No clinically relevant difference in the exposure of crizotinib between Asian patients (N=523) and non-Asian patients (N=691).

Age: Age has no effect on the exposure of crizotinib based on the population pharmacokinetic analysis from Studies 1, 2 and 3.

Body weight and gender: No clinically relevant effect of body weight or gender on the exposure of crizotinib based on the population pharmacokinetic analysis from Studies 1, 2 and 3.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity studies with crizotinib have not been conducted.

Crizotinib was genotoxic in an *in vitro* micronucleus assay in Chinese Hamster Ovary cultures, in an *in vitro* human lymphocyte chromosome aberration assay, and in *in vivo* rat bone marrow micronucleus assays. Crizotinib was not mutagenic *in vitro* in the bacterial reverse mutation (Ames) assay.

No specific studies with crizotinib have been conducted in animals to evaluate the effect on fertility; however, crizotinib is considered to have the potential to impair reproductive function and fertility in humans based on findings in repeat-dose toxicity studies in the rat. Findings observed in the male reproductive tract included testicular pachytene spermatocyte degeneration in rats given greater than or equal to 50 mg/kg/day for 28 days (greater than 1.7 times the AUC at the recommended human dose). Findings observed in the female reproductive tract included single-cell necrosis of ovarian follicles of a rat given 500 mg/kg/day (approximately 10 times the recommended human daily dose on a mg/m^2 basis) for 3 days.

14 CLINICAL STUDIES

ALK-positive metastatic NSCLC-Study 1

The efficacy and safety of XALKORI as monotherapy for the treatment of 347 patients with metastatic ALK-positive NSCLC, previously treated with one platinum-based chemotherapy regimen, was demonstrated in a randomized, multicenter, open-label, active-controlled study (Study 1). The major efficacy outcome was progression-free survival (PFS) as assessed by independent radiology review (IRR). Additional efficacy outcomes included objective response rate (ORR) as assessed by IRR and overall survival (OS).

Patients were randomized to receive XALKORI 250 mg orally twice daily (n=173) or chemotherapy (n=174). Chemotherapy consisted of pemetrexed 500 mg/m^2 (if pemetrexed naïve; n=99) or docetaxel 75 mg/m^2 (n=72) intravenously (IV) every 21 days. Patients in both treatment arms continued treatment until documented disease progression, intolerance to therapy, or the investigator determined that the patient was no longer experiencing clinical benefit. Randomization was stratified by ECOG performance status (0-1, 2), brain metastases (present, absent), and prior EGFR tyrosine kinase inhibitor treatment (yes, no). Patients were required to have ALK-positive NSCLC as identified by the FDA-approved assay, Vysis ALK Break-Apart FISH Probe Kit, prior to randomization. A total of 112 (64%) patients randomized to the chemotherapy arm subsequently received XALKORI after disease progression.

The demographic characteristics of the overall study population were 56% female, median age of 50 years, baseline ECOG performance status 0 (39%) or 1 (52%), 52% White and 45% Asian, 4% current smokers, 33% past-smokers, and 63% never smokers. The disease characteristics were metastatic disease in at least 95% of patients and at least 93% of patients' tumors were classified as adenocarcinoma histology.

Study 1 demonstrated a statistically significant improvement in PFS in the patients treated with XALKORI. Table 5 and Figure 1 summarize the efficacy results.

Table 5. ALK-Positive Metastatic NSCLC - Efficacy Results

	XALKORI (N=173)	Chemotherapy (N=174)
Progression-free Survival (Based on IRR)		
Number of Events (%)	100 (58%)	127 (73%)
Progressive Disease	84 (49%)	119 (68%)
Death	16 (9%)	8 (5%)
Median, Months (95% CI)	7.7 (6.0, 8.8)	3.0[a] (2.6, 4.3)
HR (95% CI)[b]	0.49 (0.37,0.64)	
P-value[c]	<0.001	
Overall Survival[d]		
Number of Events (%)	49 (28%)	47 (27%)
Median, Months (95% CI)	20.3 (18.1,NR)	22.8 (18.6,NR)
HR (95% CI)[b]	1.02 (0.68,1.54)	
P-value[c]	0.54	
Tumor Responses (Based on IRR)		
Objective Response Rate % (95% CI)	65% (58, 72)	20% (14, 26)
CR, n (%)	1 (0.6%)	0
PR, n (%)	112 (65%)	34 (20%)
P-value[e]	<0.001	
Duration of Response		
Median, Months (95% CI)	7.4 (6.1, 9.7)	5.6 (3.4, 8.3)

HR = Hazard Ratio; CI = confidence interval; NR= not reached; CR = complete response; PR = partial response

[a] For pemetrexed, the median PFS was 4.2 months. For docetaxel, the median PFS was 2.6 months.

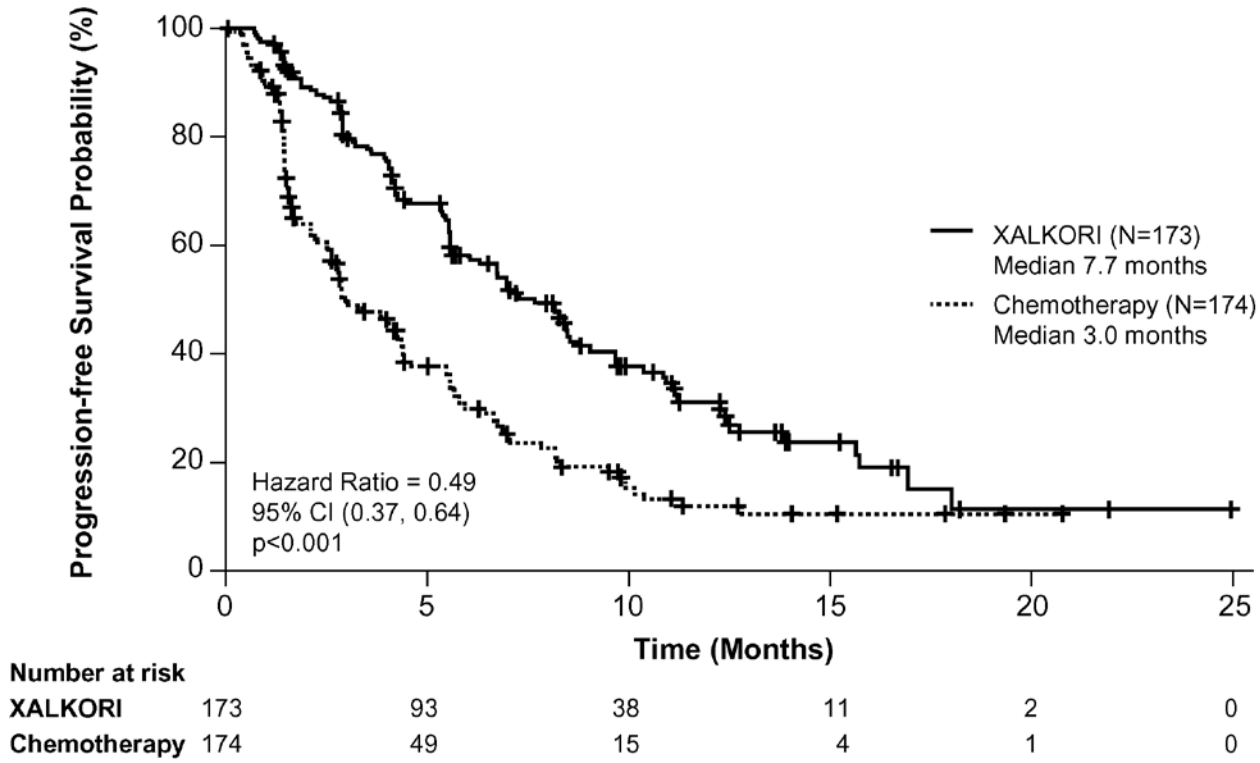
[b] Based on the Cox proportional hazards stratified analysis

[c] Based on the stratified Log-rank test

[d] Interim OS analysis conducted at 40% of total events required for final analysis

[e] Based on the stratified Cochran-Mantel-Haenszel test

Figure 1. Kaplan-Meier Curves of Progression-Free Survival as Assessed by IRR in Study 1



Single-arm studies in ALK-positive metastatic NSCLC- Studies 2 and 3

The safety and anti-tumor activity of single-agent XALKORI in the treatment of metastatic ALK-positive NSCLC was demonstrated in two multinational, single-arm studies (Studies 2 and 3). The major outcome in both studies was investigator-assessed ORR according to RECIST. Patients in both studies received 250 mg of XALKORI orally twice daily.

In Study 2 (n=934) the demographic characteristics were 57% female, median age of 52 years, baseline ECOG performance status of 0/1 (82%) or 2/3 (18%), 52% White and 44% Asian, 4% current smokers, 30% past-smokers, and 66% never smokers. The disease characteristics were 92% metastatic; 94% of the cancers were classified as adenocarcinoma histology.

Of the 934 ALK-positive metastatic NSCLC patients who received XALKORI in Study 2, 765 were ALK-positive as identified by Vysis ALK Break-Apart FISH Probe Kit and evaluable for response; demographic characteristics were similar to that of the overall population for this study. The median duration of treatment was 5.5 months. Based on investigator assessments, there were 8 complete and 357 partial responses for an ORR of 48% (95% CI: 44, 51) and the median DR was 11.0 months.

In Study 3 (n=119) the demographic characteristics were 50% female, median age of 51 years, baseline ECOG performance status of 0 (35%) or 1 (53%), 62% White and 29% Asian, less than 1% were current smokers, 27% past-smokers, and 72% never smokers. The disease characteristics were 96% metastatic, 98% of the cancers were classified as adenocarcinoma histology, and 13% had no prior systemic therapy for metastatic disease.

In Study 3, 119 patients with metastatic ALK-positive NSCLC were treated with XALKORI with a median duration of treatment of 32 weeks. Based on investigator assessments, the ORR was 61% (95% CI: 52%, 70%) and the median DR was 11.1 months.

16 HOW SUPPLIED/STORAGE AND HANDLING

250 mg capsules
Hard gelatin capsule with pink opaque cap and body, printed with black ink "Pfizer" on the cap, "CRZ 250" on the body; available in:
Bottles of 60 capsules: NDC 0069-8140-20

200 mg capsules
Hard gelatin capsule with pink opaque cap and white opaque body, printed with black ink "Pfizer" on the cap, "CRZ 200" on the body; available in:
Bottles of 60 capsules: NDC 0069-8141-20

Store at room temperature 20° to 25°C (68° to 77°F); excursions permitted between 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information).

- Inform patients of the symptoms of hepatotoxicity, and that they should be reported immediately *[see Warnings and Precautions (5.1)]*.

- Advise patients to immediately report any new or worsening pulmonary symptoms *[see Warnings and Precautions (5.2)]*.

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

- Inform patients that nausea, diarrhea, vomiting, and constipation are the most commonly reported gastrointestinal adverse events occurring in patients who received XALKORI. Nausea and vomiting began most commonly during the first few days of treatment *[see Adverse Reactions (6)]*.

- Inform patients that visual changes such as perceived flashes of light, blurry vision, light sensitivity, and floaters are commonly reported adverse events and may occur while driving or operating machinery. The onset of visual disorders most commonly occurs during the first week of treatment *[see Adverse Reactions (6)]*.

- Inform patients to avoid grapefruit or grapefruit juice while taking XALKORI. Advise patients to inform their health care providers of all concomitant medications, including prescription medicines, over-the-counter drugs, vitamins, and herbal products *[see Drug Interactions (7)]*.

- Advise patients to take XALKORI with or without food and swallow XALKORI capsules whole.

- If a patient misses a dose, advise the patient to take it as soon as remembered unless it is less than 6 hours until the next dose, in which case, advise the patient not to take the missed dose. If a patient vomits after taking a dose of XALKORI, advise the patient not to take an extra dose, but to take the next dose at the regular time.

- Inform patients of childbearing potential to use adequate contraceptive methods during therapy and for at least 90 days after completing therapy. Advise patients to inform their doctor if they or their partners are pregnant or think they may be pregnant. Also advise patients not to breastfeed while taking XALKORI *[see Use in Specific Populations (8.1 and 8.3)]*.

This product's label may have been updated. For full prescribing information, please visit www.XALKORI.com.

LAB-0440-11.2

PATIENT INFORMATION

XALKORI® (zal-KOR-ee)

(crizotinib)

Capsules

Read this patient information leaflet before you start taking XALKORI and each time you get a refill. There may be new information. This information does not take the place of talking to your doctor about your condition or treatment.

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

XALKORI may cause serious side effects, including:

Liver problems. XALKORI may cause life-threatening or fatal liver injury. Your doctor should do blood tests at least every month to check your liver while you are taking XALKORI. Tell your doctor right away if you get any of the following:

- your skin or the whites of your eyes turn yellow
- you feel tired
- your urine turns dark or brown (tea color)
- you have nausea or vomiting
- you have a decreased appetite
- you have pain on the right side of your stomach
- you bleed or bruise more easily than normal
- you have itching

Lung problems (pneumonitis). XALKORI may cause life-threatening or fatal 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 or shortness of breath
- cough with or without mucous
- fever

Heart problems. XALKORI may cause very slow, very fast or abnormal heartbeats. Your doctor may check your heart during treatment with XALKORI. Tell your doctor right away if you feel dizzy or faint or have abnormal heartbeats. Tell your doctor if you take any heart or blood pressure medicines.
See "What are possible side effects of XALKORI?" for more information about side effects.

What is XALKORI?

XALKORI is a prescription medicine that is used to treat people with non-small cell lung cancer (NSCLC) that has spread to other parts of the body and is caused by a defect in a gene called ALK (anaplastic lymphoma kinase).

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

What should I tell my doctor before taking XALKORI?

Before you take XALKORI, tell your doctor if you:

- have heart problems, including a condition called long QT syndrome
- have liver or kidney problems
- have any other medical conditions
- are pregnant, or plan to become pregnant. XALKORI may harm your unborn baby.
  - Women who are able to become pregnant and men who take XALKORI should use birth control during treatment and for 3 months after stopping XALKORI.
  - Talk to your doctor about the birth control methods that may be right for you.
  - If you or your partner becomes pregnant, tell your doctor right away.
- are breastfeeding or plan to breastfeed. It is not known if XALKORI passes into your breast milk. You and your doctor should decide if you will take XALKORI or breastfeed. You should not do both.

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

Know the medicines you take. Keep a list of them to show your doctor or pharmacist when you get a new medicine.

How should I take XALKORI?

- Take XALKORI exactly as your doctor tells you.
- Swallow XALKORI capsules whole.
- You may take XALKORI with or without food.
- Do not change your dose or stop XALKORI unless your doctor tells you.
- If you miss a dose, take it as soon as you remember. If it is close to your next dose (within 6 hours), just take your next dose at your regular time.
- If you vomit after taking a dose of XALKORI, do not take an extra dose, just take your next dose at your regular time.
- Call your doctor right away if you take too much XALKORI.
- Your doctor will check your blood and heart while you are taking XALKORI.

What should I avoid while taking XALKORI?

- You should not drink grapefruit juice or eat grapefruit during your treatment with XALKORI. It may make the amount of XALKORI in your blood increase to a harmful level.
- XALKORI can cause changes in your vision, dizziness, and tiredness. If you have these symptoms avoid driving a car, using machinery, or doing anything that needs you to be alert.

What are the possible side effects of XALKORI?

XALKORI may cause serious side effects, including:

- **See "What is the most important information I should know about XALKORI?"**

The most common side effects of XALKORI include:

- Vision problems. These problems usually happen within 1 week of starting XALKORI. Tell your doctor right away if you have any change in vision, such as double vision, flashes of light, blurred vision, light hurting your eyes, new or increased floaters.
- nausea
- diarrhea
- vomiting
- constipation
- swelling of your hands and feet
- feeling tired

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of XALKORI. For more information, ask your doctor 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 XALKORI?

- Store XALKORI at room temperature between 68°F to 77°F (20°C to 25°C).

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

General information about XALKORI

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use XALKORI for a condition for which it was not prescribed. Do not give it to other people, even if they have the same symptoms you have. It may harm them.

This leaflet provides the most important information about XALKORI. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for more information about XALKORI that is written for health professionals.

For more information, go to www.XALKORI.com.

What are the ingredients in XALKORI?

Active ingredient: crizotinib

Inactive ingredients: colloidal silicon dioxide, microcrystalline cellulose, anhydrous dibasic calcium phosphate, sodium starch glycolate, and magnesium stearate

Pink opaque capsule shell contains: gelatin, titanium dioxide, and red iron oxide

White opaque capsule shell contains: gelatin and titanium dioxide

Printing ink contains: shellac, propylene glycol, strong ammonia solution, potassium hydroxide, and black iron oxide

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

LAB-0441-6.0

Revised: November 2013