XALKORI (crizotinib) is available through specialty pharmacies

THE FOLLOWING SPECIALTY PHARMACIES OFFER XALKORI

<table>
<thead>
<tr>
<th>Pharmacy</th>
<th>Website</th>
<th>Phone Number</th>
<th>Fax Number</th>
<th>Hours of Operation</th>
</tr>
</thead>
<tbody>
<tr>
<td>US Bioservices</td>
<td>usbioservices.com</td>
<td>1-877-757-0667</td>
<td>1-888-899-0067</td>
<td>Monday–Friday 8AM to 8PM (ET)</td>
</tr>
<tr>
<td>CuraScript</td>
<td>curascript.com</td>
<td>1-888-773-7376</td>
<td>1-888-773-7386</td>
<td>Monday–Friday 8AM to 9PM (ET) Saturday 9AM to 1PM (ET)</td>
</tr>
<tr>
<td>Walgreens Specialty</td>
<td>walgreenshealth.com</td>
<td>1-888-347-3416</td>
<td>1-866-889-1510</td>
<td>Monday–Friday 8AM to 7PM (ET) Saturday 9AM to 5PM (ET)</td>
</tr>
<tr>
<td>CVS Caremark Specialty Pharmacy</td>
<td>caremark.com</td>
<td>1-800-237-2767</td>
<td>1-800-323-2445</td>
<td>Monday–Friday 7:30AM to 9PM (ET)</td>
</tr>
<tr>
<td>Accredro Specialty Pharmacy</td>
<td>accredo.com</td>
<td>1-877-732-3431</td>
<td>1-888-302-1028</td>
<td>Monday–Friday 8AM to 11PM (ET) Saturday 8AM to 5PM (ET)</td>
</tr>
</tbody>
</table>

Please note that XALKORI is not available from traditional retail pharmacies

SPECIALTY PHARMACY ORDERING PROCESS

THE PROVIDER’S OFFICE
- Submits XALKORI prescriptions to the specialty pharmacy via:
  - Phone
  - Fax
  - Internet
- Submits any supporting documentation to the payer

THE SPECIALTY PHARMACY
- Verifies patient coverage for XALKORI
- Helps with prior authorization if required
- Can refer patients to the Pfizer Co-Pay Assistance Program
- Schedules shipment of product to the patient’s home
- Bills the payer for cost of the product
- Bills the patient for remaining co-pay/coinsurance

FOR ASSISTANCE WITH SPECIALTY PHARMACY OR ACCESSING XALKORI, PLEASE CALL 1-877-744-5675

The Pfizer First Resource® Program is designed to help patients get access to the Pfizer medicines they need*

- The program will help insured patients find an appropriate specialty pharmacy for reimbursement support services and to obtain their medicines
- For uninsured and underinsured patients, the program can provide eligible patients with free medicine for up to 12 months

*XFirst Resource is a part of the Pfizer Helpful Answers® family of patient assistance programs—a joint program of Pfizer Inc and the Pfizer Patient Assistance Foundation™.

XALKORI is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. This indication is based on response rate. There are no data available demonstrating improvement in patient reported outcomes or survival with XALKORI.

Please see Important Safety Information on page 2 and full Prescribing Information on pages 3-8.

For more information, please visit www.xalkorihcp.com.
XALKORI is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test.

This indication is based on response rate. There are no data available demonstrating improvement in patient reported outcomes or survival with XALKORI.

IMPORTANT SAFETY INFORMATION

Hepatotoxicity: Drug-induced hepatotoxicity with fatal outcome has occurred. Transaminase elevations generally occurred within the first 2 months of treatment. Monitor with liver function tests including ALT and total bilirubin once a month and as clinically indicated, with more frequent repeat testing for Grades 2, 3 or 4 elevation in patients who develop transaminase elevations. Temporarily suspend, dose reduce, or permanently discontinue XALKORI as indicated.

Pneumonitis: XALKORI has been associated with severe, life-threatening, or fatal treatment-related pneumonitis in clinical trials with a frequency of 4 in 255 (1.6%) patients. All of these cases occurred within 2 months after the initiation of treatment. Patients should be monitored for pulmonary symptoms indicative of pneumonitis. Other causes of pneumonitis should be excluded. XALKORI should be permanently discontinued in patients with treatment-related pneumonitis.

QT Interval Prolongation: QTc prolongation has been observed. XALKORI should be avoided in patients with congenital long QT syndrome. In patients with congestive heart failure, bradycardia, electrolyte abnormalities, or who are taking medications that are known to prolong the QT interval, periodic monitoring with electrocardiograms and electrolytes should be considered. Permanently discontinue XALKORI for grade 4 QTc prolongation. XALKORI should be withheld for grade 3 QTc prolongation until recovery to ≤ grade 1. Permanently discontinue XALKORI if grade 3 QTc prolongation recurs.

ALK Testing: Detection of ALK-positive NSCLC using an FDA-approved test, indicated for this use, is necessary for selection of patients for treatment with XALKORI.

Pregnancy: XALKORI can cause fetal harm when administered to a pregnant woman based on its mechanism of action. Women of childbearing potential should be advised to avoid becoming pregnant while receiving XALKORI. If the patient or their partner becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

Adverse Reactions: Among the 397 patients for whom information on deaths and serious adverse reactions are available, deaths within 28 days of the last dose of study drug occurred in 45 patients. Ten (2.5%) patients died within 28 days of their first dose of study drug. Causes of death included disease progression (32 patients), respiratory events (9), and other (4).

Safety of XALKORI was evaluated in 255 patients with locally advanced or metastatic ALK-positive NSCLC in 2 single-arm clinical trials (Studies A and B). The most common adverse reactions (≥25%) across both studies were vision disorder, nausea, diarrhea, vomiting, edema, and constipation. Grade 3-4 adverse reactions in ≥4% of patients in both studies included ALT increased and neutropenia.

- Vision disorders including visual impairment, photopsia, vision blurred, vitreous floaters, photophobia, and diplopia were reported in 159 (62%) patients in clinical trials. Ophthalmological evaluation should be considered, particularly if patients experience photopsia or experience new or increased vitreous floaters. Severe or worsening vitreous floaters and/or photopsia could also be signs of a retinal hole or pending retinal detachment. Caution should be exercised when driving or operating machinery by patients who experience vision disorder.
- Neuropathy attributed to study drug was reported in 34 (13%) patients. Grade 2 motor neuropathy and grade 3 peripheral neuropathy were reported in 1 patient each.
- Bradycardia has been reported in 12 (5%) patients treated with XALKORI. All of these cases were grade 1 or 2 in severity.
- Complex renal cysts have been reported in 2 (1%) patients treated with XALKORI. There were no reports of abnormal urinalyses or renal impairment in these cases.

Grade 3 or 4 laboratory abnormalities of neutropenia, thrombocytopenia, and lymphopenia were seen in 5.2%, 0.4%, and 11.4% of patients, respectively.

Drug Interactions: Caution should be exercised with concomitant use of moderate CYP3A inhibitors. Grapefruit or grapefruit juice may increase plasma concentrations of crizotinib and should be avoided. The concurrent use of strong CYP3A inducers and inhibitors should be avoided. Dose reduction may be needed for coadministered drugs that are predominantly metabolized by CYP3A.

Nursing Mothers: Given the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or discontinue XALKORI.

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. Treatment with XALKORI should be used with caution in patients with hepatic impairment.

Renal Impairment: No starting dose adjustment is needed for patients with mild and moderate renal impairment. No data are available for patients with end-stage renal disease. Caution should be used in patients with severe renal impairment or patients with end-stage renal disease.
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: August 2011

INDICATIONS AND USAGE
XALKORI is a kinase inhibitor indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) that is anaplastic lymphoma kinase (ALK)-positive as detected by an FDA-approved test. (1) This indication is based on response rate. There are no data available demonstrating improvement in patient reported outcomes or survival with XALKORI.

DOSEAGE AND ADMINISTRATION
• 250 mg taken orally twice daily with or without food. (2.1)
• Dosing interruption and/or dose reduction to 200 mg taken orally twice daily may be required based on individual safety and tolerability, then to 250 mg taken orally once daily if further reduction is necessary. (2.2)

DOSE FORMS AND STRENGTHS
• XALKORI Capsules: 250 mg and 200 mg. (3)

CONTRAINDICATIONS
• None (4)

WARNINGS AND PRECAUTIONS
• Hepatotoxicity: Drug-induced hepatotoxicity with fatal outcome has occurred. Monitor monthly and as clinically indicated with more frequent testing in patients with Grade 2-4 elevations. Temporarily suspend, dose reduce, or permanently discontinue XALKORI as indicated. (5.1)

ADVERSE REACTIONS
The most common adverse reactions (>25%) are vision disorder, nausea, diarrhea, vomiting, edema, and constipation. (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: Dose reduction may be needed for coadministered drugs that are predominantly metabolized by CYP3A. 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: 12/2011

FULL PRESCRIBING INFORMATION: CONTENTS *

1 INDICATIONS AND USAGE
2 DOSEAGE AND ADMINISTRATION
  2.1 Recommended Dosing
  2.2 Dose Modification
3 DOSE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
  5.1 Hepatotoxicity
  5.2 Pneumonitis
  5.3 QT Interval Prolongation
  5.4 ALK Testing
  5.5 Pregnancy
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
  7.1 Drugs That May Increase Crizotinib Plasma Concentration
  7.2 Drugs That May Decrease Crizotinib Plasma Concentration
  7.3 Drugs Whose Plasma Concentrations May Be Altered By Crizotinib
8 USE IN SPECIFIC POPULATIONS
  8.1 Pregnancy
  8.3 Nursing Mothers
  8.4 Pediatric Use
  8.5 Geriatric Use
  8.6 Hepatic Impairment
  8.7 Renal Impairment
9 SAFETY INFORMATION
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
  12.1 Mechanism of Action
  12.3 Pharmacokinetics
  12.4 Cardiac Electrophysiology
13 NONCLINICAL TOXICOLOGY
  13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
  17.1 Hepatotoxicity
  17.2 Gastrointestinal Effects
  17.3 Visual Effects
  17.4 Effects on Ability to Drive and Use Machines
  17.5 Concomitant Medications
  17.6 Instructions for Taking XALKORI
  17.7 Pregnancy and Nursing
  17.8 FDA-Approved Patient Labeling

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

Table 1: XALKORI Dose Modification – Hematologic Toxicities*

<table>
<thead>
<tr>
<th>CTCAE Grade</th>
<th>XALKORI Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3</td>
<td>Withhold until recovery to Grade ≤2, then resume at the same dose schedule</td>
</tr>
<tr>
<td>Grade 4</td>
<td>Withhold until recovery to Grade ≤2, then resume at 250 mg twice daily*</td>
</tr>
</tbody>
</table>

*Except lymphopenia (unless associated with clinical events, e.g. opportunistic infections).

Table 2: XALKORI Dose Modification – Non-Hematologic Toxicities

<table>
<thead>
<tr>
<th>CTCAE Grade</th>
<th>XALKORI Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 3 or 4 alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevation with Grade ≥1 total bilirubin elevation</td>
<td>Withhold until recovery to Grade ≤1 or baseline, then resume at 200 mg twice daily*</td>
</tr>
<tr>
<td>Grade 2, 3 or 4 ALT or AST elevation with concurrent Grade 2, 3 or 4 total bilirubin elevation (in the absence of cholestasis or hemolysis)</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Any Grade pneumonitis</td>
<td>Permanently discontinue</td>
</tr>
<tr>
<td>Grade 3 QTc prolongation</td>
<td>Withhold until recovery to Grade ≤1, then resume at 200 mg twice daily*</td>
</tr>
<tr>
<td>Grade 4 QTc prolongation</td>
<td>Permanently discontinue</td>
</tr>
</tbody>
</table>

*In case of recurrence, withhold until recovery to Grade ≤1, then resume at 250 mg once daily. Permanently discontinue in case of Grade 4 recurrence.

**Not attributable to NSCLC progression, other pulmonary disease, infection, or radiation effect.
Complete blood counts including differential white blood cell counts should be monitored monthly and as clinically indicated, with more frequent repeat testing if Grade 3 or 4 abnormalities are observed, or if fever or infection occurs. Liver function tests should be monitored monthly and as clinically indicated, with more frequent repeat testing if Grade 2, 3 or 4 abnormalities are observed.

3. DOSAGE FORMS AND STRENGTH

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 has occurred. These cases have occurred during XALKORI treatment in less than 1% patients in clinical trials. Concurrent elevations in ALT greater than 3 x ULN and total bilirubin greater than 2 x ULN without elevated alkaline phosphatase have been observed in less than 1% patients in clinical trials. Grade 3 or 4 ALT elevation was observed in 7% of patients in Study A and in 4% of patients in Study B. Grade 3 and 4 elevations were generally asymptomatic and reversible upon dosing interruption. Patients usually resumed treatment at a lower dose without recurrence; however, 3 patients from Study A (2%) and 1 patient from Study B (less than 1%) required permanent discontinuation from treatment. Transaminase elevations generally occurred within the first 2 months of treatment. Monitor with liver function tests including ALT and total bilirubin once a month and as clinically indicated, with more frequent repeat testing for Grades 2, 3 or 4 elevation in patients who develop transaminase elevations [see Dosage and Administration (2.2) and Adverse Reactions (6)].

5.2 Pneumonitis

XALKORI has been associated with severe, life-threatening, or fatal treatment-related pneumonitis in clinical trials with a frequency of 4 in 255 (1.6%) patients across Studies A and B. All of the cases occurred within 2 months after the initiation of treatment. Patients should be monitored for pulmonary symptoms indicative of pneumonitis. Other causes of pneumonitis should be excluded. XALKORI should be permanently discontinued in patients diagnosed with treatment-related pneumonitis [see Dosage and Administration (2.2)].

5.3 QT Interval Prolongation

QTc prolongation has been observed. XALKORI should be avoided in patients with congenital long QT syndrome. In patients with congestive heart failure, bradynrhythmias, electrolyte abnormalities, or taking medications that are known to prolong the QT interval, periodic monitoring with electrocardiograms (ECGs) and electrolytes should be considered. Permanently discontinue XALKORI in patients who develop Grade 4 QTc prolongation. Withhold XALKORI in patients who develop Grade 3 QTc prolongation until recovery to less than or equal to Grade 1, then resume XALKORI at 200 mg twice daily. In case of recurrence of Grade 3 QTc prolongation, withhold XALKORI until recovery to less than or equal to Grade 1, then resume XALKORI at 250 mg once daily. Permanently discontinue XALKORI if Grade 3 QTc prolongation recurs [see Dosage and Administration (2.2) and Clinical Pharmacology (12.4)].

5.4 ALK Testing

Detection of ALK-positive NSCLC using an FDA-approved test, indicated for this use, is necessary for selection of patients for treatment with XALKORI [see Clinical Studies (14)]. Assessment for ALK-positive NSCLC should be performed by laboratories with demonstrated proficiency in the specific technology being utilized. Improper assay performance can lead to unreliable test results.

Refer to an FDA-approved test’s package insert for instructions on the identification of patients eligible for treatment with XALKORI.

5.5 Pregnancy

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 and above those observed in humans at the recommended clinical dose of 250 mg orally 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, the patient should be apprised of the potential hazard to a fetus [see Use in Specific Populations (8.1)].

6. ADVERSE REACTIONS

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.

In Studies A and B, patients with locally advanced or metastatic ALK-positive NSCLC received crizotinib 250 mg orally twice daily continuously. Among the 255 patients for whom data on Grade 1-4 adverse reactions are available, median exposure to study drug was 5.1 months in Study A and 7.8 months in Study B. Dosing interruptions occurred in 36% and 45% of patients in Studies A and B, and lasted greater than 2 weeks in 13% and 19% of patients in Studies A and B, respectively. Dose reductions occurred in 44% and 29% of patients in Studies A and B, respectively. The rates of treatment-related adverse events of Grade 1-4 discontinuation were 6% in Study A and 3% in Study B. The most common adverse reactions (≥25%) across both studies were vision disorder, nausea, diarrhea, vomiting, edema, and constipation. Grade 3-4 adverse reactions in at least 4% of patients in both studies included ALT increased and neutropenia. Among the 397 patients for whom information on deaths and serious adverse reactions are available, deaths within 28 days of the last dose of study drug occurred in 45 patients. Ten (2.5%) patients died within 28 days of their first dose of study drug. Causes of death included disease progression (32 patients), respiratory events (9), and other (4). Respiratory causes of death included pneumonia (2), hypoxia (2), ARDS (1), dyspnea (1), respiratory arrest (1), and pulmonary hemorrhage (1). Other causes of death included septic shock, DIC, cardiovascular event, and death due to unknown cause (1 each). Serious adverse events in greater than or equal to 2% of patients included pneumonia, dyspnea, and pulmonary embolism.

Table 3 lists the common adverse reactions on Studies A and B in patients receiving XALKORI.

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Treatment Emergent N=255</th>
<th>Treatment Related N=255</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eye Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vision Disorder2</td>
<td>163 (64%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>145 (57%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>124 (49%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>116 (45%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Constipation</td>
<td>98 (38%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Esophageal Disorder2</td>
<td>51 (20%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Abdominal Pain4</td>
<td>40 (16%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Stomatitis</td>
<td>27 (11%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>General Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edema</td>
<td>97 (38%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>90 (35%)</td>
<td>6 (2%)</td>
</tr>
<tr>
<td>Chest Pain/Discontinuation2</td>
<td>30 (12%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Fever</td>
<td>30 (12%)</td>
<td>2 (1%)</td>
</tr>
<tr>
<td><strong>Infections and Infestations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Infection3</td>
<td>50 (20%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine Aminotransferase</td>
<td>38 (15%)</td>
<td>17 (7%)</td>
</tr>
<tr>
<td>Aspartate Aminotransferase</td>
<td>29 (11%)</td>
<td>7 (3%)</td>
</tr>
<tr>
<td><strong>Metabolism and Nutrition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>69 (27%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td><strong>Musculoskeletal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>29 (11%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>28 (11%)</td>
<td>2 (&lt;1%)</td>
</tr>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness4</td>
<td>60 (24%)</td>
<td>0</td>
</tr>
<tr>
<td>Neutropathy8</td>
<td>58 (23%)</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>Headache</td>
<td>34 (13%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>33 (13%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Psychiatric Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>30 (12%)</td>
<td>8 (3%)</td>
</tr>
<tr>
<td><strong>Respiratory Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea</td>
<td>57 (22%)</td>
<td>16 (6%)</td>
</tr>
<tr>
<td>Cough</td>
<td>54 (21%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td><strong>Skin Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>41 (16%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Study A used CTCAE v4.0, and Study B used CTCAE v3.0.

Includes diplopia, photopsia, photophobia, vision blurred, visual field defect, visual impairment, vitreous floaters, visual brightness, and visual acuity reduced.

Includes dyspnea, dysphagia, epigastric discomfort/pain/blister, esophagitis, esophageal obstruction/pain/spasm/ulcer, gastroesophageal reflux, ophthalmic and reflex esophagitis.

Includes abdominal discomfort, abdominal pain, abdominal pain upper, and abdominal tenderness.

Includes mouth ulceration, glossodynia, glossitis, cheilitis, mucosal inflammation, oropharyngeal pain/discomfort, oral pain, and stomatitis.

Includes edema, edema localized, and peripheral edema.

Includes chest pain, chest discomfort, and musculoskeletal chest pain.

Includes nasopharyngitis, rhinitis, pharyngitis, and upper respiratory tract infection.

Includes balance disorder, dizziness, and presyncope.

Includes burning sensation, dysesthesia, hyperesthesia, hypoesthesia, neuralgia, paresthesia, peripheral neuropathy, peripheral motor neuropathy, and peripheral sensory neuropathy.

Vision disorders include visual impairment, photopsia, vision blurred, vitreous floaters, photophobia, and diplopia were reported in 159 (62%) patients in clinical trials. These events generally started within two weeks of drug administration. Ophthalmological evaluation should be considered, particularly if patients experience photopsia or experience new or increased vitreous floaters. Severe or worsening vitreous floaters and/or photopsia could also be signs of a retinal hole or pending retinal detachment. Caution should be exercised when driving or operating machinery by patients who experience vision disorder [see Patient Counseling Information (17)].

Neuropathy as defined in Table 3 and attributed to study drug by the investigator was reported in 34 (13%) patients. While most events were Grade 1, Grade 2 motor neuropathy and Grade 3 peripheral neuropathy were reported in 1 patient each. Dizziness and...
dysgeusia were also very commonly reported in these studies, but were all Grade 1 or 2 in severity. Bradycardia has been reported in 12 (5%) patients treated with XALKORI. All of these cases were Grade 1 or 2 in severity. Complex renal cysts have been reported in 2 (1%) patients treated with XALKORI. There were no reports of abnormal urinalyses or renal impairment in these cases.

**Laboratory Abnormalities**
Grade 3 or 4 neutropenia, thrombocytopenia, and lymphopenia were seen in 5.2%, 0.4%, and 11.4% of patients, respectively.

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)]. The concurrent use of strong CYP3A inhibitors, including but not limited to atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, troleandomycin, and voriconazole, should be avoided. Grapefruit or grapefruit juice may also increase plasma concentrations of crizotinib and should be avoided. Caution should be exercised 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)]. The concurrent use of strong CYP3A inducers, including but not limited to carbamazepine, phenobarbital, rifabutin, rifampin, and St. John’s Wort, should be avoided.

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)]. Dose reduction may be needed for coadministered drugs that are predominantly metabolized by CYP3A. Coadministration of crizotinib with CYP3A substrates with narrow therapeutic indices, including but not limited to alfentanil, cyclosporine, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus, should be avoided.

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 and above 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 1.2 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 250 mg/kg/day (approximately 5 times the AUC at the recommended human dose) or in rabbits at doses of up to 60 mg/kg/day (approximately 3 times the AUC at the recommended human dose), though fetal body weights were reduced at these doses. Women of childbearing potential should be advised 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 30 days after completing therapy. If this drug is used during pregnancy or if the patient or their partner becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to a fetus.

8.2 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, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

8.3 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 10 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.

8.4 Geriatric Use
Of the 136 patients in Study A, 19 (14%) were 65 years or older. Of the 119 patients in Study B, 18 (13%) were 65 years or older. No overall differences in safety or efficacy were observed in comparison with younger patients.

8.5 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. Treatment with XALKORI should be used with caution in patients with hepatic impairment [see Clinical Pharmacology (12.3)].

8.6 Renal Impairment
No starting dose adjustment is needed for patients with mild (creatinine clearance [CLCr] 60 to 90 mL/min) and moderate renal impairment (CLCr 30 to 60 mL/min), as steady-state trough concentrations in these two groups were similar to those in patients with normal renal function (CLCr greater than 90 mL/min) in Study B. The potential need for starting dose adjustment in patients with severe renal impairment cannot be determined, as clinical and pharmacokinetic data were available for only one patient. In addition, no data are available for patients with end-stage renal disease. Therefore, caution should be used in patients with severe renal impairment (CLCr less than 30 mL/min) or patients with end-stage renal disease [see Clinical Pharmacology (12.3)].

10. OVERDOSAGE
There have been no known cases of XALKORI overdose. Treatment of overdose with XALKORI should consist of general supportive measures. There is no antidote for XALKORI.

11. DESCRIPTION
XALKORI (crizotinib) is an oral receptor tyrosine kinase inhibitor. The molecular formula for crizotinib is C_{18}H_{24}Cl_{2}FN_{6}O. 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)-1H-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 500 mg of crizotinib, with a coating of hydroxypropyl 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 oxide II. 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 (HGF/ c-Met), and Receptor 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 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 Pharmacokinetics

Absorption
Following oral single-dose administration, 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_s 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 the administration of a single 250 mg oral dose. A high-fat meal reduced crizotinib AUC, and C_s by approximately 14%. XALKORI can be administered with or without food [see Dosage and Administration (2.1)].

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
In vitro studies demonstrated that 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. In vitro studies in human liver microsomes demonstrated that crizotinib is a time-dependent inhibitor of CYP3A.

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/hr) after 250 mg twice daily than that after a single 250 mg oral dose (100 L/hr), which was likely due to autoinhibition of CYP3A by crizotinib after multiple dosing.
Drug Interactions

Coadministration of Crizotinib and CYP3A Substrates

Crizotinib inhibits CYP3A both in vitro and in vivo. Coadministration of crizotinib (250 mg twice daily for 28 days) in patients resulted in a geometric mean oral midazolam AUC that was 3.7-fold that observed when midazolam was administered alone, suggesting that crizotinib is a moderate inhibitor of CYP3A [see Drug Interactions (7.3)].

Coadministration of Crizotinib and CYP3A Inhibitors

Coadministration of a single 150 mg oral dose of crizotinib in the presence of ketoconazole (200 mg twice daily), a strong CYP3A inhibitor, resulted in increases in crizotinib systemic exposure, with crizotinib AUC\(_0\) and C\(_{\text{max}}\) values that were approximately 3.2-fold and 1.4-fold, respectively, those seen when crizotinib was administered alone. However, the magnitude of effect of CYP3A inhibitors on steady-state crizotinib exposure has not been evaluated [see Drug Interactions (7.2)].

Coadministration of Crizotinib and Antiacids

The aqueous solubility of crizotinib is pH dependent, with higher pH resulting in lower solubility. Drugs that elevate the gastric pH (such as proton pump inhibitors, H\(_2\) blockers, or antacids) may decrease the solubility of crizotinib and subsequently reduce its bioavailability. However, no formal studies have been conducted.

Coadministration With Other CYP Substrates

In vitro studies indicated that clinical drug-drug interactions are unlikely to occur as a result of crizotinib-mediated inhibition of the metabolism of substrates for CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, or CYP2D6. An in vitro study in human hepatocytes indicated that clinical drug-drug interactions are unlikely to occur as a result of crizotinib-mediated inhibition of the metabolism of substrates for CYP1A2 or CYP3A.

Coadministration With Substrates of Transporters

Crizotinib is an inhibitor of P-glycoprotein (P-gp) in vitro. Therefore, crizotinib may have the potential to increase plasma concentrations of coadministered substrates of P-gp.

In vitro, crizotinib did not inhibit the human hepatic uptake transport proteins OATP1B1 or OATP1B3 at therapeutic concentrations. Therefore, clinical drug-drug interactions are unlikely to occur as a result of crizotinib-mediated inhibition of the uptake of substrates for these transporters.

Pharmacokinetics in Special 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 Special Populations (8.6)].

Renal Impairment: No dedicated renal impairment trial for XALKORI has been conducted. In Study B, steady-state trough concentrations in patients with mild (CLCR 60 to 90 mL/min, N=47) and moderate renal impairment (CLCR 30 to 60 mL/min, N=27) were similar to those in patients with normal renal function (CLCR greater than 90 mL/min, N=33). Limited data (N=1) are available in patients with severe renal impairment, and no data are available in patients with end-stage renal disease [see Use in Special Populations (8.7)].

Ethnicity: After 250 mg twice daily dosing, steady-state crizotinib C\(_{\text{max}}\) and AUC in Asian patients were 1.57- and 1.50-fold those seen in non-Asian patients, respectively.

12.4 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 on crizotinib on QT intervals. Four of 308 patients (1.3%) were found to have QTcF (corrected QT by the Fridericia method) greater than or equal to 500 msec, and 10 of 289 patients (3.5%) had an increase from baseline QTcF greater than or equal to 60 msec by automated machine-read evaluation of ECG. A pharmacokinetic/pharmacodynamic analysis suggested a concentration-dependent increase in QTcF [see Warnings and Precautions (5.3)].

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, and an in vitro human lymphocyte chromosome aberration assay, and in in vivo rat bone marrow micronuclear 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 animals based on findings in repeat-dose toxicity studies in the rat. Findings observed in the male reproductive tract included testicular pachytcne spermatocyte degeneration in rats given greater than or equal to 50 mg/kg/day for 28 days (greater than 3 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/m² basis) for 3 days.

14. CLINICAL STUDIES

The use of single-agent XALKORI in the treatment of locally advanced or metastatic ALK-positive NSCLC was investigated in 2 multi-center, single-arm studies (Studies A and B). Patients enrolled into these studies had received prior systemic therapy, with the exception of 15 patients in Study B who had no prior systemic treatment for locally advanced or metastatic disease. In Study A, ALK-positive NSCLC was identified using the Vysis ALK Break-Apart FISH Probe Kit. In Study B, ALK-positive NSCLC was identified using a number of local clinical trial assays. The primary efficacy endpoint in both studies was Objective Response Rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST). Response was evaluated by the investigator and by an independent radiology review panel. Duration of Response (DR) was also evaluated. Patients received 250 mg of XALKORI orally twice daily. Demographic and disease characteristics for Studies A and B are provided in Table 4.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Study A N=136</th>
<th>Study B N=119</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>64 (47)</td>
<td>59 (50)</td>
</tr>
<tr>
<td>Female</td>
<td>72 (53)</td>
<td>60 (50)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>52 (29-82)</td>
<td>51 (21-79)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>87 (64)</td>
<td>74 (62)</td>
</tr>
<tr>
<td>Black</td>
<td>5 (4)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Asian</td>
<td>43 (32)</td>
<td>34 (29)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1)</td>
<td>8 (7)</td>
</tr>
<tr>
<td>Smoking status, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>92 (68)</td>
<td>86 (72)</td>
</tr>
<tr>
<td>Former smoker</td>
<td>39 (29)</td>
<td>32 (27)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>5 (4)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Disease stage, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Locally advanced</td>
<td>9 (7)</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Metastatic</td>
<td>127 (93)</td>
<td>114 (96)</td>
</tr>
<tr>
<td>Histological classification, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>130 (96)</td>
<td>116 (98)</td>
</tr>
<tr>
<td>Large cell carcinoma</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Adenosquamous carcinoma</td>
<td>3 (2)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (2)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Prior systemic therapy for locally advanced or metastatic disease — number of regimens, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
<td>15 (13)</td>
</tr>
<tr>
<td>1</td>
<td>13 (10)</td>
<td>34 (29)</td>
</tr>
<tr>
<td>2</td>
<td>37 (27)</td>
<td>20 (17)</td>
</tr>
<tr>
<td>≥3</td>
<td>37 (27)</td>
<td>17 (14)</td>
</tr>
<tr>
<td>≥4</td>
<td>49 (36)</td>
<td>33 (28)</td>
</tr>
</tbody>
</table>

Table 4: Demographic and Disease Characteristics in Studies A and B

*Includes 1 patient with an ECG0 PS of 1 at screening but was 3 at baseline.

One hundred thirty-six patients with locally advanced or metastatic ALK-positive NSCLC from Study A were analyzed at the time of data cutoff. The median duration of treatment was 22 weeks. Based on investigator assessments, there was 1 complete and 67 partial responses for an ORR of 50% (95% CI: 42%, 59%). Seventy-nine percent of objective tumor responses were achieved during the first 8 weeks of treatment. The median response duration was 41.9 weeks.

One hundred nineteen patients with locally advanced or metastatic ALK-positive NSCLC were enrolled into Study B at the time of data cutoff. The median duration of treatment was 32 weeks. Based on investigator assessments, there were 2 complete and 69 partial responses for an ORR of 61% (95% CI: 52%, 70%). Fifty-five percent of objective tumor responses were achieved during the first 8 weeks of treatment. The median response duration was 48.1 weeks.

Efficacy data from Studies A and B are provided in Table 5.

<table>
<thead>
<tr>
<th>Efficacy Parameter</th>
<th>Study A N=136</th>
<th>Study B N=119</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORR (CR+PR) (%) (95% CI)</td>
<td>50% (42%, 59%)</td>
<td>61% (52%, 70%)</td>
</tr>
<tr>
<td>Number of Responders</td>
<td>68</td>
<td>71</td>
</tr>
<tr>
<td>Duration of Response (\text{Median (range) weeks})</td>
<td>41.9 (6.1+; 42.1+)</td>
<td>48.1 (4.1+; 76.6+)</td>
</tr>
</tbody>
</table>

*Response as assessed by the Investigator.

*One patient was not evaluable for response in Study A; 3 patients were not evaluable for response in Study B.

*Preliminary estimate using Kaplan-Meier method.

+Censored values
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 treatment.

What is the most important information for me to know about XALKORI?

XALKORI may cause serious side effects, such as:

Liver problems – XALKORI may cause life-threatening and/or fatal liver injury. Your doctor should do blood tests 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

Swelling of the lungs (pneumonitis) - XALKORI may cause life-threatening and/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

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 is advanced or 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, non-prescription medicines, vitamins, and herbal supplements. Especially tell your doctor if you take:

- St. John’s Wort (Hypericum perforatum)
- Medicines for:
  - depression (antidepressants)
  - fungal infections (antifungals)
  - bacterial infections (antibiotics)
  - tuberculosis (TB)
  - HIV/AIDS
  - heart conditions
  - seizures

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.
- Do not crush, dissolve, or open capsules.
- 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.
- Do not take more than 1 dose of XALKORI at a 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, use caution when 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:

- See “What is most important for me to know about XALKORI?”
- Changes in your heartbeat (called QT interval prolongation), very fast or abnormal heartbeats. Your doctor may check your heart during treatment with XALKORI. Tell your doctor right away if you have abnormal heartbeats, feel dizzy, or faint. These may be symptoms related to QT interval prolongation.

The most common side effects of XALKORI include:

- Vision problems
- These problems usually happen within 2 weeks of starting XALKORI. Tell your doctor right away if you have any change in vision, such as:
  - flashes of light
  - blurred vision
  - light hurting your eyes
  - new or increased floaters
- nausea
- diarrhea
- vomiting
- swelling of your hands and feet
- constipation

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 do I store XALKORI?**

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

- Keep XALKORI in the original container, and keep the container closed tightly.
- Do not touch or handle crushed or broken XALKORI capsules. XALKORI is made with a capsule to prevent contact with the active ingredient.

**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 to know more about XALKORI talk with your doctor. You can ask your doctor or pharmacist for more information about XALKORI.

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-0441-3.0
Revised: December 2011

*Pfizer*
Division of Pfizer Inc, NY, NY 10017