Your doctor is the best resource for medical advice and information. The health information contained herein is provided for educational / awareness purposes only and is not intended to replace discussions with a medical practitioner and/or medical advice or be construed as a promotional information.

Package Leaflet: Information for the user
Crizotinib
200 mg Hard Capsules
250 mg Hard Capsules
CRIZALK™

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What CRIZALK (Crizotinib) is and what it is used for
2. What you need to know before you take CRIZALK (Crizotinib)
3. How to take CRIZALK (Crizotinib)
4. Possible side effects
5. How to store CRIZALK (Crizotinib)
6. Contents of the pack and other information

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1. What CRIZALK (Crizotinib) is and what it is used for

CRIZALK (Crizotinib) is an anticancer medicine containing the active substance crizotinib used to treat patients with a type of lung cancer called locally advanced or metastatic (spread outside lungs or to other parts of the body) non-small cell lung cancer (NSCLC), that is anaplastic lymphoma kinase (ALK)-positive as detected by an IHC/FISH test.

CRIZALK (Crizotinib) can be prescribed for the treatment of patients with metastatic (tumor has spread to other parts of the body) NSCLC whose tumors are ROS1-positive.

If you have any questions about how CRIZALK (Crizotinib) works or why this medicine has been prescribed for you, ask your doctor.

2. What you need to know before you take CRIZALK (Crizotinib)

Do not take CRIZALK (Crizotinib)

- If you are allergic to crizotinib or any of the other ingredients of this medicine (listed in Section 6, "What CRIZALK (Crizotinib) contains").

Warnings and precautions

When assessing either ALK or ROS1 status of a patient, it is important that a well-validated and robust methodology is chosen to avoid false negative or false positive determinations. Talk to your doctor before taking CRIZALK (Crizotinib):

- If you ever had/have liver disease.
- If you have reduced white cell count.
- If you have ever had any other lung problems. Some lung problems may get worse during treatment with CRIZALK (Crizotinib), as CRIZALK (Crizotinib) may cause inflammation of the lungs during treatment. Symptoms may be similar to those from lung cancer. Tell your doctor right away if you have any new or worsening symptoms including difficulty in breathing, shortness of breath, or cough with or without mucous, or fever.
- If you have been told that you have an abnormality of your heart tracing after an electrocardiogram (ECG) known as prolonged QT interval.
- If you have slower heart rate.
- If you ever had/have heart problems which can cause shortness of breath or ankle swelling.
- If you have ever had stomach or intestine problems such as holes (perforation), or if you have conditions causing diverticulitis, or if you have spread of cancer inside the abdomen (metastasis).

- If you have vision disorders
- If you ever had/have kidney disease.
- If you are currently treated with any of the medicines listed in section **Other medicines and CRIZALK (Crizotinib).**

Talk to your doctor right away after having taken CRIZALK (Crizotinib):

- If you are experiencing severe stomach or abdominal pain, fever, chills, shortness of breath, fast or slow heartbeat, partial or complete loss of vision (in one or both eyes) or changes in bowel habits.

Most of the available information is available in patients with some specific histology type of ALK-positive and ROS1-positive NSCLC (adenocarcinoma) and limited information is available in the other histologies.

Children and adolescents

Crizalk is not recommended below the age of 18 years.

Other medicines and CRIZALK (Crizotinib)

Tell your doctor if you are taking, have recently taken or might take any other medicines, including herbal medicines and medicine obtained over the counter.

In particular, the following medicines (including but not limited to) can affect CRIZALK (Crizotinib) plasma level:

- Following medicine may increase plasma level of CRIZALK (Crizotinib): atazanavir, ritonavir, cobicistat, itraconazole, ketoconazole, posaconazole, voriconazole, clarithromycin, telithromycin, erythromycin, diltiazem or verapamil, and grapefruit or grapefruit juice

The following medicines may reduce plasma level of CRIZALK (Crizotinib):

- Carbamazepine, phenobarbital, phenytoin, rifampicin, and St. John's Wort, efavirenz or rifabutin

Plasma level of following medicine may change by CRIZALK (Crizotinib):

- Midazolam, alfentanil, cisapride, cyclosporine, ergot derivatives, fentanyl, pimozide, quinidine, sirolimus, and tacrolimus. bupropion, efavirenz, oral contraceptives, raltegravir, irinotecan, digoxin, dabigatran, colchicine, pravastatin, metformin, procainamide, class IA [quinidine, disopyramide] or class III [e.g., amiodarone, sotalol, dofetilide, ibutilide], methadone, cisapride, moxifloxacin, antipsychotics, non-dihydropyridine calcium channel blockers such as verapamil and diltiazem, beta-

blockers, clonidine, guanfacine, mefloquine, anticholinesterases, pilocarpine etc, Alfentanil and other short acting opiates such as fentanyl.

Consult your doctors before taking these medicines.

Oral contraceptives

If you take CRIZALK (Crizotinib) whilst using oral contraceptives, the oral contraceptives may be ineffective.

CRIZALK (Crizotinib) with food and drink

You can take CRIZALK (Crizotinib) with or without food; however, you should avoid drinking grapefruit juice or eating grapefruit while on treatment with CRIZALK (Crizotinib) as they may change the amount of CRIZALK (Crizotinib) in your body.

Sun protection

Avoid spending prolonged time in sunlight. CRIZALK (Crizotinib) can make your skin sensitive to the sun (photosensitivity), and you may burn more easily. You should wear protective clothing and/or use sunscreen that covers your skin to help protect against sunburn if you have to be in the sunlight during treatment with CRIZALK (Crizotinib).

Pregnancy and breast-feeding

Talk to your doctor before taking this medicine if you are pregnant, may become pregnant or are breast-feeding.

It is recommended that women avoid becoming pregnant and that men do not father children during treatment with CRIZALK (Crizotinib) because this medicine could harm the baby. If there is any possibility that the person taking this medicine may become pregnant or father a child, they must use adequate contraception during treatment, and for at least 90 days after completing therapy as oral contraceptives may be ineffective while taking CRIZALK (Crizotinib).

Do not breast-feed during treatment with CRIZALK (Crizotinib). CRIZALK (Crizotinib) could harm a breast-fed baby.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

Driving and using machines

CRIZALK (Crizotinib) has minor influence on the ability to drive and use machines. You should take special care when driving and using machines as patients taking CRIZALK (Crizotinib) may experience fainting, dizziness, low blood pressure, vision disorder or, fatigue.

Crizalk (Crizotinib) contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per 200 mg or 250 mg capsule, that is to say essentially 'sodium-free'.

3. How to take CRIZALK (Crizotinib)

Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

- The recommended dose is one capsule of 250 mg taken orally twice daily (total amount 500 mg/day).
- Take the capsule once in the morning and once in the evening.
- Take the capsules at about the same time each day.
- You can take the capsules with or without food always avoiding grapefruit.
- Swallow the capsules whole and do not crush, dissolve or open the capsules.

If necessary, your doctor may decide to reduce the dose to 200 mg to be taken orally twice daily (total amount 400 mg) and if further dose reduction is necessary, to reduce it to 250 mg to be taken orally once daily. Your doctor may decide to permanently discontinue your treatment if you are unable to tolerate CRIZALK (Crizotinib) 250 mg taken orally once daily.

If you take more CRIZALK (Crizotinib) than you should

If you accidentally take too many capsules, tell your doctor right away. You may require medical attention.

If you forget to take CRIZALK (Crizotinib)

What to do if you forget to take a capsule depends on how long it is until your next dose.

- If your next dose is in **6 hours or more**, take the missed capsule as soon as you remember. Then take the next capsule at the usual time.
- If your next dose is in **less than 6 hours**, skip the missed capsule. Then take the next capsule at the usual time.

Tell your doctor about the missed dose at your next visit.

Do not take a double dose (two capsules at the same time) to make up for a forgotten capsule.

If you vomit after taking a dose of CRIZALK (Crizotinib), do not take an extra dose; just take your next dose at your regular time.

If you stop taking CRIZALK (Crizotinib)

It is important to take CRIZALK (Crizotinib) every day, as long as your doctor prescribes it to you. If you are not able to take the medicine as your doctor prescribed, or you feel you do not need it anymore, contact your doctor right away.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you experience any side effects, talk to your doctor,. This also includes any possible side effects not listed in this leaflet.

Some side effects could be serious. You should immediately contact your doctor if you experience any of the following serious side effects (see also section 2 “What you need to know before you take CRIZALK (Crizotinib):

- **Liver failure**

  Tell your doctor right away if you feel more tired than usual, your skin and whites of your eyes turn yellow, your urine turns dark or brown (tea colour), you have pale stools and fever, you have nausea, vomiting, or decreased appetite, you have pain on the right side of your stomach, you have itching, or if you bruise more easily than usual. Your doctor may do blood tests to check your liver function, and if the results are abnormal, your doctor may decide to reduce the dose of CRIZALK (Crizotinib) or stop your treatment.

- **Lung inflammation**

  Tell your doctor right away if you experience difficulty in breathing, weakness; especially if associated with cough or fever.

- **Reduction in the number of white blood cells (including neutrophils)**

  Tell your doctor right away if you experience fever or infection. Your doctor may do blood tests and if the results are abnormal, your doctor may decide to reduce the dose of CRIZALK (Crizotinib).

- Slower heart beat, dizziness, and fainting

  Tell your doctor right away if you experience these symptoms which could be signs of QT prolongation (Abnormal ECG heart tracing). Your doctor may perform electrocardiograms to check there are no problems with your heart during treatment with CRIZALK (Crizotinib).

- **Partial or complete loss of vision in one or both eyes**

Tell your doctor right away if you experience any loss of vision or any change in vision such as difficulty seeing out of one or both eyes. Your doctor may stop CRIZALK (Crizotinib) treatment and refer you to an ophthalmologist.

Other side effects of CRIZALK (Crizotinib) may include:

Very common side effects (may affect 1 or > in 10 people)

- Visual effects (Diplopia - Double vision, Halo vision, Photophobia, Photopsia, Vision blurred, Visual acuity reduced, Visual brightness, Visual impairment, Visual perseveration, Vitreous floaters often started within the first week of CRIZALK (Crizotinib) administration
- Vomiting, diarrhoea, nausea
- Excessive fluid in the body (oedema)
- Constipation
- Increased liver enzymes
- Decreased appetite
- Tiredness (fatigue)
- Dizziness
- A disorder of the nerves which can causes weakness, tingling or numbness (Neuropathy)
- Dysgeusia
- Pain in the abdomen
- Reduced number of white cells in the blood (Neutropenia), Reduction in red blood cells which can make the skin pale and cause weakness or breathlessness (Anaemia), low white cell count (Leucopenia)
- Skin rash
- Reduced heart rate

*Common side effect*s (may affect up to 1 or > in 100 and <1 in 10)

- Indigestion
- Increased blood levels of creatinine
- Increased levels of the enzyme alkaline phosphatase in the blood
- Hypophosphataemia

- Kidney cysts
- Fainting
- Inflammation of the oesophagus
- Decreased levels of testosterone
- Heart failure
- ECG QT prolongation

*Uncommon side effect*s (may affect up to <1 or > in 1,000 to <1 in100)

- Gastrointestinal perforation
- Kidney failure
- Liver failure
- Sensitivity to sunlight (photosensitivity)
- Increased levels of tests that check for muscle damage (creatine phosphokinase levels)

5. How to store CRIZALK (Crizotinib)

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the bottle or blister foil and carton after "EXP". The expiry date refers to the last day of that month.
- Store under controlled room temperature e.g., 15°C to 30°C.
- Keep in the original container.
- Do not use any pack that is damaged or shows signs of tampering.

Do not throw away any medicines via wastewater or household waste. Ask your doctor how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What CRIZALK (Crizotinib) contains

– The active pharmaceutical ingredient (API) in CRIZALK is crizotinib

CRIZALK 200 mg: Each hard gelatin capsule contains 200 mg crizotinib

CRIZALK 250 mg: Each hard gelatin capsule contains 250 mg crizotinib

– The other ingredients present in hard gelatin capsule along with API:

Colloidal silicon dioxide, microcrystalline cellulose, anhydrous dibasic calcium phosphate, sodium starch glycolate, magnesium stearate, and hard gelatin capsule shells.

Capsule shell: Gelatin, titanium dioxide, and ferric oxide red. The hard gelatin capsule shell contains titanium dioxide and ferric oxide red as colorant.

Printing ink is made up of: Shellac, propylene glycol, strong ammonia solution, potassium hydroxide, and black iron oxide.

What CRIZALK (Crizotinib) looks like and contents of the pack

CRIZALK (Crizotinib) 200 mg is supplied as CRIZALK 200 mg hard capsules, white opaque and pink opaque hard capsule, with "Pfizer" imprinted on the cap and "CRZ 200" on the body.

CRIZALK (Crizotinib) 250 mg is supplied as CRIZALK 250 mg hard capsules, pink opaque hard capsule, with "Pfizer" imprinted on the cap and "CRZ 250" on the body.

CRIZALK (Crizotinib) capsules (200 mg and 250 mg) are packaged in PVC/ Alu foil blisters. It contains 6 blister strips of 10 capsules each.

All strengths/presentations mentioned in this document might not be available in the market.

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Pfizer Products India Private Limited, The Capital - B Wing, 1802, 18th Floor Plot No. C-70, G Block, Bandra Kurla Complex, Bandra (East), Mumbai 400 051, India.

Manufacturer

Pfizer Manufacturing Deutschland GmbH Betriebssatatte Freiburg,

Mooswaldallee 1, 79090 Freiburg, Germany

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