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Kingdom of Saudi Arabia

Kingdom of Saudi Arabia
22nd of December, 2015

XALKORI (crizotinib) Hard Capsules 200 and 250 mg for oral use Inclusion of a new warning regarding cardiac failure

Dear Healthcare Professional,

Pfizer in an agreement with the Saudi Food and Drug Authority- Drug Sector would like to inform you of the following:

- Severe, sometimes fatal, cases of cardiac failure have been reported in patients with ALK-positive NSCLC treated with crizotinib.
- Cardiac failure occurred in patients with or without pre-existing cardiac disorders, receiving crizotinib.
- Patients should be monitored for signs and symptoms of heart failure (dyspnea, oedema, rapid weight gain).
- If symptoms of cardiac failure are observed, appropriate measures such as dosing interruption, dose reduction, or discontinuation should be considered.

Background information on the safety concern

- XALKORI is a medicinal product containing crizotinib.
- Crizotinib is indicated for the treatment of anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC).
- A safety review of crizotinib based on data from clinical trials and reports from clinical practice concluded that there is a risk of cardiac failure following the use of crizotinib. Across clinical studies in patients with ALK-positive NSCLC (n=1669), a total of 19 (1.1%) patients treated with crizotinib had any grade cardiac failure, 8 (0.5%) patients had Grade 3 or 4, and 3 (0.2%) patients had fatal outcome.
- In the post marketing experience, as of 25 February 2015, it is estimated that more than 14700 patients have received crizotinib and cardiac failure was reported in 40 patients (reporting rate 0.27%). The majority occurred during the first month of treatment. A fatal outcome was reported for 15 of them. Seven cases have been identified where symptoms of cardiac failure resolved after discontinuation of crizotinib, and in three of these cases symptoms reoccurred when crizotinib was subsequently re-introduced. In 3 out of these 7 cases, no confounding cardiac disorders (past medical history, comorbid conditions, and concurrent medications) were identified.
- In order to prevent or minimize the above risk, the text in the Annex has been added to the XALKORI Summary of Product Characteristics (SmPC).

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Call for reporting

Healthcare professionals are reminded to report any adverse reactions suspected to be associated with the use of XALKORI in accordance with the national spontaneous reporting system:

1. **The National Pharmacovigilance & Drug Safety Centre (NPC)**
   Fax: +966-11-205-7662
   Call NPC at +966-11-2038222, Ext: 2317-2356-2353-2354-2334-2340.
   Toll free phone: 8002490000
   E-mail: npc.drug@sfda.gov.sa
   Website: www.sfda.gov.sa/npc

Or

2. **The Pharmacovigilance Department in Pfizer:**
   Email: SAU.AEReporting@Pfizer.com
   Tel.: 012 22 93520

For further information or any questions on cardiac failure associated with the use of XALKORI please contact:

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Sincerely,
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ANNEX: Changes to the SmPC for XALKORI

Warnings and precautions

- Cardiac failure

  In clinical studies with crizotinib and during post marketing surveillance, severe, life-threatening, or fatal adverse reactions of cardiac failure were reported.

  Patients with or without pre-existing cardiac disorders, receiving crizotinib, should be monitored for signs and symptoms of heart failure (dyspnea, oedema, rapid weight gain from fluid retention). Dosing interruption, dose reduction, or discontinuation should be considered as appropriate if such symptoms are observed.

- Undesirable effects
  Adverse reactions reported in crizotinib randomized Phase 3 Study 1.
  Cardiac failure (common, 1%)

  Cardiac failure (Cardiac failure, Cardiac failure congestive, Ejection fraction decreased, Left ventricular failure, Pulmonary oedema). Across clinical studies (n=1669), 19 (1.1%) patients treated with crizotinib had any grade cardiac failure, 8 (0.5%) patients had Grade 3 or 4, and 3 (0.2%) patients had fatal outcome.