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Worldwide Biopharmaceutical Businesses

Direct Healthcare Professional Communication

10-AUG-2023

Xalkori (crizotinib): Vision disorders, including risk of severe visual loss, need for monitoring in paediatric patients

Dear Healthcare Professional,

Pfizer Limited in agreement with the European Medicines Agency as well as the Medicines and Healthcare products Regulatory Agency would like to inform you of the following:

Summary

- Vision disorders are a known risk with crizotinib and have been reported in 61% of paediatric patients with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) or recurrent or refractory anaplastic lymphoma kinase (ALK)-positive unresectable inflammatory myofibroblastic tumour (IMT), in crizotinib clinical trials.
- As paediatric patients may not report or notice changes in vision spontaneously, healthcare professionals should inform patients and caregivers of the symptoms of vision disorders and the risk of visual loss, and to contact their healthcare provider if visual symptoms or visual loss develop.
- Paediatric patients should be monitored for vision disorders. A baseline ophthalmologic examination should be undertaken prior to starting crizotinib, with follow-up examinations within 1 month, every 3 months thereafter, and upon observation of new visual symptoms.
- In paediatric patients, a dose reduction should be considered if Grade 2 ocular disorders arise and crizotinib should be permanently discontinued for Grade 3 or 4, unless another cause is identified.

Background information

Xalkori has been authorised since 2012 as a monotherapy in adults for the treatment of patients with ALK-positive advanced non-small cell lung cancer (NSCLC) and in *ROS1*-positive NSCLC since 2016.

In adults, vision disorders have been reported in 1084 of the 1722 (63%) clinical trial patients with ALK-positive or *ROS1*-positive advanced NSCLC treated with Xalkori. Grade 4 vision loss was reported in 4 (0.2%) patients. Optic atrophy and optic nerve disorder have been reported as potential causes of vision loss.

Since May 2023, Xalkori is also indicated in paediatric patients (age ≥ 6 to < 18 years) as monotherapy for the treatment of patients with relapsed or refractory systemic ALK-positive ALCL or patients with recurrent or refractory ALK-positive unresectable IMT.

In paediatric patients (age ≥ 6 to < 18 years), vision disorders were reported in 25 out of 41 (61%) patients treated with crizotinib for these indications in clinical trials. The most common visual symptoms were blurred vision (24%), visual impairment (20%), photopsia (17%) and vitreous floaters (15%). Of the 25 patients who experienced vision disorders, one patient experienced grade 3 optic nerve disorder.

Vision disorders are more challenging to detect in paediatric patients, as they may not report or notice changes in vision without specific questioning of symptoms and examinations. For these reasons, the following is recommended for paediatric patients with ALK-positive ALCL or ALK-positive IMT:

- Inform patients and caregivers of the symptoms of vision disorders (e.g., perceived flashes of light, blurry vision, light sensitivity, floaters) and potential risk of visual loss.
- Obtain a baseline ophthalmologic examination for young patients with ALCL or IMT prior to starting crizotinib.
- Conduct follow-up ophthalmologic examinations within 1 month of starting crizotinib, every 3 months thereafter, and upon presentation of any new visual symptoms. Ophthalmological evaluation should consist of best corrected visual acuity, retinal photographs, visual fields, optical coherence tomography (OCT) and other evaluations as appropriate.
- For Grade 2 ocular disorders, symptoms should be monitored and reported to an eye specialist with consideration of a dose reduction
- Withhold crizotinib pending evaluation for any Grade 3 or 4 ocular disorders, and permanently discontinue crizotinib for Grade 3 or 4 ocular disorders unless another cause is identified.

The product information and the educational material for patients and caregivers are being updated to contain instructions/recommendations in paediatric patients about the risk of vision disorders, including severe vision loss.

Call for adverse event reporting

Healthcare professionals are asked to report adverse events to the Yellow Card Scheme electronically.

Report via the website <https://www.gov.uk/yellowcard>, the free Yellow Card app available from the Apple App Store or Google Play Store, and some clinical IT systems (EMIS, SystemOne, Vision, MiDatabank) for healthcare professionals. Suspected side effects can also be reported by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

Suspected adverse drug reactions may also be reported to Pfizer Medical Information on 01304 616 161.

Company contact point

If you have any questions about this letter or for more information about Xalkori, please contact Pfizer Medical Information at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS or Telephone: 01304 616 161.

Pfizer Medical Information can also be found online at: <https://www.pfizer.com/products/product-contact-information>

Yours sincerely,

DocuSigned by:
July 31, 2023
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Pfizer Limited