Pfizer Inc
235 E 42nd Street
New York, NY 10017

IMPORTANT DRUG WARNING

Subject: Ocular toxicity, including risk of severe visual loss, with Xalkori® (crizotinib) in patients with ALCL

19 January 2021

Dear Health Care Provider:

The purpose of this letter is to inform you of an important safety warning in the Xalkori® (crizotinib) prescribing information regarding the recent approval in patients 1 year of age and older and young adults with relapsed or refractory, systemic anaplastic large cell lymphoma (ALCL) that is anaplastic lymphoma kinase (ALK)-positive.

Risks of Severe Ocular Toxicity

In a study of 121 patients who were ≤21 years of age treated with Xalkori, 26 patients with ALCL were included and vision disorders were reported in 65% of these patients. The most common visual symptoms were blurred vision and visual impairment. Similarly, the most common visual symptoms for the 121 patients treated with Xalkori were blurred vision and visual impairment, with median onset of approximately 1 week. Other visual symptoms included photopsia, vitreous floaters, and photophobia.

Severe visual loss has occurred in 0.2% of 1719 recipients of Xalkori who were treated for metastatic non-small cell lung cancer. Optic atrophy and optic nerve disorder have been reported as potential causes of partial or complete visual loss. The US Prescribing Information (USPI) for Xalkori includes a Warning and Precaution for severe visual loss.

Visual problems and ocular toxicity are more challenging to detect in children who are pre-verbal or not performing activities where defects in vision are often first noticed (e.g., reading, sports). Young patients may not report or notice changes in vision without specific questioning of symptoms and examinations. For these reasons, guidance on ophthalmologic examinations is provided in Section 5 (Warnings and Precautions) of the USPI.

Prescriber Actions

Recommended actions include but are not limited to:

- Obtain a baseline ophthalmologic examination for patients with ALCL prior to starting Xalkori.
- Conduct follow-up ophthalmologic examinations including retinal examination within 1 month of starting Xalkori, every 3 months thereafter, and upon any new visual symptoms.

Ophthalmological evaluations should consist of best corrected visual acuity, retinal photographs, visual fields, optical coherence tomography (OCT) and other evaluations as appropriate.

- Assess for visual symptoms monthly during treatment. Report visual symptoms to an eye specialist.
- Consider a dose reduction of Xalkori for patients who develop Grade 2 ocular disorders.
- Withhold Xalkori pending evaluation for any Grade 3 or 4 ocular disorders, and permanently discontinue Xalkori for Grade 3 or 4 ocular disorders unless another cause is identified.

Patient counseling includes but is not limited to:

Inform patients and caregivers of the symptoms of ocular toxicity (e.g., perceived flashes of light, blurry vision, light sensitivity, floaters) and potential risk of visual loss, and to immediately contact their healthcare provider if visual symptoms or visual loss develops.

Reporting Adverse Events

Healthcare professionals, caregivers, and/or patients are encouraged to report all serious adverse events suspected to be associated with the use of Xalkori to Pfizer at 1-800-438-1985 (US only) or www.XALKORI.com. The Medical Community can further our understanding of adverse events by reporting all cases to the FDA via the MedWatch program by phone at 1-800- FDA-1088, by fax at 1-800-FDA-0178, via the MedWatch website at www.fda.gov/medwatch or by mail: MEDWATCH Food and Drug Administration 5600 Fishers Lane, Rockville, MD 20852-9787.

This letter is not intended as a complete description of the benefits and risks related to the use of Xalkori for ALCL. Please refer to the enclosed full US prescribing information and Medication Guide. Should you have any questions regarding the prescribing information or the use of Xalkori, please call the Pfizer Medical Information Department at 1-800-438-1985.

Sincerely,

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