Pfizer Healthcare Ireland
9 Riverwalk, National Digital Park,
Citywest Business Campus, Dublin 24
Telephone: 01 4676500 Facsimile 01 4676501
Freephone: 1800 460 900
www.pfizer.ie

Direct Healthcare Professional Communication

PLEASE READ

IMPORTANT MEDICINE SAFETY INFORMATION

APPROVED BY THE HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

03-NOV-2022

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

Dear Healthcare Professional,

Pfizer Healthcare Ireland in agreement with the European Medicines Agency (EMA) and the Health Products Regulatory Authority (HPRA) 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.

Pfizer Healthcare Ireland
9 Riverwalk, National Digital Park,
Citywest Business Campus, Dublin 24
Telephone: 01 4676500 Facsimile 01 4676501
Freephone: 1800 460 900
www.pfizer.ie

Since 28 October 2022, 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.
- Consider a dose reduction of crizotinib for patients who develop Grade 2 ocular disorders.
- 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 have been updated to contain instructions/recommendations in paediatric patients about the risk of vision disorders, including severe vision loss.

Call for reporting

You can assist us with monitoring the safety of Xalkori® by reporting suspected adverse reactions. Suspected adverse drug reactions (ADRs) should be reported to the Health Products Regulatory Authority (HPRA):

- Online Reporting via the HPRA Website www.hpra.ie
- Using downloadable form from the HPRA website. An adverse reaction report form can be downloaded from the HPRA Website. This can be sent by Freepost to the HPRA or by email to medsafety@hpra.ie.
- By telephoning the Pharmacovigilance Section of the HPRA, (01) 676 4971

Suspected adverse drug reactions may also be reported to Pfizer Medical Information on 1800 633 363.

For more information about Xalkori®, please contact Pfizer Medical Information at https://www.pfizer.com/products/product-contact-information

Yours sincerely,

DocuSigned by:
Orlaith Gavan
E8073D7B6136470...

Orlaith Gavan
Country Medical Director
Pfizer Healthcare Ireland

PP-XLK-IRL-0229 November 2022