Scientific Office of
Hoffmann-La Roche Ltd

المكتب العلمي
هوفمان لاروش المحدودة

19 Feb 2017

Important Drug Warning: Risk of Dupuytren's Contracture and Plantar Fascial Fibromatosis with Zelboraf® (vemurafenib)

Dear Healthcare Professional,
F. Hoffmann-La Roche Ltd/Genentech Inc. Saudi Arabia would like to inform you of the following:

Summary

- Cases of Dupuytren's contracture and plantar fascial fibromatosis have been reported with Zelboraf use.
- The majority of cases were mild or moderate in severity. However, severe, disabling cases of Dupuytren's contracture have also been reported.
- Dupuytren's contracture and plantar fascial fibromatosis should be managed using temporary interruption or treatment discontinuation of Zelboraf, as outlined in the current Zelboraf label.

This information is being sent in agreement with the National Competent Authorities Saudi Food and Drug Authority (SFDA).

Further information on the safety concern and recommendations

The reported cases of Dupuytren's contracture seen with Zelboraf were characterized by thickening or appearance of visible cords in the palm of one or both hands. The median time to onset was 224 days from the initial dose of Zelboraf. In the majority of patients, the event persisted when Zelboraf treatment was maintained, while in cases where Zelboraf was either interrupted or discontinued, the majority of patients had improvement of symptoms or resolution of the event. One patient with a pre-existing Dupuytren's contracture experienced an exacerbation of the condition after Zelboraf use. In addition to Dupuytren's contracture, rare cases of mild and moderate plantar fascial fibromatosis were also reported with Zelboraf use. Sequential involvement of the hands and feet was observed in one case.

Healthcare providers should inform patients of this risk and should exercise caution in patients with pre-existing Dupuytren's contracture and plantar fascial fibromatosis. Healthcare providers are advised to follow the dose modification guidance for adverse events as outlined in the Zelboraf label: for moderate and severe fibromatosis, it is recommended that treatment with Zelboraf is interrupted until event is resolved or improved; dose should be reduced by 240 mg increment at resumption of treatment. Treatment interruption with dose reduction should be attempted twice and permanently

discontinued if no resolution or improvement. Dose reduction resulting in a dose below 480 mg twice daily is not recommended.

Roche is working closely with health authorities to update the product label to reflect the risk of Dupuytren's contracture and plantar fascial fibromatosis. Please see the accompanying, current prescribing information for a complete discussion of the other risks associated with Zelboraf.

Call for reporting

As a reminder, there is a need to report any suspected adverse reactions suspected to be associated with the use of Zelboraf to:

Roche Pharmacovigilance Department:

Telephone: +966 11 4545039
Email: jeddah.drug_safety@roche.com
Fax: +966 11 4545896

Or, report to SFDA:

The National Pharmacovigilance and Drug Safety Centre NPC:
Email: npc.drug@sfda.gov.sa
Fax: +966112057662
Toll free phone: 8002490000
Online: https://ade.sfda.gov.sa/

Company contact point

Should you have any questions regarding the use of Zelboraf, please feel free to contact us at:
Telephone: +966 11 4545039
Fax: +966 11 4545896
Website: www.roche.com

Sincerely,

Saud Alsubait
Qualified Person Responsible for Pharmacovigilance

S. Alsubait