IMPORTANT SAFETY UPDATE – ZELBORAF® (vemurafenib)
Risk of Dupuytren's Contracture and Plantar Fascial Fibromatosis

23 March 2017

Dear Healthcare Provider,

Roche Products (New Zealand) Limited ("Roche") would like to inform you of safety updates for Zelboraf.

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 Data Sheet.

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 Data Sheet: for moderate and severe fibromatosis, it is recommended that treatment with Zelboraf is interrupted until the event has resolved or improved. The 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.

Updated Safety Information in the Zelboraf Data Sheet

Following Medsafe review Dupuytren's contracture and plantar fascial fibromatosis have been included under the Precautions and Adverse Effects sections of the Zelboraf Data Sheet. Before prescribing, please review the full Zelboraf Data Sheet available at www.medsafe.govt.nz.

If you have any questions or require additional information regarding the use of Zelboraf please contact Roche Medical Information on 0800 276 243 or email at Auckland.medinfonz@roche.com.

Reporting Adverse Events

Roche will continue to monitor the safety of Zelboraf through established reporting mechanisms and notify regulatory authorities of any serious adverse events for evaluation.
Please report any suspected adverse events via email to Roche Drug Safety at nz.drugsafety@roche.com. Alternatively, this information may be reported to the Centre for Adverse Reactions Monitoring (CARM) in Dunedin by telephone on (03) 479 7247, online at https://nzphvc.otago.ac.nz/reporting, by email to nzphvc@otago.ac.nz or by fax on (03) 479 7150.

Yours sincerely

Roche Products (New Zealand) Limited
Jan Campbell
Director Medical Affairs