Health Canada Endorsed Important Safety Information on ZELBORAF® (vemurafenib)

Roche

Date 08/20/2013

Dear Health Care Professional:

Subject: ZELBORAF® (vemurafenib) and the Risks of Malignancy Progression and Drug Rash with Eosinophilia and Systemic Symptoms (DRESS Syndrome)

Hoffmann-La Roche Limited (Roche Canada), in collaboration with Health Canada, would like to inform you of important new safety information associated with ZELBORAF regarding the risk of malignancy progression as well as the risk of Drug Rash with Eosinophilia and Systemic Symptoms (DRESS Syndrome).

ZELBORAF is indicated as a monotherapy for the treatment of proto-oncogene serine/threonine-protein kinase B-Raf (BRAF) V600 mutation-positive unresectable or metastatic melanoma. A validated test is required to identify BRAF V600 mutation status.

Progression of Malignancies Associated with Rat Sarcoma Viral Oncogene (RAS) Mutation

- Based on its mechanism of action, ZELBORAF may cause progression of cancers associated with RAS mutations.
- A recent article[1] reported a case of accelerated growth of a pre-existing neuroblastoma RAS (NRAS)-mutated chronic myelomonocytic leukemia in a 76-year-old patient shortly after he had initiated a treatment with ZELBORAF. These findings suggest that ZELBORAF can cause paradoxical activation of extracellular signal-regulated kinase (ERK) signaling in the RAS-mutant leukemic cell population, which could lead to leukemic cell proliferation.
- ZELBORAF should be used with caution in patients with prior or concurrent cancers associated with RAS mutation.

Drug Rash with Eosinophilia and Systemic Symptoms (DRESS Syndrome)

- Cases of DRESS syndrome have been reported with the use of ZELBORAF.
- The cases of DRESS syndrome were characterized by rash, eosinophilia, and systemic involvement (e.g. fever, lymphadenopathy, elevated transaminases and renal insufficiency). The typical time to onset was 7-25 days.
- ZELBORAF treatment should be permanently discontinued in patients who develop DRESS syndrome.

Roche Canada will be working with Health Canada to implement appropriate revisions to the ZELBORAF Product Monograph.

Managing marketed health product-related adverse reactions depends on health care professionals and consumers reporting them. Reporting rates determined on the basis of spontaneously reported post-marketing adverse reactions are generally presumed to underestimate the risks associated with health product treatments. Any case of adverse reactions due to use of ZELBORAF or other serious or unexpected adverse reactions in patients receiving ZELBORAF should be reported to Roche Canada or Health Canada.

Hoffmann-La Roche Limited
Drug Safety Department
2455 Meadowpine Boulevard
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or call toll free at: 1-888-762-4388
or fax at: 905-542-5864
or email to: mississauga.drug_safety@roche.com

To correct your mailing address or fax number, contact Hoffmann-La Roche Limited.

You can report any suspected adverse reactions associated with the use of health products to Health Canada by:

- Calling toll-free at 1-866-234-2345; or
- Visiting MedEffect Canada's Web page on Adverse Reaction Reporting (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) for information on how to report online, by mail or by fax

For other health product inquires related to this communication, contact Health Canada at:
Marketed Health Products Directorate (MHPD)
E-mail: mhpd_dpsc@hc-sc.gc.ca
Tel: (613) 954-6522
Fax: (613) 952-7738

Should you have any questions or require additional information regarding the use of ZELBORAF, please contact the Drug Information Department at Hoffmann-La Roche Limited at 1-888-762-4388, Monday to Friday, between 8:30 a.m. and 4:30 p.m. (Eastern Standard Time).

Original signed by

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References

1. Callahan MK, et al. Progression of RAS-mutant leukemia during RAF inhibitor treatment. N Engl J Med. 2012 Dec 13;367(24):2316-21.