



Summary of Investigation Results

Encorafenib, binimetinib

January 10, 2023

Non-proprietary name

- a. Encorafenib
- b. Binimetinib

Brand name (marketing authorization holder)

- a. Braftovi Capsules 50 mg, 75 mg (Ono Pharmaceutical Co., Ltd.)
- b. Mektovi Tablets 15 mg (Ono Pharmaceutical Co., Ltd.)

Japanese market launch

- a. 50 mg: February 2019
75mg: November 2020
- b. February 2019

Indications

- a., b.
- Unresectable malignant melanoma with *BRAF* mutation
 - Unresectable, advanced or recurrent colorectal cancer with *BRAF* mutation that has progressed after cancer chemotherapy

Summary of revisions

1. The language concerning tumour lysis syndrome should be added to the IMPORTANT PRECAUTIONS section.
2. "Tumour lysis syndrome" should be added to the Clinically Significant Adverse Reactions section in ADVERSE REACTIONS.

Pharmaceuticals and Medical Devices Agency

3-3-2 Kasumigaseki, Chiyoda-ku, Tokyo 100-0013 Japan
E-mail: safety.info@pmda.go.jp



This English version is intended to be a reference material for the convenience of users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

Investigation results and background of the revision

Cases involving tumour lysis syndrome were evaluated. Cases for which a causal relationship of encorafenib and binimetinib to tumour lysis syndrome was reasonably possible have been reported. As a result of consultation with expert advisors regarding the causality assessment of the cases and the necessity of revision of PRECAUTIONS, the MHLW/PMDA concluded that revision of PRECAUTIONS was necessary.

Reference: Number of cases* and patient mortalities involving tumour lysis syndrome reported in Japan and overseas

a., b.,

A total of 5 cases have been reported in Japan to date. (A causal relationship between the drugs and event was reasonably possible for 3 cases, including 1 case in which the drugs were administered outside the approved indications.)

No patient mortalities have been reported in Japan to date.

A total of 13 cases have been reported overseas to date (including 5 cases for which a causal relationship between the drugs and event was reasonably possible).

One instance of patient mortality has been reported overseas to date. (A causal relationship between the drugs and death subsequent to the event could not be established for this case.)

*Cases collected in the PMDA's database for adverse drug reactions, etc. reports

The expert advisors present at the Expert Discussion regarding the current investigation were nominated based on their conflict of interest declarations concerning the relevant products, pursuant to the "Rules for Convening Expert Discussions, etc., by the Pharmaceuticals and Medical Devices Agency" (PMDA Administrative Rule No. 20-8, dated December 25, 2008).