衞生署藥物辦公室
藥物資訊及進出口管制科
香港九龍觀塘巧明街 100 號
Landmark East 友邦九龍大樓
20 樓 2002-05 室

DEPARTMENT OF HEALTH
DRUG OFFICE
DRUG INFORMATION AND
IMPORT/EXPORT CONTROL DIVISION
Suites 2002-05, 20/F, AIA Kowloon Tower,
Landmark East, 100 How Ming Street,
Kwun Tong, Kowloon, Hong Kong

電話號碼 Tel. No.: (852) 3974 4175
詢問處 Enquiries (852) 3974 4175
傳真號碼 Faxline No.: (852) 2803 4962
本署檔號 OUR REF.: DH DO DIMC/7-30/1

(來函請敍明此檔案號碼)
(IN REPLY PLEASE QUOTE THIS FILE REF.)

29 Apr 2024

Dear Healthcare Professionals,

CHMP recommended new contraindications on the co-administration of Reyataz (Atazanavir) with encorafenib and ivosidenib, and with carbamazepine, phenobarbital, and phenytoin

Your attention is drawn to the European Medicines Agency's (EMA) announcement that the Committee for Medicinal Products for Human Use (CHMP) adopted a positive opinion on 25 April 2024, recommending a change to the terms of the marketing authorisation for the medicinal product Reyataz. The marketing authorisation holder for this medicinal product is Bristol-Myers Squibb Pharma EEIG.

The CHMP adopted a change to sections 4.3 and 4.5 of the summary of product characteristics (SmPC) to reclassify drug-drug interactions to new contraindications. The new contraindications are:

- Co-administration with encorafenib and ivosidenib (see section 4.5).
- Co-administration with carbamazepine, phenobarbital, and phenytoin (see section 4.5).

For information, the full contraindications for Reyataz will be as follows:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Reyataz is contraindicated in patients with severe hepatic insufficiency (see sections 4.2, 4.4 and 5.2). Reyataz with ritonavir is contraindicated in patients with moderate hepatic insufficiency (see sections 4.2, 4.4, and 5.2).
- Co-administration with simvastatin or lovastatin (see section 4.5).
- Combination of rifampicin (see section 4.5).
- Combination of the PDE5 inhibitor sildenafil when used for the treatment of pulmonary

arterial hypertension (PAH) only (see section 4.5). For co-administration of sildenafil for the treatment of erectile dysfunction see sections 4.4 and 4.5.

- Co-administration with medicinal products that are substrates of the CYP3A4 isoform of cytochrome P450 and have narrow therapeutic windows (e.g., quetiapine, lurasidone, alfuzosin, astemizole, terfenadine, cisapride, pimozide, quinidine, bepridil, triazolam, midazolam administered orally (for caution on parenterally administered midazolam, see section 4.5), lomitapide, and ergot alkaloids, particularly, ergotamine, dihydroergotamine, ergonovine, methylergonovine) (see section 4.5).
- Co-administration with grazoprevir-containing products, including elbasvir/grazoprevir fixed-dose combination (see section 4.5).
- Co-administration with glecaprevir/pibrentasvir fixed-dose combination (see section 4.5).
- Co-administration with products containing St. John's wort (Hypericum perforatum) (see section 4.5).
- Co-administration with apalutamide, encorafenib and ivosidenib (see section 4.5).
- Co-administration with carbamazepine, phenobarbital, and phenytoin (see section 4.5).

Detailed recommendations for the use of this product will be described in the updated SmPC, which will be published in the revised European public assessment report (EPAR) and made available in all official European Union languages after a decision on this change to the marketing authorisation has been granted by the European Commission.

Please refer to the following website in EMA for details:
https://www.ema.europa.eu/en/medicines/human/variation/reyataz

In Hong Kong, there are 4 registered pharmaceutical products containing atazanavir. All products are prescription-only medicines. So far, with regard to atazanavir, the Department of Health (DH) has received 2 cases of adverse drug reaction, but these cases were not related to co-administration with encorafenib, ivosidenib, carbamazepine, phenobarbital, and phenytoin.

In light of the above EMA's announcement, the matter will be discussed by the Registration Committee of the Pharmacy and Poisons Board.

Please note that this letter serves as a means for the DH to communicate important new safety information about registered pharmaceutical products with healthcare professionals in Hong Kong and is not intended to serve as guidelines or to replace professional clinical judgement. Healthcare professionals are advised to balance the risk of possible adverse effects against the benefit of treatment.

Please report any adverse events caused by drugs to the Clinical Trials and Pharmacovigilance Unit of the DH (tel. no.: 2319 2920, fax: 2319 6319 or email: adr@dh.gov.hk). For details, please refer to the website at Drug Office under "ADR Reporting": http://www.drugoffice.gov.hk/adr.html. You may wish to visit the Drug Office's website for subscription and browsing of "Drug News" which is a monthly digest of drug safety news and information issued by Drug Office.

Yours faithfully,

(Terence MAN)
for Assistant Director (Drug)