[National Pharmaceutical Regulatory Agency (NPRA) letterhead]

Our ref: NPRA/007/06/R/001(83) Vol.3
Date: 22 January 2024

To:
All Product Registration Holders,
All Applicants of the Evaluation on the Need for BE Study Specific Inspection (BEDE),
All Applicants for Bioequivalence (BE) Centre Inspections,

YBhg. Datuk / Dato' / Prof. / Dr. / Sir / Madam,

REJECTION OF BE STUDIES CONDUCTED AT THE BE CENTRE SYNAPSE LABS PVT. LTD., INDIA FOLLOWING INSPECTION FINDINGS BY THE EUROPEAN MEDICINES AGENCY (EMA)

With due respect, the matter above is referred.

2. For your information, the EMA had issued a notification to pharmaceutical companies via the EMA website on 15 December 2023 stating that all clinical and bioanalytical studies conducted at the BE Centre Synapse Labs Pvt. Ltd. at the following addresses will not be accepted in marketing authorisation applications.

Facility 1: Synapse Labs. Pvt. Ltd., Majestic Plaza, S No. 21/5, Kharadi-Mundhwa Bypass, Kharadi, Pune – 411014, Maharashtra India.
Facility 2: Synapse Labs. Pvt. Ltd., Krushna Complex, Kharadi-Mundhwa Bypass, Kharadi, Pune – 411014, Maharashtra India.

3. This notification was issued following inspection findings on the BE centre's quality management system where the data integrity of BE studies conducted are in doubt. Accordingly, the EMA decided to suspend approximately 345 products which were supported by BE studies conducted between 2009 to 2023. Alternative data showing that the products meet bioequivalence requirements must be submitted to lift the suspension status of the effected products. Product marketing authorisation applications with the EMA supported by only BE studies from the effected BE centre mentioned above will not be approved. Additional information on the EMA notification can be accessed via the link https://www.ema.europa.eu/en/documents/referral/synapse-article-31-referral-synapse-labs-pvt-ltd-ema-recommends-suspension-medicines-over-flawed-studies_en.pdf

4. Following the notification by the EMA, the National Pharmaceutical Regulatory Agency (NPRA) in the Committee for Premises and Study Inspections Meeting No. 1/2024 on 8 January 2024 decided **TO REJECT** all BE studies conducted at the affected BE Centre mentioned above. This decision will involve the following:

i. Rejection of all application for the Evaluation on the Need for BE Study Inspection (BEDE) on BE studies conducted on or before 2023;
ii. Cancellation of all BE study inspection exemptions granted via BEDE applications;
iii. Cancellation of all letters of acceptance issued via the BE Inspection Report Evaluation applications (BEIR);
iv. Delisting of the BE centre from the NPRA BE Centre Compliance Programme. However, two of the following BE studies may be accepted to support product registration evaluation at the NPRA.
    - Study Protocol: 14-064; Product name: Erlotinib 150mg Film-coated Tablets.
    - Study Protocol: 15-004; Product name: Darunavir 8000mg Film-coated Tablets.

5. NPRA also decided that acceptance of BE studies from the affected BE centre to support product registration evaluation by the Centre of Product & Cosmetic Evaluation can only be considered if the BE studies are conducted at the BE centres on or after 2024 **AND** undergo Study Specific Inspections. BEDE applications will not be considered by the NPRA.

5. This decision will be enforced with **IMMEDIATE EFFECT**.

6. Should you require any additional information on this matter, kindly get in touch with our officers via the email beec@npra.gov.my. The cooperation and attention from YBhg. Datuk/ Dato'/ Prof./ Dr./ Sir/ Madam is highly appreciated.

Thank you.

"MALAYSIA MADANI"
"TO SERVE THE COUNTRY"

I who carries out the trust,
{signature}
(ROSILAWATI BINTI AHMAD) RPh. 1413
Director
National Pharmaceutical Regulatory Agency,
Ministry of Health Malaysia.

[administrative information]

c.c. Deputy Director, Centre of Product & Cosmetic Evaluation
Deputy Director, Centre of Compliance & Quality Control
Deputy Director, Centre of Regulatory Coordination & Strategic Planning