



GMP Compliance Menu

Search

[GMP Certificates](#)[Non-Compliance Report](#) Exclude Teleconference info

Malta Medicines Authority

Report No: MT/002/NCR/2023

STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GMP non-compliance at a manufacturer⁽¹⁾

Part 1

Issued following an inspection in accordance with :
Art. 111(7) of Directive 2001/83/EC as amended

The competent authority of Malta confirms the following:

The manufacturer: **Beximco Pharmaceuticals Limited**

Site address: **Tongi, 126 Kathaldia Auchpara, Gazipur, 1711, Bangladesh**

OMS Organisation Id. / OMS Location Id.: **ORG-100014998 / LOC-100060917**

Other

(Human) Application for a GMP certificate for MA registration in Malta (Latanoprost 0.005mg/ml + Timolol 5mg/ml eyedrops)

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on **2023-08-01**, it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

• The principles and guidelines of Good Manufacturing Practice laid down in Directive (EU) 2017/1572 and Commission Delegated Regulation (EU) 2017/1569

(1) The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and 80(7) of Directive 2001/82/EC, as amended, shall also be required for imports coming from third countries into a Member State.

Part 2

Human Medicinal Products

1 NON-COMPLIANT MANUFACTURING OPERATIONS

1.1 Sterile products

1.1.1 Aseptically prepared (processing operations for the following dosage forms)
1.1.1.6 Other: Eye drops(en)

Part 3

Nature of non-compliance: PharmSol Europe Limited, Malta as proposed MAH is reserved a dossier filing slot in Malta (Malta as RMS) for the product Latanoprost 0.005 mg/ml + Timolol 5 mg/ml eyedrops in the month of October 2023 stating Beximco as finished product manufacturer (assigned DCP no. is MT/H/0708/001/DC). PharmSol Europe as Applicant applied for a GMP certificate with the scope of aseptically prepared sterile medicinal products, small volume liquids, eye drops with Malta Medicines Authority. A product specific GMP inspection with the scope of Latanoprost 0.005 mg/ml + Timolol 5mg/ml eyedrops (Latanoprost & Timolol PharmSol 0.05mg/ml+5mg/ml Eye Drops) was conducted on 28th July – 1st August 2023. The inspectors found one critical, three major and fifteen other deficiencies. The outcome of this inspection was discussed at the Inspection Review Group (IRG) at the Malta Medicines Authority who decided that a Statement of Non-Compliance with the principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC is to be issued about the site. Main inspection findings: One critical and three major deficiencies were found during the course of this inspection. The critical finding is related to: -the TAC Vista Building Management System (BMS), version 5.1.7.219 was not working and there is some issues with facility design -Environmental (EM) conditions such as temperature, relative humidity and differential pressure cannot be continuously monitored since BMS system is not working. All specific alarm files (.txt) and audit trails (named as 'Events') have been lost. -Currently actual temperature, humidity and delta pressure values in the facility are documented manually only twice daily. If alert levels are exceeded, alarms are not triggered, although there are issues with power supply as well (from 2019 twenty-one deviations were opened related to power cuts and failures). When power cut occurs, it takes 5-10 minutes to recover the electricity. This issue was also highlighted during the last EU GMP inspection. The three major deficiencies were found in the areas of: -GMP manufacturing activities, including aseptic processes in the Vision Unit (BLD-002) and their validation -Quality Management System (QMS) -Data integrity For further details the post-inspection letter (dated: 11th August 2023) that lists all findings is available by request to National Competent Authorities. Assessment of first CAPAs for critical finding: The company's first CAPA-plan related to the critical finding was received on 17th August 2023. After evaluation the Inspection Team found them unsatisfactory since no proposal for final preventive actions were proposed to avoid re-occurrence of the same issues (re critical deficiency). Second CAPAs with supporting evidence documents related to the critical finding will be submitted by Beximco on 31st October except for installation of new BMS for which target timeline, 31st March 2024 was provided. Assessment of main inspection findings on concerned medicinal products: The critical, major and other deficiencies, indicate that the sterility assurance of products manufactured in the inspected block cannot be guaranteed at all times in view that: the environmental monitoring, including delta-p, is not continuously monitored, with frequent electricity failures being experienced during which differential partial pressures fail, aseptic process stimulations (APS) carried out until June 2023 do not reflect the actual practice during aseptic manufacturing, deviations are not always logged and preventive actions are either missing or when taken are generally weak, plus issues with the integrity of retained GMP related data were also identified, amongst other deficiencies as listed in the post inspection letter. These all indicate strongly towards a lack of proper quality assurance as required with respect to the manufacture of sterile products.

Action taken/proposed by the NCA:

Withdrawal, of current valid GMP certificate No. DE_BW_01_GMP_2020_0001

It is recommended to withdraw issued GMP compliance certificate DE_BW_01_GMP_2020_0001 (issued by Baden – Württemberg (Regierungspräsidium Tübingen Leitstelle Arzneimittelüberwachung) on 27th January 2020.

Prohibition of supply

Prohibition of supply to EU/EEA markets.

Others

No new marketing authorisation applications, line extensions or variations to existing marketing authorisations applications should be authorised with

this site as a site of manufacture until the non-compliance is in place.

Teleconference Date:

Teleconference Time (CET):

Dial in no.:

2023-09-07

Name and signature of the authorised person of the Competent Authority of Malta

Confidential

Malta Medicines Authority

Tel: **Confidential**

Fax: **Confidential**

The EudraGMDP database is maintained and operated by the EMA. Access to the general public is granted in order to enhance availability of information related to the EMA mandate. The content of the database is provided by the National Competent Authorities (NCA) of the EEA. For this reason, the EMA accepts no responsibility or liability whatsoever (including but not limited to any direct or consequential loss or damage it might occur to you and/or any other third party) arising out of or in connection with the information on this database. Any questions about the content should be addressed to the relevant NCA. Please [click here](#) to get list of NCA's.

Due to the restrictions caused by COVID-19, the period of validity GMP and GDP certificates issued by EEA authorities is automatically extended until the end of 2023, except where clarifying remarks in the document state otherwise. Manufacturers, and importers and distributors must continue to comply with GMP/GDP and all other legal obligations. On-site inspections are conducted where and when possible. Competent authorities reserve the right to perform risk based supervision of sites by either on-site inspections or distant assessments and, based on the outcome, may continue to issue, withdraw or restrict GMP certificates, as appropriate.

For the UK, as from 1.1.2021, EU Law applies only to the territory of Northern Ireland (NI) to the extent foreseen in the Protocol on Ireland/NI.

Documents issued by UK authorities up to and including 31 December 2020 remain available for consultation in EudraGMDP. However, they are no longer included or updated from 1 January 2021, with the exception of the documents pertaining to sites located in Northern Ireland.

As of 28 January 2022, the source of organisational data will change. Additional information and instructions are available on [EMA's website](#)

[EMA © 2014. EudraGMDP 6.5.0.9-bugfix3 build 2023/09/01 13:02]