TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

TMDA
Tanzania Medicines & Medical Devices Authority

BETA DRUGS LIMITED
PUBLIC GMP INSPECTION REPORT

December, 2020

Part 1: General information about the company

Manufacturers details	
Name of manufacturer	Beta Drugs Limited (Unit of Adley Group, Oncology Division)
Corporate address of manufacturer	Village Nandpur, Kharuni-Lodhimajra Road, Baddi, District Solan, Himachal Pradesh 173205, India
Inspected site	
Name & address of inspected manufacturing site	Beta Drugs Limited (Unit of Adley Group, Oncology Division), Village Nandpur, Kharuni-Lodhimajra Road, Baddi, District Solan, Himachal Pradesh 173205, India
Unit number	Unit of Adley Group, Oncology Division
Inspection details	
Date of inspection	13th – 14th June, 2019
Type of inspection	Pre – Registration GMP Inspection
Introduction	
General information about the company and site	Beta Drugs Limited facility is located at a Village Nandpur, Kharuni-Lodhimajra Road, Baddi, District Solan, Himachal Pradesh, India, 55 km from Chandigarh Railway Station, 58 km from Chandigarh Airport and about 58 km from Interstate Bus Terminus Sector 43 Chandigarh. The company had license No. MNB/09/748 and MB/09/749 issued by the Drugs Controller of Himachal Pradesh to manufacture injectables and oral solid dosage forms (capsules and tablets) oncology.
History	The facility was inspected by the local regulatory authority, Drugs Controller of Himachal Pradesh and issued with a GMP compliant certificate No. HFW-H (DCA) 98/09. The facility has also been inspected and certified by

	other national regulatory authorities such as Cote D'Ivoire, Kenya, Nepal and Philippines. This was the second inspection done by TMDA following the previous inspection that was conducted from 14th – 15th December, 2018.
Brief report of the activities undertaken	
Areas inspected	Areas inspected were external surroundings, utilities, raw materials and packaging materials warehouses, manufacturing areas and their packing lines, finished goods warehouse, quality control laboratory. The inspection also verified the qualification of key personnel, training, premises layout, design, sanitation and hygiene, state of the buildings and equipment used in various manufacturing operations, laboratory instruments, complaints handling and recalls, self-inspection, documentation, qualification and validation as well as production and quality control practices.
Restrictions	None
Out of scope	Production lines other than the inspected ones.
Production lines inspected by TMDA	Oncology injectables (liquid and lyophilized) and Oncology oral solid dosage form (tablets and capsules) production lines.
Abbreviations	**Meaning**
AHU	Air Handling Unit
EAC	East African Community
ETP	Effluent Treatment Plant
cGMP	Current Good Manufacturing Practices
HPLC	High Performance Liquid Chromatography
HVAC	Heating, ventilation and air conditioning
PW	Purified Water
QC	Quality Control
RO	Reverse Osmosis
SOP's	Standard Operating Procedures
TMDA	Tanzania Medicines and Medical Devices Authority
TOC	Total Organic Carbon

TPIR	TMDA Public Inspection Report
UV	Ultraviolet
WFI	Water for Injection

Part 2: Brief summary of the findings and comments

The surroundings of the facility including the utilities were inspected followed by tracing the logical flow of production from incoming raw materials to the finished goods warehouses. During inspection various relevant working documents were evaluated and technical staffs interviewed on various aspects of GMP relevant to their areas of work.

1. Personnel

The facility had an adequate number of personnel and each was provided by job descriptions in line with their qualification and organogram. The latter suggested that, Production manager and Quality Control (QC) manager were independent from each other. Also, key positions were occupied by fulltime, qualified and experienced personnel.

The training records were reviewed and noted that, trainings were conducted as per training program. Induction training was offered immediately after employment followed by on job trainings which were conducted once per year and whenever the need arises.

The procedures for medical examinations and medical records were reviewed and observed that pre-employment and annual medical examinations were carried out and being implemented as per procedures.

Adequate measures were put in place for personnel hygiene e.g. presence of entry and exit SOPs which were supported by pictorial presentations.

2. Premises

i. Layout and Design

The facility was well designed and spacious enough to minimize the chance of mix-up, cross-contamination as well as to ensure unidirectional flow of personnel and material. Different production lines had separate production areas (floors) in the same building.

The walls, floors and ceiling were constructed by using hard non-porous and non-shedding materials with smooth finish to ensure effective cleaning of the building. The

critical manufacturing areas were epoxy coated. The doors with interlocking mechanism were provided in all critical areas. Airlocks were available at entry and exit points.
Generally, the facility was provided with all necessary areas as per Good Manufacturing Practices (GMP) guidelines and the premises were suitably located, constructed and maintained to suit the operations which were carried out.

ii. Sanitation and Hygiene

The facility surroundings and manufacturing areas were clean, well maintained. There were traps to prevent entrance of insects and rodents. Personnel change rooms were provided with entry and exit SOPs, wash area/toilet, cabinets for keeping street gowns and shoes, step over benches and sanitizing solutions. The doors with interlocking mechanism were provided in all critical areas and airlocks at entry and exit points. The facility had a good system (Effluent Treatment Plant - ETP) for managing generated waste.

3. Production

Received raw materials were being verified, cleaned and weighed as per SOP before taken to the quarantined area. Common warehouses were provided for injectables and oral solid dosage forms. Quarantined, under test, approved and rejected materials/finished goods were clearly identified, demarcated and well arranged.

Printed labels were secured under lock and key. Sampling and dispensing rooms were available and well equipped. Reverse Laminar Air Floor (RLAF) booths were provided to these rooms. The sampling of Active Pharmaceutical Ingredients (API) and excipients were 100%. Generally, production operations were carried out as per written procedures and records (for both batch manufacturing and packaging) maintained. Status labels were provided for each manufacturing steps.

Production line I (Injectables)

The manufacturing process in this line involved the following steps; bulk manufacturing, vial filling and sealing, followed by terminal sterilization, leak test, optical inspection, secondary packing and quality check prior to distribution. The vials were subjected into a thorough wash using purified water and water for injection, depyrogenated and dried before use.

Production line II (Oral Solid Dosage Form)

Manufacturing process involved dispensing, sifting, mixing, granulation, drying, compression and packaging. While capsule production steps included dispensing, sifting, mixing, drying, filling and packaging.

4. Quality Control

The quality control laboratory was divided into subdivisions namely chemical, instrumental and microbiological sections. Each section was well equipped and had sufficient number of qualified and experienced staff to facilitate effective analysis of raw materials, in process and finished products.

Microbiology laboratory was responsible for testing raw materials and finished pharmaceutical products.

Samples, reference standards and microorganisms were stored as per SOP. HPLC Columns were coded and appropriately managed. All preparations and analytical tests conducted in the laboratory were done in accordance to the procedure. Control samples of starting materials and finished products were confirmed to be reserved in the sample room. The stability studies were also being performed by the facility and stability chambers were available.

5. Equipment

The manufacturing facility had sufficient number of equipment which were located, designed, installed, qualified, calibrated, adapted and maintained to suit the operations to be carried out. The layout and design of equipment minimize the risk of errors and permit effective cleaning and maintenance in order to avoid cross-contamination, build-up of dust or dirt. All equipment were labeled for identification and those available in the quality control laboratory were provided with user logbooks.

6. Water Treatment System

Water was sourced from bore well and pumped to underground tank. The raw water was chlorinated and stored in two (2) overhead tanks, then de-chlorinated prior to addition of NaOH to control acidity and removal of heavy metals. The purified water (PW) was produced by Reverse Osmosis (RO) and subjected to UV light which was then passed through multicolumn distillation plant to produce water for injection (WFI).

The system was well labeled to show direction of water flow, various stages and sampling points. Conductivity, PH, TOC and total microbial count were carried out to monitor the quality of water as per schedule and records maintained. Sanitization of the system were performed as per procedures and records maintained. Generally, the

purified water system was suitably designed, installed, validated, maintained, calibrated and monitored.

7. Heating, Ventilation and Air Conditioning

Heating, Ventilation and Air Conditioning (HVAC) system was installed in each block (i.e injectable production block and oral solid dosage block) to prevent cross-contamination. The Air Handling Units (AHUs) installed were sufficient in number and clearly labeled to indicate the rooms they supply and direction of air flow.

All AHUs were well designed, qualified, calibrated, validated and subjected to preventive maintenances as scheduled and in accordance to written SOPs.

8. Document Review

Documents were designed and prepared as per GMP requirements and were approved, signed and dated by the appropriate responsible persons. The document review was done in timely manner and records were kept up to date.

Part 3: Conclusion

Based on the areas inspected, the people met and the documents reviewed and considering the findings of the inspection and assessment of compliance report, **Beta Drugs Limited (Unit of Adley Group, Oncology Division) located at Village Nandpur, Kharuni - Lodhimajra Road, Baddi, District Solan, Himachal Pradesh, India** was considered to be operating at an acceptable level of compliance with EAC GMP Guidelines for the manufacturing of Oncology injectables (liquid and lyophilized) and Oncology oral solid dosage form (tablets and capsules).

This TPIR will remain valid for three (3) years from the date of approval for GMP compliance provided that the outcome of any inspection conducted during this period is positive.

Part 4: References

1. EAC, (2014), *Compendium of Good Manufacturing Practice Guidelines Technical Documents for Harmonization of Medicines Regulations,* EAC Secretariat, Arusha, Tanzania.

2. TMDA *Good Manufacturing Practices Regulations, Manual and SOPs*, Tanzania Medicines and Medical Devices Authority, Dar es Salaam, Tanzania.

3. Tanzania Medicines and Medical Devices Act, Cap 219.

4. Beta Drugs Limited (Unit of Adley Group, Oncology Division) – CAPA response