World Health Organization

20, AVENUE APPIA – CH-1211 GENEVA 27 – SWITZERLAND – TEL CENTRAL +41 22 791 2111 – FAX CENTRAL +41 22 791 3111 – WWW.WHO.INT

Prequalification Unit Inspection Services
WHO INSPECTION REPORT
(WHOPIR)
Desk Assessment of Active Pharmaceutical Ingredient (API) Manufacturer

Part 1	**General information**	
Company information		
Name of Manufacturer	Cdymax (India) Pharma Private Limited	
Corporate address of manufacturer	Cdymax (India) Pharma Private Limited, [Formerly known as Acebright (India) Pharma Private Limited] No. 116/117, KIADB Industrial Area, Jigani, 2nd phase Bangalore - 560 105. Karnataka, India. Tel: +91 9343720118, +91 9980587638	
Contact person	Mrs. Manorama Avinash, Executive Director Tel: +91 8110 415502, +91 8110 415540 Email: rnanorama@cdymax.in	
Inspected site		
Name & address of manufacturing site	Cdymax (India) Pharma Private Limited, [Formerly known as Acebright (India) Pharma Private Limited] No. 116/117, KIADB Industrial Area, Jigani, 2nd phase Bangalore - 560 105. Karnataka, India. Latitude:12° 28'N & Longitude: 77°2 3'E FEI Number:3009882550 D-U-N-S Number: 91-651-2426	
Synthetic Unit/Block/Workshop	Block 01: line 1 and line 2	
Manufacturing license number	The Department of Drugs Control, Government of Karnataka issued a manufacturing license for the manufacture of APIs under Form 25, document reference DCD/MFG/SR-51/2020-21, bearing Mfg. License No. KTK/25/506/2005, valid 15/7/2020 – 14/7/2025.	
Desk assessment details		
Start and end dates of review	22 – 23 December 2023	
Inspection record number	INSP-API-2020-0075	
APIs covered by this desk assessment	APIMF173 Efavirenz APIMF219 Tenofovir Disoproxil Fumarate APIMF394 Atazanavir Sulfate	
Any documents missing?	None	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments**	
COFEPRIS, Mexico	Dates of inspection:	12 – 16 February 2023
	Type of inspection:	Virtual real-time GMP inspection
	Block/Unit/Workshop:	Building Block 2, Lines 1,2, and 3

	APIs covered:	Dasatinib, Sunitinib, Palbociclib, Capecitabine and Erlotinib Hydrochloride.
	Description of CAPA:	Not available
Malta Medicines Authority, Malta	Dates of inspection:	25 – 29 January 2023
	Type of inspection:	1st GMP inspection
	Block/Unit/Workshop:	The inspection scope was limited to the GMP (Part I) compliance status of the manufacturing, testing, storage and distribution activities of non-sterile and non-sensitising finished product intermediates (human and investigational medicinal products) with a particular focus on Enzalutamide Solid Dried Dispersion (SDD).
	APIs covered:	Enzalutamide
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	The most recent WHO inspection of Cdymax formally known as Acebright was performed by PQT from 22 to 24 July 2019. This was the 5th inspection of the site. The inspection concluded that the site is considered to be compliant with WHO GMP guidelines for API after submission and implementation of CAPAs in response to the identified deficiencies.	
Brief summary of manufacturing activities	Active Pharmaceutical Ingredients of oncology and general APIs are manufactured at this site. There were two manufacturing blocks on site (Production Block-1 (PB-1) and Production Block-2 (PB-2)) and an R&D unit. Each Production Block had a Kilo lab, a dedicated QC laboratory, dedicated Warehouse and dedicated Utilities and personnel. General APIs were manufactured in PB-1, while Oncology APIs were manufactured in PB-2. PB-2 has three production lines. Hazardous and sensitising substances like β-lactums, Cephalosporins, Hormone substances or veterinary products are not handled or manufactured at the site. The General API Production Building (PB-1) had two manufacturing lines (Line 1 and Line 2) with equivalent equipment where the WHO products were manufactured: • Efavirenz USP/Ph. Int. and Tenofovir Disoproxil Fumarate Ph.Int./IP were manufactured in both lines. • Atazanavir Sulphate IP was manufactured in Line 1.	
General information about the company and manufacturing site	Cdymax (India) Pharma Pvt. Ltd., Bangalore, was formerly known as Acebright (India) Pharma Private Limited, and before that, it was known as Cdymax (India) Pharma Pvt. Ltd and Intermed Labs Pvt. Ltd. The facility was established in 1991 to manufacture drug intermediates and active pharmaceutical ingredients (APIs). The site is located in Jigani, approximately 25 km from Bangalore and 70 km from Kempegowda International Airport and commenced production operations in 1991. There were two production blocks in Unit 2. General APIs were manufactured in PB-1, and oncology APIs in PB-2. Separate and dedicated utilities were provided for each production building. There were also separate QC laboratories.	
Focus of the last WHO inspection	Routine GMP inspection	
Areas inspected	Workshops, Utilities, Warehousing, Solvent Storage, Production Blocks, Analytical and Microbiological Laboratories explicitly used for the manufacture of WHO PQ APIs	

Out of scope and restrictions (last WHO inspection)	Parts of the site that were not concerned with the manufacture of WHO PQ APIs were not inspected.
WHO APIs covered by the last WHO inspection	APIMF173 Efavirenz APIMF219 Tenofovir Disoproxil Fumarate APIMF-2019-0017 Atazanavir Sulfate (under assessment)
Additional products to be covered by this desk assessment:	Not Applicable
Abbreviations	**Meaning**
BMR	Batch manufacturing record
BPR	Batch production record
CAPA	Corrective and preventive action
CC	Change control
GMP	Good manufacturing practices
NC	Non conformity
NRA	National regulatory agency
PQR	Product quality review
PQS	Pharmaceutical quality system
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure

Part 4	**Summary of the assessment of supporting documentation**

a) Manufacturing authorization and GMP certificate granted by the local authority:
A manufacturing license for manufacturing of APIs was issued by the Department of Drugs Control, Government of Karnataka under Form 25, document reference, DCD/MFG/SR-51/2020-21, bearing Mfg. License No. KTK/25/506/2005 with validity 15/7/2020 – 14/7/2025.

A GMP certificate has been issued by the Drugs Controller, Government of Karnataka as per document reference DCD/SPL-1/CR-292/2023-24 with an issue date of 14/6/2023 and valid until 14/06/2024.

b) Site master file (SMF):
A 31 page (plus annexures) Site Master File was submitted. The SMF was found acceptable.

c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:
The list has been provided and reviewed as part of this desk assessment.

d) List of all regulatory inspections performed in the last 3 years and their outcomes:

Product name	Manufacturing facility/rooms	Manufacturing equipment	Packaging line	Product dedicated yes/no	If shared, specify type of products	Covered by (SRA name and date of inspection)?
Efavirenz	Production block-1, line-1.	Enclosed list of equipments	Production block-1, line-1 and clean room.	No, multiproduct	Antiretroviral	Name of Authority: USFDA, Date of Inspection: 27.01.20 to 31.01.20
Tenofovir Disoproxil Fumarate	Production block-1, line-1 and Line-2	Enclosed list of equipments	Production block-1, line-1 & 2, clean room.	No, multiproduct	Antiretroviral	
Atazanavir Sulphate	Production block-1, Line-2	Enclosed list of equipments	Production block-1, line-2, clean room.	No, multiproduct	Antiretroviral	
Efavirenz	Production block-1, line-1.	Enclosed list of equipments	Production block-1, line-1 and clean room.	No, multiproduct	Antiretroviral	Name of Authority: WHO, Date of Inspection: 22.07.19 to 24.07.19
Tenofovir Disoproxil Fumarate	Production block-1, line-1 and Line-2	Enclosed list of equipments	Production block-1, line-1 & 2, clean room.	No, multiproduct	Antiretroviral	
Atazanavir Sulphate	Production block-1, Line-2	Enclosed list of equipments	Production block-1, line-2, clean room.	No, multiproduct	Antiretroviral	

e) Most recent product quality review(s) (PQR)(s) of the concerned WHO API(s):
The PQR was reviewed for the period January – December 2022 for active ingredients Efavirenz, Tenofovir and Atazanavir, obtaining the following:

Batches	Efavirenz	Tenofovir	Atazanavir
Manufacturing area	Block 01: line 1 & line 2	Block 01: line 1 & line 2	Block 1: line 2
Manufactured	0 # manufactured	281 # manufactured	0 # manufactured
Approved	0 # approved	281 #	0 # approved
Rejected	0 #	0 #	0 #
Deviation	0 #	0 #	0 #
Analytical incidents	0 #	4 #	0 #
OOS	0 #	1 #	1 #
OOT	0 #	1 #	0 #
Reprocessing	0 #	0 #	0 #
Change Control	0 #	9 related to documents, specifications & processes	4 related to facility & equipment
Complaints	0 #	0 #	0 #
Returns	0 #	0 #	0 #
Recalls	0 #	0 #	0 #
CAPAs	0 #	1 #	0 #

From the data presented, it was concluded that each manufacturing process was robust, the acceptance criteria were met, and no findings were detected in the documentation reviewed.

f) Batch manufacturing and packaging record(s), including the analytical part, for the most recently released batch of relevant API(s):
Batch manufacturing and packaging record(s), including the analytical part of the last commercial batches of Tenofovir, Efavirenz and Atazanavir were submitted. These were generally found acceptable.

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:
The master batch production, control records and batch packaging records of Tenofovir, Efavirenz and Atazanavir were submitted. These were generally found acceptable.

h) Recalls in the past three years related to APIs with quality defects:
Cdymax submitted a confirmation dated 9/12/2023 that during the past three years no recalls have been implemented.

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the API(s) has been performed and all matters dealt with:
Cdymax submitted a confirmation dated 20/12/2023 that a full self-inspection had been conducted.

j) Copy of any warning letter, or equivalent regulatory action, issued by any authority for their market, to which the site provides or has applied to provide the API(s):
Cdymax submitted a confirmation dated 9/12/2023 stating that no warning letter or equivalent regulatory action had been issued/considered by any regulatory authority.

k) Out-of-stock situations:
Cdymax submitted a confirmation dated 20/12/2023 that an out-of-stock situation is not foreseen.

l) Additional documents submitted:
Not applicable

Part 5	Conclusion – Desk assessment outcome

Based on the previous WHO inspections and on the GMP evidence received and reviewed, it is considered that a desk assessment is acceptable in lieu of a WHO onsite inspection. The site ***Cydmax (India) Pharma Pvt. Ltd,*** located at ***77D & 116/117 KIADB Industrial Area, Jigani, Bangalore, Karnataka, 560 105, India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines for APIs.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted by this period is positive.

Part 6	List of guidelines referenced in this inspection report

1. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eight Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2.
   Short name: WHO TRS No. 986, Annex 2
   https://www.who.int/publications/m/item/trs986-annex2

2. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2.
   Short name: WHO TRS No. 957, Annex 2
   https://www.who.int/publications/m/item/annex-2-trs-957

3. WHO guidance on good practices for desk assessment of compliance with good manufacturing practices, good laboratory practices and good clinical practices for medical products regulatory decisions. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report. Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 9.
   Short name: WHO TRS 1010, Annex 9
   https://www.who.int/publications/m/item/trs1010-annex9

4. WHO Good Manufacturing Practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-fifth Report. Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 3.
   Short name: WHO TRS No. 1033, Annex 3
   https://www.who.int/publications/m/item/annex-3-trs-1033

5. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
   Short name: WHO TRS No. 929, Annex 4
   https://www.who.int/publications/m/item/annex-4-trs-929

6. WHO good practices for pharmaceutical quality control laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957, Annex 1.
   Short name: WHO TRS No. 957, Annex 1
   https://www.who.int/publications/m/item/trs957-annex1

7. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
   Short name: WHO TRS No. 957, Annex 3
   https://www.who.int/publications/m/item/trs957-annex3

8. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8.
   Short name: WHO TRS No. 1010, Annex 8
   https://www.who.int/publications/m/item/Annex-8-trs-1010

9. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. Part 2: Interpretation of Guidelines on heating, ventilation and air-conditionning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1019), Annex 2.
   Short name: WHO TRS No. 1019, Annex 2
   https://www.who.int/publications/m/item/trs1019-annex2

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 4
    https://cdn.who.int/media/docs/default-source/medicines/norms-and-standards/guidelines/production/trs1044-annex4-technology-transfer-in-pharmaceutical-manufacturing.pdf

11. WHO good manufacturing practices for sterile pharmaceutical products. Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2022 (WHO Technical Report Series, No. 1044), Annex 4.
    Short name: WHO TRS No. 1044, Annex 2

https://www.who.int/publications/m/item/trs1044-annex2

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-First Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
https://www.who.int/publications/m/item/trs943-annex3

13. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
Short name: WHO TRS No. 961, Annex 2
https://www.who.int/publications/m/item/trs961-annex2

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2.
Short name: WHO TRS No. 981, Annex 2
https://www.who.int/publications/m/item/trs981-annex2

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3.
Short name: WHO TRS No. 981, Annex 3
https://www.who.int/publications/m/item/annex-3-trs-981

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14.
Short name: WHO TRS No. 961, Annex 14
https://www.who.int/publications/m/item/tr961-annex14

17. Good Manufacturing Practices: Guidelines on validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Third Report Geneva, World Health Organization, 2019 (WHO Technical Report Series, No. 1019), Annex 3.
Short name: WHO TRS No. 1019, Annex 3
https://www.who.int/publications/m/item/trs1019-annex3

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4.
Short name: WHO TRS No. 992, Annex 4
https://www.who.int/publications/m/item/trs992-annex4

19. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9.
Short name: WHO TRS No. 961, Annex 9
https://www.who.int/publications/m/item/trs961-annex9-modelguidanceforstoragetransport

20. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5.
Short name: WHO TRS No. 992, Annex 5
https://www.who.int/publications/m/item/trs992-annex5

21. WHO Recommendations for quality requirements when plant – derived artemisinin is used as a starting material in the production of antimalarial active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-Ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 6.
Short name: WHO TRS No. 992, Annex 6
https://www.who.int/publications/m/item/trs-992-annex-6

22. Guideline on data integrity. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 4.
Short name: WHO TRS No. 1033, Annex 4
https://www.who.int/publications/m/item/annex-4-trs-1033

23. WHO general guidance on variations to multisource pharmaceutical products. *WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifties Report* Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
Short name: WHO TRS No. 996, Annex 10
https://www.who.int/publications/m/item/trs966-annex10

24. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10. ***Short name: WHO TRS No. 1010, Annex 10***
https://www.who.int/publications/m/item/trs1010-annex10

25. Points to consider when including Health-Based Exposure Limits in cleaning validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fifth Report Geneva, World Health Organization, 2021 (WHO Technical Report Series, No. 1033), Annex 2.
Short name: WHO TRS No. 1033, Annex 2
https://www.who.int/publications/m/item/annex-2-trs-1033

26. Points to consider for manufacturers and inspectors: environmental aspects of manufacturing for the prevention of antimicrobial resistance. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 6.
Short name: WHO TRS No. 1025, Annex 6
https://www.who.int/publications/m/item/trs-1025-annex-6

27. Production of water for injection by means other than distillation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 3.
Short name: WHO TRS No. 1025, Annex 3
https://www.who.int/publications/m/item/trs-1025-annex-3-water-for-injection

27. Good chromatography practice. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-Fourth Report. Geneva, World Health Organization, 2020 (WHO Technical Report Series, No. 1025), Annex 4.
Short name: WHO TRS No. 1025, Annex 4
https://www.who.int/publications/m/item/trs1025-annex4