World Health Organization

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Prequalification Unit Inspection services
WHO PUBLIC INSPECTION REPORT

Desk Assessment of Finished Product Manufacturer

Part 1	General information
Company information	
Name of Manufacturer	Hetero Labs Limited Unit 3 (Jeedimetla)
Corporate address of manufacturer	Hetero Labs Ltd. Hetero Corporate, H.No. 7-2-A2, Industrial Estates, Sanath Nagar, Hyderabad –500 018, Telangana, India
Inspected site	
Name & address of manufacturing site	Hetero Labs Limited Unit 3 (Jeedimetla) Hetero Labs Ltd, Unit3, Survey No.51, Plot No 22-110 IDA, Jeedimetla, Hyderabad, Telangana, 500 055, India GPS coordinates: 17° 32' 00.7" N- 78° 26' 05.5" E
Production Block/Unit	Block-A, Block-B
Manufacturing license number	License: No 22/RR/AP/2001/F/R valid up to 29-03-2021, Form 25 & 28 GMP certificate: L.Dis.No.7337/E1/2018, dated 17-1-2019
Desk assessment details	
Start and end dates of review	21 September - 02 October 2020
Products covered by this desk assessment	1. Lamivudine Tablet 300mg 2. Lamivudine/Zidovudine Tablet 150mg/300mg 3. Lamivudine Tablet, Film-coated 150mg 4. Lopinavir/Ritonavir Tablet 100mg/25mg 5. Lamivudine Solution, Oral 10mg/ml 6. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg 7. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg 8. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg 9. Zidovudine Solution, Oral 50mg/5ml 10. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg 11. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg 12. Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg 13. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg 14. Lopinavir/Ritonavir Tablet, Film-coated 100mg/25mg 15. Dolutegravir (Sodium) Tablet, Film-coated 50mg 16. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg 17. Darunavir (Ethanolate)/Ritonavir Tablet, Film-coated 400mg/50mg 18. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg

	19. HA758 Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg
List of documents submitted	1) FDA EIR, dates of inspection 30 May 2019 and 3 – 7 June 2019 2) Hetero response CAPAs to FDA inspection 30 May 2019 and 3 – 7 June 2019 3) Annexures to the Hetero response to FDA inspection 30 May 2019 and 3 – 7 June 2019 4) CAPA status, dated 14.08.2020 5) Supporting exhibits to CAPAs 6) SMF with Annexures 7) Executed BMR/BPR and analytical raw data: 1. Lamivudine/Zidovudine Tablet 150mg/300mg 2. Lamivudine Tablet, Film-coated 150mg 3. Lopinavir/Ritonavir Tablet 100mg/25mg 4. Lamivudine Solution, Oral 10mg/ml 5. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg 6. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg 7. Zidovudine Solution, Oral 10mg 8. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg 9. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg 10. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg 11. Dolutegravir (Sodium) Tablet, Film-coated 50mg 12. Darunavir (Ethanolate)/Ritonavir Tablet 400mg/50mg 13. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg 14. Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg Note: 15. Lamivudine Tablet 300mg – *(not commercialized as per WHO dossier)* 16. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg *(not commercialized on 2018 onwards)* 17. Lopinavir/Ritonavir Tablet, Film-coated 100mg/25mg *(not commercialized as per WHO dossier)* 18. Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg *(not commercialized as per WHO dossier)* 19. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg *(not commercialized as per WHO dossier)* 8) Master batch records: 1. Lamivudine Tablet 300mg 2. Lamivudine/Zidovudine Tablet 150mg/300mg 3. Lamivudine Tablet, Film-coated 150mg 4. Lopinavir/Ritonavir Tablet 100mg/25mg 5. Lamivudine Solution, Oral 10mg/ml 6. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg 7. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg

	8. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg 9. Zidovudine Solution, Oral 50mg/5ml 10. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg 11. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg 12. Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg 13. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg 14. Lopinavir/Ritonavir Tablet, Film-coated 100mg/25mg 15. Dolutegravir (Sodium) Tablet, Film-coated 50mg 16. Dolutegravir/Lamivudine/Tenofovir Disoproxil Fumarate tablet, Film-coated 50mg/300mg/ 300mg 17. Darunavir (Ethanolate)/Ritonavir Tablet, Film-coated 400mg/50mg 18. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg 19. Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg 9) List of all regulatory inspections performed in the last 5 years and their outcomes 10) Details of recalls in last 3 years 11) Products covered by SRA inspections in the last 3 years 12) Declaration: self-inspection 13) PQRs: 1. Lamivudine Tablet 300mg 2. Lopinavir/Ritonavir Tablet 100mg/25mg 3. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg 4. Darunavir (Ethanolate)/Ritonavir Tablet, film-coated 400mg/50mg 5. Lamivudine Tablet, Film-coated 150mg 6. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg and Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg 7. Zidovudine Solution, Oral 50 mg/5ml 8. Lamivudine Solution, Oral 10mg/ml 9. Lamivudine/Zidovudine Tablet 150mg/300mg 10. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg 11. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg 12. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg 13. Dolutegravir (Sodium) Tablet, Film-coated 50mg 14. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg 15. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg
Any documents missing?	N/A

Part 2	Summary of SRA/NRA inspection evidence considered (from most recent to last) and comments	
US FDA, FDA	Dates of inspection:	30 May 2019 and 03 – 07 June 2019
	Type of inspection:	Surveillance GMP inspection
	Block/Unit:	Block A and B
	Type of products/Dosage forms covered:	• Simvastatin Tablets USP 80mg • Finasteride Tablets USP 5mg • Methocarbamol Tablets 750 mg • Levetiracetam Tablets USP 500 mg • Levocetirizine dihydrochloride Tablets 5mg • Torsemide tablets USP 5 mg • Metoprolol Succinate Extended Release Tablets USP 200 mg • Metoprolol Tablets USP 50 mg and 100 mg • Hydralazine hydrochloride Tablets USP 20 mg • Lithium Carbonate Capsules UPS 300 mg • Indomethacin Capsules USP 50 mg WHO products under PQ were not specifically covered
Date of inspection and conclusion of most recent WHO inspection	Last on-site inspection was performed by WHO 09-12 June 2015. Initial conclusion: "Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the deficiencies listed in the Inspection Report, a decision on the compliance of Hetero Labs Unit 3 Jeedimetha (blocks A and B), located at Survey No 51, Plot No 22-110 IDA, Jeedimetla, Hyderabad, Telangana 500 055,India with WHO GMP guidelines will be made after the manufacturer's response to the deficiencies has been assessed". CAPAs were submitted and assessed by the PQT: Inspection Team and the inspection, following the review of the CAPA, was closed 28 October 2015 as compliant with the standards of GMP published by WHO. In addition, a Desk assessment of an inspection conducted by the Spanish Agency for Medicines and Medical Devices, Medicines Control Department and that of the USFDA was performed and closed on 5 September 2018 as compliant.	
Summary of manufacturing activities as of *June 2015*	Manufacturing of solid dosage forms • Tablets (uncoated and coated) • Capsules • Oral liquids • Primary and secondary packaging • Storage • Quality control	

General information about the company and manufacturing site as of *June 2015*	Hetero Labs Ltd, a division of Hetero group was established in 1993. Hetero Labs Limited Unit 3 was located about 45 km from Hyderabad international airport. There were two blocks (Block-A and Block-B) involved with different multi-product formulation and packaging modules.
Focus of the last WHO inspection	• Lamivudine Tablet, Film-coated 150mg • Nevirapine Tablet 200mg • Lamivudine/Nevirapine/Stavudine Tablet 150mg/200mg/40mg • Lamivudine/Nevirapine/Stavudine Tablet 150mg/200mg/30mg • Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg • Efavirenz Tablet, Film-coated 600mg • Lamivudine/Tenofovir disoproxil (fumarate) Tablet 300mg/300mg • Zidovudine Tablet, Film-coated 300mg • Zidovudine Solution, Oral 50mg/5ml • Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg • Abacavir (sulfate) Solution, Oral 20mg/mL • Emtricitabine/Tenofovir disoproxil (fumarate) Tablet, Film-coated 200mg/300mg • Tenofovir disoproxil (fumarate) Tablet, Film-coated 300mg • Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg • Lamivudine Tablet 300mg • Stavudine Capsules, hard 15mg • Stavudine Capsules, hard 20mg • Stavudine Capsules, hard 30mg • Stavudine Capsules, hard 40mg • Lamivudine/Zidovudine Tablet 150mg/300mg • Abacavir (sulfate) Tablet 300mg • Lamivudine/Tenofovir disoproxil (fumarate) Tablet 300mg/300mg • Efavirenz/Lamivudine/Tenofovir disoproxil (fumarate) Tablet, Film-coated 600mg/300mg/300mg • Ritonavir Tablet, Film-coated 100mg • Abacavir (sulfate) Tablet, Film-coated 300mg • Atazanavir (sulfate)/Ritonavir Tablet, Film coated 300mg/100mg • Lamivudine/Tenofovir disoproxil (fumarate) Tablet, film-coated 75mg/75mg • Lopinavir/Ritonavir Tablet 100mg/25mg
Areas inspected	• Quality Assurance • Sanitization and hygiene • Qualification and validation • Complaints • Recalls • Supplier qualification • Personnel • Training • Personal hygiene • Premises • Equipment • Materials

	• Documentation • Production • Quality control • Quality Risk Management (QRM) • Product Quality Review (PQR) • Deviations and Incidents • Change control (CC) • SAP (enterprise resource planning) system • Validation Master Plan (VMP) • Self-inspection and quality audit ▪ Items for self-inspection ▪ Self-inspection team ▪ Frequency of self-inspection ▪ Follow-up action ▪ Quality audit • Personnel ▪ Job descriptions ▪ Training ▪ Personnel hygiene • Premises ▪ Ancillary areas ▪ Storage areas ▪ Production workshops ▪ Quality control areas • Equipment ▪ Preventive maintenance (PM) ▪ Calibration and qualification ▪ HVAC ▪ Compressed air ▪ Purified Water • Materials ▪ Suppliers audit and approval ▪ Starting materials ▪ Finished products • Documentation ▪ Labels ▪ Specifications and testing procedures ▪ Batch processing records • Good practices in production ▪ Cleaning procedures • Good Practices in quality control ▪ Control of starting materials and intermediate, bulk and finished products ▪ Specifications and analytical test methods ▪ Microbiological laboratory (MB) ▪ Retention samples ▪ Reference materials

Out of scope and restrictions (last WHO inspection)	Products out of WHO PQ
Abbreviations	Meaning
BMR	Batch manufacturing record
BPR	Batch Packaging record
EIR	Establishment inspection report
FPP	Finished pharmaceutical product
GMP	Good manufacturing practices
PQR	Product quality review
SMF	Site master file

Part 4	Summary of the assessment of supporting documentation

a) List of all regulatory inspections performed in the last 5 years and their outcomes:

Regulatory agency	Dates of inspection	Outcome
U.S. Food and Drug Administration, USA	30-05-2019 to 07-06-2019	EIR issued, VAI
	22-10-2018 to 26-10-2018	
	19-03-2018 to 23-03-2018	
	17-10-2016 to 26-10-2016	
	27-07-2015 to 31-07-2015	
Agencia Espanola De Medicamentors Y Productos Sanitarious (AEMPS) - Spain	27-02-2017 to 03-03-2017	GMP certificate issued
Berlin Health Authorities - Germany	17-11-2015 to19-11-2015	GMP certificate issued
Agencia National De Vigilancia Sanitaria (ANVISA) - Brazil	30-10-2017 to 03-11-2017	GMP certificate issued
Pharmacy and Medicines Regulatory Authority (PMRA), - Malawi	06-03-2020 to 07-03-2020	GMP certificate issued
Food, Medicine and Healthcare Administration and Control Authority, (EFMHACA) - Ethiopia	19-10-2019 to 22-10- 2019	GMP certificate issued
Saudi Food and Drug Authority (Kingdom of Saudi Arabia) - Saudi Arabia	15-10-2019 to16-10-2019	GMP certificate issued
Tanzania Medicines and Medical Devices Authority - Tanzania	28-08-2019 to 29-08-2019	GMP certificate under receipt
Ministry of Health – Belarus	01-08-2018 to 03-08-2018	GMP certificate issued
Sultanate of Oman - Oman	18-04-2018 to 19-04-2018	GMP certificate issued
State Institute of Medicinal Products and Good Practices – Russia	07-11-2018 to 08-11-2018	GMP certificate issued
NDA (National Drug Authority) - Uganda	20-11-2017 to 21-11-2017	GMP certificate issued
Pharmacy & Poisons Board - Kenya	12-12-2016 to14-12-2016	GMP certificate issued
Medicines Control Authority of Zimbabwe – (MCAZ) - Zimbabwe	22-02-2016 to 23-02-2016	GMP certificate issued

National Medicines and Poisons Board (NMPB) - Sudan	25-11-2015 to 28-11-2015	GMP certificate issued
COFEPRIS (Comision Federal Para La Proteccion Contra Reisgos Sanitarios) - Mexico	20-07-2015 to 31-07-2015	GMP certificate issued
Sierra Leone -Salone	08-07-2015	GMP certificate issued
Instiluto Acional De Vigilancia de Medicamentos Y Alimentos (INVIMA) - Columbia	16-02-2015 to 20-02-2015	GMP certificate issued

b) Manufacturing authorization granted by national authorities:
License: No 22/RR/AP/2001/F/R valid up to 29-03-2021, Form 25 & 28
GMP certificate: L.Dis.No.7337/E1/2018, dated 17-1-2019

c) Site master file:
SMF submitted and reviewed. SMF written according to the WHO TRS No. 961, Annex 14

d) List of all the products and dosage forms manufactured on-site:

S.No.	Name of the Product	Therapeutic Group
1.	Abacavir Tablets USP 300 mg	Anti-retro viral
2.	Atazanavir Sulfate and Ritonavir Tablets 300/100 mg.	Anti-retro viral
3.	Amlodipine Tablets 5 mg and 10 mg.	Anti-hypertensive
4.	Clobazam Tablets 10mg and 20mg	Anti-Convulsant
5.	Darunavir Tablets 400 mg and 600 mg	Anti-retro viral
6.	Dolutegravir tablets 50mg	Anti-retro viral
7.	Dolutegravir, Lamivudine and Tenofovir Disoproxil Fumarate Tablets 50/300/300mg	Anti-retro viral
8.	Efavirenz Tablets USP 600 mg	Anti-retro viral
9.	Etoricoxib Tablets 30mg/60mg/90mg/120mg	Osteoarthritis and Rheumatoid arthritis
10.	Emtricitabine and Tenofovir Disoproxil Fumarate Tablets 200/300 mg	Anti-retro viral
11.	Emtricitabine and Tenofovir Disoproxil Tablets 200mg/245mg	Anti-retro viral
12.	Efavirenz, Lamivudine and Tenofovir Disoproxil Fumarate Tablets 600 / 300/ 300 mg	Anti-retro viral
13.	Esomeprazole Gastro Resistant Tablets 20mg & 40 mg	Proton pump inhibitor
14.	Finasteride Tablets USP 1 mg	Treatment of male pattern hair loss (Androgenetic alopecia)

S.No.	Name of the Product	Therapeutic Group
15.	Finasteride Tablets USP 5 mg	Treatment of symptomatic benign prostatic hyperplasia (BPH)
16.	Fenofibrate Tablets USP 48 mg and 145 mg	Anti-hyper cholesterol emic/ Hypertriglyceridemia (Lipid regulating agent)
17.	Hydralazine Hydrochloride Tablets USP 10 mg, 25 mg, 50 mg and 100 mg	Anti-hypertensive
18.	Imatinib Mesylate Tablets 100mg and 400mg	Anti-cancer drug
19.	Levocetirizine Dihydrochloride Tablets 5 mg	Anti-allergic
20.	Lamivudine Tablets 150 mg and 300 mg	Anti-retro viral
21.	Lamivudine, Zidovudine and Nevirapine Tablets 150/300/200 mg	Anti-retro viral
22.	Levetiracetam Tablets 250 mg, 500 mg, 750 mg and 1000 mg	Anti-Convulsant
23.	Lamivudine and Tenofovir Tablets 300 mg/ 300 mg	Anti-retro viral
24.	Lopinavir and Ritonavir Tablets USP 200 mg/ 50 mg & 100/25 mg	Anti-retro viral
25.	Methocarbamol Tablets USP 500 mg and 750 mg	Central nervous system depressant drug
26.	Nevirapine Tablets USP 200 mg	Anti-retro viral
27.	Nevirapine Prolonged-Release Tablets 400 mg	Anti-retro viral
28.	Raltegravir Tablets 400 mg	Anti-retro viral
29.	Roflumilast Tablets 250mcg, 500 mcg	Severe Chronic obstructive Pulmonary disease
30.	Ritonavir Tablets 100 mg	Anti-retro viral
31.	Simvastatin Tablets USP 5 mg, 10 mg, 20 mg, 40 mg and 80 mg	Anti-Hyperlipidemic drug
32.	Sofosbuvir Tablets 400mg	Chronic Hepatitis-C drug
33.	Sildenafil Tablets USP 20mg,25mg,50 mg and 100 mg	Treatment of Erectile Dysfunction
34.	Tadalafil tablets USP 2.5mg,5mg,10mg,20mg	Phosphodiesterase Type 5 inhibitor
35.	Tenofovir DF Tablets 300 mg	Anti-retro viral
36.	Tenofovir Disoproxil Tablets 245mg	Anti-retro viral
37.	Torsemide Tablets 5 mg, 10 mg, 20 mg and 100 mg	Diuretic
38.	Valaciclovir Tablets 500mg	Anti-viral

S.No.	Name of the Product	Therapeutic Group
39.	Zidovudine Tablets USP 300 mg	Anti-retro viral
40.	Zidovudine + Lamivudine Tablets USP 300 mg/150 mg	Anti-retro viral
41.	Atazanavir capsules 150mg,200mg and 300mg	Anti-retro viral
42.	Duloxetine Hydrochloride DR Capsules USP 20 mg, 30 mg, 40mg and 60 mg	Anti-depressant agent
43.	Dimethyl Fumarate Delayed - Release Capsules 120mg, 240mg	Used to treat relapsing forms of multiple sclerosis
44.	Esomeprazole Magnesium DR Capsules 20 mg and 40 mg	Proton pump inhibitor
45.	Indomethacin Capsules USP 25 mg and 50 mg	Anti-inflammatory drug
46.	Indomethacin ER Capsules USP 75 mg	Anti-inflammatory drug
47.	Lithium Carbonate Capsules USP 150 mg, 300 mg and 600 mg	Treatment of manic episodes of bipolar disorder
48.	Lansoprazole Delayed Release Pellets (9.2 %w/w of Lansoprazole), Capsules 15 mg and 30 mg	Anti-ulcerative
49.	Omeprazole Gastro-Resistant Capsules 10 mg, 20 mg and 40 mg (13.4% m/m Pellets)	Anti-ulcerative
50.	Oseltamivir Phosphate Capsules USP 30 mg 45 mg and 75	Anti-viral
51.	Pregabalin Capsules 25 mg, 50 mg, 75 mg, 100 mg, 150 mg, 200 mg, 225 mg and 300 mg	Anti-epileptic drug
52.	Silodosin Capsules 4mg, 8mg	For the treatment of the signs and symptoms of benign prostatic hyperplasia (BPH)
53.	Tolterodone Tartarate ER Capsules 2mg, 4mg	Anti-muscarinic agent
54.	Abacavir Oral Solution USP 20 mg/mL	Anti-retro viral
55.	Atovaquone Oral suspension USP 750mg/5mL	Anti-Protozoal drug
56.	Cetirizine Hydrochloride Oral Solution USP 1mg/mL	Anti-allergic
57.	Citalopram Hydrobromide Oral Solution 10 mg /5mL	Anti-depressant drug
58.	Clobazam Oral Suspension 2.5mg/mL	Anti-Convulsant
59.	Escitalopram Oxalate Oral Solution 5 mg/5mL	Anti-retro viral
60.	Lamivudine Oral Solution 10 mg/mL	Anti-retro viral
61.	Levetiracetam Oral Solution USP 100 mg/ml	Anti-Convulsant
62.	Levocetirizine Dihydrochloride oral Solution 2.5mg/5mL	Anti-allergic
63.	Zidovudine Oral solution USP 50 mg/5m.	Anti-retro viral

e) Most recent product quality reviews (PQRs) of the concerned WHO products:

Submitted:

1. Lamivudine Tablet 300mg
2. Lopinavir/Ritonavir Tablet 100mg/25mg
3. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg

Submitted and checked:

1. Darunavir (Ethanolate)/Ritonavir Tablet, Film-coated 400mg/50mg
2. Lamivudine Tablet, Film-coated 150mg
3. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg and Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg
4. Zidovudine Solution, Oral 50 mg/5ml
5. Lamivudine Solution, Oral 10mg/ml
6. Lamivudine/Zidovudine Tablet 150mg/300mg
7. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg
8. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg

Submitted and reviewed:

1. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg
2. Dolutegravir (Sodium) Tablet, Film-coated 50mg
3. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg
4. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg

f) Batch manufacturing and packaging records, including the analytical part, for the most recently released batch of relevant products:

Submitted:

1. Lamivudine Tablet, Film-coated 150mg
2. Lopinavir/Ritonavir Tablet 100mg/25mg
3. Lamivudine Solution, Oral 10mg/ml
4. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg
5. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg
6. Dolutegravir (Sodium) Tablet, Film-coated 50mg
7. Darunavir (Ethanolate)/Ritonavir Tablet, film-coated 400mg/50mg
8. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg
9. Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg

Submitted and reviewed:

10. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg
11. Zidovudine Solution, Oral 50mg/5ml
12. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg
13. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg
14. Lamivudine/Zidovudine Tablet 150mg/300mg

Note:

15. Lamivudine Tablet 300mg – *(not commercialized as per WHO dossier)*

16. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg *(not commercialized on 2018 onwards)*
17. Lopinavir/Ritonavir Tablet, Film-coated 100mg/25mg *(not commercialized as per WHO dossier)*
18. Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg *(not commercialized as per WHO dossier)*
19. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg *(not commercialized as per WHO dossier)*

g) Master batch manufacturing and packaging records of the products of interest:
Submitted:

1. Lamivudine Tablet 300mg
2. Lamivudine/Zidovudine Tablet 150mg/300mg
3. Lamivudine Tablet, Film-coated 150mg
4. Lopinavir/Ritonavir Tablet 100mg/25mg
5. Lamivudine Solution, Oral 10mg/ml
6. Dolutegravir (Sodium)/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 50mg/300mg/300mg
7. Lamivudine/Nevirapine/Zidovudine Tablet, Film-coated 150mg/200mg/300mg
8. Lamivudine/Tenofovir disoproxil fumarate Tablet 300mg/300mg
9. Zidovudine Solution, Oral 50mg/5ml
10. Lopinavir/Ritonavir Tablet, Film-coated 200mg/50mg
11. Emtricitabine/Tenofovir disoproxil fumarate Tablet, Film-coated 200mg/300mg
12. Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg
13. Efavirenz/Lamivudine/Tenofovir disoproxil fumarate Tablet, Film-coated 600mg/300mg/300mg
14. Lopinavir/Ritonavir Tablet, Film-coated 100mg/25mg
15. Dolutegravir (Sodium) Tablet, Film-coated 50mg
16. Dolutegravir (Sodium)/Lamivudine/Tenofovir Disoproxil Fumarate tablet, Film-coated 50mg/300mg/ 300mg
17. Darunavir (Ethanolate)/Ritonavir Tablet, Film-coated 400mg/50mg
18. Darunavir/Ritonavir Tablet, Film-coated 400mg/50mg
19. Darunavir/Ritonavir Tablet, Film-coated 800mg/100mg

h) If any of the products are sterile, the completed batch records for the most recent media fill validation that is relevant to the products of interest and report on its outcome:
N/A

i) Recalls in the past three years related to products with quality defects:

Complaint receipt date	Product Name / Batch Number	Reason for Recall / CAPA
09-09-2017	Levetiracetam oral solution 100 mg/ml / E170436	Found an inch screw in a bottle. CAPA: Metal detectors installed on liquid filling lines.
11-07-2017	Simvastatin Tablets 40 mg / E171280	Found a Metal piece (like razor blade) in a bottle. Metal contaminant from HDPE bottle supplier. CAPA implemented with cleaning of HDPE bottles.
16-06-2018	Indomethacin Capsules USP 50 mg / E180315	Some of the Capsules were deformed, clumped, misshaped, looks melted and stuck together. Reason was due to lower temperature. CAPA: temperature monitoring for capsule consignments.

22-08-2018	Fenofibrate Tablets, USP 145 mg / E181370	One foreign tablet found in Fenofibrate tablet bottle. CAPA: gowning procedure were strengthened with packaging line specific gowns were marked to avoid cross-contamination.

j) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the product) has been performed and all matters dealt with:
Declaration submitted: that a full self-inspection or external audit dedicated to the product) has been performed and all matters dealt with

k) **Copy of any warning letter, or equivalent regulatory action, issued by any authority to which the site provides or has applied to provide the product:**
Declaration submitted: no warning letters or equivalent regulatory actions issued

k) Out-of-stock situations:
Declaration submitted: no out-of-stock situations

l) Additional documents submitted:
N/A

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 ***Hetero Labs Ltd, Unit 3, Block-A, Block-B*** located at ***Survey No. 51, Plot No 22-110 IDA, Jeedimetla, Hyderabad, Telangana, 500 055 India*** is considered to be operating at an acceptable level of compliance with WHO GMP guidelines.

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

Part 6	List of guidelines referenced in this inspection report

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11. 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
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21. WHO general guidance on variations to multisource pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 10.
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