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 PUBLIC INSPECTION REPORT
(WHOPIR)
Desk Assessment of Active Pharmaceutical Ingredient (API) Manufacturer

Part 1	**General information**	
Company information		
Name of Manufacturer	**Sun Pharmaceutical Industries Limited**	
Corporate address of manufacturer	Sun Pharmaceutical Industries Limited Sun House, 201 B/1, Western Express Highway, Goregaon (East), Mumbai, 400063, India	
Name & address of manufacturing site		
Synthetic Unit/Block/Workshop		
Desk assessment details		
Date of review	18 – 21 May 2020	
APIs covered by this desk assessment	Atazanavir Sulphate	
List of documents submitted	1. A list of regulatory inspections performed in the last 5 years 2. A copy of the inspection report issued by German Regulatory Agency (in German language) 3. A copy of the response submitted to the queries raised by German Agency 4. EU GMP certificate dated 31 October 2016 5. A copy of Manufacturing License 6. Site Master File 7. List of API and related manufacturing premises 8. The recent product quality review (PQR) of the Atazanavir Sulfate 9. A signed declaration regarding self-inspection 10. Master batch manufacturing and packaging records for Atazanavir Sulfate Stage-1, Atazanavir Sulfate Stage-2 and Atazanavir Sulfate Stage-Final 11. Analytical reports for Atazanavir Sulfate Stage-1, Atazanavir Sulfate Stage-2 and Atazanavir Sulfate Stage-Final	
Part 2	**Summary of SRA/NRA inspection evidence considered (from most recent to last)**	
Landesamter fur Gesundheit and Soziales Berlin, Germany	Dates of inspection:	24 – 25 October, 2016
	Type of inspection:	GMP inspection
	Block/Unit/Workshop:	Not specified
	Type of APIs covered:	

US Food & Drugs administration	Dates of inspection:	30 April, 1 May and 3, 4 May 2018
	Type of inspection:	Surveillance GMP inspection
	Block/Unit/Workshop:	Plant 2 Plant 6
	Type of APIs covered:	Atorvastatin Calcium Trihydrate
Part 3	**Summary of the last WHO inspection**	
Date and conclusion of most recent WHO inspection	No on-site inspection performed by WHO.	
Abbreviations	**Meaning**	
CAPA	Corrective and preventive action	
GMP	Good manufacturing practices	
SOP	Standard operating procedure	

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

a) Manufacturing authorization and GMP certificate granted by the local authority:

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

c) List of all the APIs or other products (intermediates, dosage forms) manufactured on-site:

	Name of the API (Manufactured at Plant 2, packaging at block 05A)
1.	Acamprosate Calcium
2.	Amitriptyline Hydrochloride
3.	Apremilast
4.	Aripiprazole
5.	Armodafinil
6.	Asenapine Maleate
7.	Atazanavir Sulfate
8.	Buprenorphine Hydrochloride
9.	Cetirizine Hydrochloride
10.	Cinacalcet Hydrochloride
11.	Dapagliflozin
12.	Deferasirox
13.	Dimethyl Fumarate
14.	Esomeprazole Sodium
15.	Empagliflozin
16.	Fosphenytoin Sodium
17.	Dalfampridine
18.	Isotritinoin
19.	Ivacaftor
20.	Lacosamide
21.	Levocetirizine Dihydrochloride
22.	Methylphenidate Hydrochloride

23.	Mirtazapine
24.	Naltrexone Hydrochloride
25.	Ondansetron Base
26.	Ondansetron Hydrochloride Dihydrate
27.	Orlistat
28.	Rasagiline Mesylate
29.	Repaglinide
30.	Riluzole
31.	Risperidone
32.	Rosuvastatin Calcium
33.	Sitagliptin Phosphate
34.	Tamsulosin Hydrochloride
35.	Tiagabine Hydrochloride
36.	Topiramate
37.	Zonisamide Hydrochloride

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

Regulatory Agency	Inspection Date	Inspection Status
CDSCO & FDCA	April, 2015	GMP certificate received
	April, 2017	GMP certificate received
	March, 2019	GMP certificate received
USFDA	July, 2015	EIR Received
	April-May, 2018	EIR Received
EU-GMP (Berlin Authority)	October, 2016	GMP certificate received
Cofepris (Mexico)	June, 2015	GMP certificate received

e) Most recent product quality reviews (PQR) of the concerned WHO API:
Reviewed for Atazanavir Sulfate. Review period: Match 2018 – February 2019. No batches manufactured.

f) Batch manufacturing and packaging records, including the analytical part, for the most recently released batch of relevant API:
Reviewed for Atazanavir Sulfate Stage-1, Atazanavir Sulfate Stage-2 and Atazanavir Sulfate Stage-Final, analytical reports for Atazanavir Sulfate Stage-1, Atazanavir Sulfate Stage-2 and Atazanavir Sulfate Stage-Final.

g) Master batch manufacturing and packaging record(s) of the API(s) of interest:
Reviewed for Atazanavir Sulfate Stage-1, Atazanavir Sulfate Stage-2 and Atazanavir Sulfate Stage-Final.

h) Recalls in the past three years related to APIs with quality defects:
Not reported.

i) Confirmation by the senior quality assurance representative that a full self-inspection or external audit dedicated to the APIs has been performed and all matters dealt with:
Submitted.

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 APIs:
Not reported.

k) Out-of-stock situations:
Not reported.

l) Additional documents submitted:
PQR for PQR Atorvastatin Calcium Trihydrate

Part 5	Conclusion – Desk assessment outcome

Based 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 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 during this period is positive.

Part 6	List of guidelines referenced in this inspection report

1. 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 GMP for APIs or WHO TRS No. 957, Annex 2***
   http://apps.who.int/medicinedocs/documents/s20119en/s20119en.pdf

2. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO TRS No. 986, Annex 2***
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
   Short name: WHO TRS No. 970, Annex 2
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

4. 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
   http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. 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**
   http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

6. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
   Short name: WHO TRS No. 937, Annex 4
   http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

7. 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. 961, 957), Annex 1
   http://www.who.int/medicines/publications/44threport/en/

8. 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 2.
   Short name: WHO TRS No. 957, Annex 2
   http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile 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 6.
   Short name: WHO TRS No. 961, Annex 6
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
    Short name: WHO TRS No. 961, Annex 7
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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***
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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
    http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

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
    http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

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***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3.
Short name: WHO TRS No. 992, Annex 3
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. 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***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

20. WHO Recommendations for quality requirements when plant – derived artemisin 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
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
Short name: WHO GDRMP guidance or WHO TRS No. 996, Annex 5
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

22. 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.
Short name: WHO Multisource guidance or WHO TRS No. 996, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

23. 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
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf

24. 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-detail/978-92-4-000182-4

25. 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-detail/978-92-4-000182-4

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-detail/978-92-4-000182-4

27. 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/medicines/areas/quality_safety/quality_assurance/TRS1010annex9.pdf?ua=1