WHO Prequalification Programme
WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

SYMFI LO [1]

International Nonproprietary Name (INN):
Efavirenz/Lamivudine/Tenofovir Disoproxil Fumarate 400mg/300mg/300mg tablets

Abstract

SYMFI LO, manufactured at Mylan Laboratories Limited, Madhya Pradesh, India was submitted to be considered for prequalification in 2018 when the product was licensed / registered in the USA and subsequently accepted for the WHO list of prequalified products for the treatment of HIV/AIDS on 31 October 2018.

The "Procedure for prequalification of pharmaceutical products[2]"defines specific evaluation mechanisms for products approved by regulatory authorities, which apply similar stringent standards for quality, safety and efficacy as those required by WHO.

The prequalification of this product by the WHO Prequalification of Medicines Programme (PQP) is based on the approval by a stringent regulatory authority (SRA), namely the United States "Food and Drug Administration" (https://www.fda.gov) in line with the "Guidelines on submission of documentation for prequalification of finished pharmaceutical products approved by stringent regulatory authorities"[3].

Hence, no assessment of the data underlying this approval has been undertaken within the WHO Prequalification Programme. However, according to the SRA guideline WHO may request additional data when considered necessary for the safe use of the product in regions relevant for prequalified products and such information may be included in the WHOPAR as a separate piece of information. In order to safeguard product quality throughout its entire intended shelf-life, stability studies under the conditions defined for Climatic Zones IVb have been requested from the Applicant.

Based on the submitted stability data WHO PQTm considers the following storage condition appropriate for the product when distributed in regions with zone III, IVa and IVb climatic conditions, based on available stability information:

"Do not store above 30°C. Store in the original container. Protect from light.
The shelf-life at this storage condition is 24 months."

This WHOPAR refers to the information available at the approving stringent regulatory authority in terms of the assessment of the quality, efficacy and safety as well as steps taken after the prequalification
(https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/208255Orig1s000TOC.cfm).

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[1] Trade names are not prequalified by WHO. This is the National Medicines Regulatory Authority's (NMRA) responsibility. Throughout this WHOPAR the proprietary name is given as an example only.

[2] http://www.who.int/medicines/areas/quality_safety/quality_assurance/TRS961_Annex10.pdf

[3] http://apps.who.int/prequal/info_general/documents/TRS986/TRS986_ANNEX-5_SRA-Guide.pdf https://extranet.who.int/prequal/sites/default/files/documents/75%20SRA%20clarification_February2017_0.pdf

Parts 2a, 2b, 5 and 7 of the WHOPAR for SYMFI LO are included here.

SYMFI LO contains efavirenz/lamivudine/tenofovir disoproxil fumarate. Its WHO recommended use is for the treatment of HIV/AIDS.

The most frequent adverse events observed during treatment with efavirenz, lamivudine and tenofovir disoproxil were rash, diarrhoea, nausea, vomiting, dizziness, asthenia, and hypophosphataemia.
The most serious safety concerns with efavirenz, lamivudine and tenofovir disoproxil are related to the kidneys (e.g. renal impairment, renal failure and proximal renal tubulopathy), the psyche (e.g. suicide and neurosis) the liver (e.g. acute hepatitis, hepatic failure and hepatic steatosis), the skin (e.g. Stevens-Johnson syndrome), and the muscles and bones (e.g. rhabdomyolysis and osteomalacia).
Discontinuation of therapy with Efavirenz/Lamivudine/Tenofovir Disoproxil Fumarate 600 mg/300 mg/300 mg Tablets, in patients co-infected with HIV and HBV may be associated with severe acute exacerbations of hepatitis.

The efficacy and safety profile of efavirenz, lamivudine and tenofovir disoproxil is well established based on the extensive clinical experience in the treatment of HIV/AIDS.

Summary of Prequalification Status for SYMFI LO

	Initial Acceptance	
	Date	**Outcome**
Status on PQ list,	31 Oct 2018	listed
Dossier Evaluation	26 Oct 2018	MR

MR: meets requirements

The table represents the status of relevant completed activities only.