WHO Prequalification Programme
WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

Combivir 150 mg/300 mg film-coated tablets[1]

International Nonproprietary Name (INN):
Lamivudine/Zidovudine 150mg/300mg Tablets

Abstract

Combivir 150 mg/300 mg film-coated tablets, manufactured at Glaxo Operations UK Limited, UK, and GlaxoSmithKline Pharmaceuticals S.A., Poznań, Poland, was submitted to be considered for prequalification in 2001 when the product was licensed / registered in the European Union and subsequently accepted for the WHO list of prequalified products for the treatment of HIV/AIDS on 18 March 2002.

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 "European Medicines Agency" (EMA http://www.ema.europa.eu/ema/) 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.
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 (http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000190/human_med_000719.jsp&mid=WC0b01ac058001d124).

[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

WHOPAR part		**Reference**[4, 5]
Part 1	Summary for the Public	http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Summary_for_the_public/human/000190/WC500032324.pdf
Part 3	Package Leaflets	http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000190/WC500032326.pdf
Part 4	Summaries Product Characteristics	http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000190/WC500032326.pdf
Part 5	Labelling	http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000190/WC500032326.pdf
Part 6	Discussion	http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Scientific_Discussion/human/000190/WC500032320.pdf
Part 8	Steps taken following Autho-rization	http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Procedural_steps_taken_and_scientific_information_after_authorisation/human/000190/WC500032325.pdf

Parts 2a, 2b and 7 of the WHOPAR for Combivir 150 mg/300 mg film-coated tablets are included here.

Combivir 150 mg/300 mg film-coated tablets contains lamivudine and zidovudine.
Its WHO recommended use is for the treatment of HIV/AIDS in combination with other antiretroviral products.

The most frequent adverse reactions observed during treatment with lamivudine and zidovudine are headache , nausea, vomiting, diarrhoea, abdominal pain, dizziness, hair-loss, fatigue, muscle pain, anaemia, leucopenia, neutropenia and transient elevation of liver enzymes and of bilirubin.
The most serious adverse reactions of lamivudine and zidovudine are are related to zidovudine: The most serious adverse reactions of zidovudine are severe lactic acidosis and hepatic steatosis with hepatic failure, which can be fatal.
In patients with chronic hepatitis B infection discontinuation of lamivudine therapy can lead to hepatic deterioration and hepatitis flare.

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

[4] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/epar_search.jsp&mid=WC0b01ac058001d125
[5] http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/000190/human_med_000719.jsp&mid=WC0b01ac058001d124

Summary of Prequalification Status for Combivir 150 mg/300 mg film-coated tablets

	Initial Acceptance		**Requalification**	
	Date	**Outcome**	**Date**	**Outcome**
Status on PQ list,	18 March 2002	listed	27 Nov 2017	listed
Dossier Evaluation	06 Sept 2001	MR	08 Nov 2017	requalified

MR: meets requirements

The table represents the status of relevant completed activities only.