WHO Prequalification Programme
WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

Ziagen 20 mg/ml oral solution[1]

International Nonproprietary Name (INN):
Abacavir (as sulfate) 20 mg/mL oral solution

Abstract

Ziagen 20 mg/ml oral solution, manufactured at GlaxoSmithKline Inc 7333 Mississauga Road North Mississauga Ontario, Canada, 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 20 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.
After first opening the container: 2 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.ema.europa.eu/en/medicines/human/EPAR/ziagen).

[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]
Part 1	Summary for the Public	https://www.ema.europa.eu/documents/overview/ziagen-epar-summary-public_en.pdf
Part 3	Package Leaflets	https://www.ema.europa.eu/documents/product-information/ziagen-epar-product-information_en.pdf
Part 4	Summaries Product Characteristics	https://www.ema.europa.eu/documents/product-information/ziagen-epar-product-information_en.pdf
Part 5	Labelling	https://www.ema.europa.eu/documents/product-information/ziagen-epar-product-information_en.pdf
Part 6	Discussion	https://www.ema.europa.eu/documents/scientific-discussion/ziagen-epar-scientific-discussion_en.pdf
Part 8	Steps taken following Authorization	https://www.ema.europa.eu/documents/procedural-steps-after/ziagen-epar-procedural-steps-taken-scientific-information-after-authorisation_en.pdf

Parts 2a, 2b and 7 of the WHOPAR for Ziagen 20 mg/ml oral solution are included here.

Ziagen 20 mg/ml oral solution contains the nucleoside reverse transcriptase inhibitors (NRTI) abacavir (as sulfate). Its WHO recommended use is for the treatment of HIV/AIDS in combination with other antiretroviral products.
The most frequent adverse events observed during treatment with abacavir were skin rash (without any other illness), nausea, vomiting, diarrhoea, abdominal pain, headache, high temperature, lethargy, fatigue and loss of appetite.

The most serious safety concern is a hypersensitivity reaction to abacavir. About 5 % of the patients treated with abacavir develop this reaction. People with a gene called HLA-B*5701 are more likely to get a hypersensitivity reaction to abacavir. Therefore, screening for carriage of the HLA-B*5701 allele is recommended in any HIV-infected patient without prior exposure to abacavir. Screening is also recommended prior to re-initiation of abacavir in patients of unknown HLA-B*5701 status who have previously tolerated abacavir.

The most common symptoms of this hypersensitivity reaction are high temperature (fever) and skin rash. Other frequently observed signs or symptoms include nausea, vomiting, diarrhoea, abdominal pain and severe tiredness. Other symptoms may include joint or muscle pain, swelling of the neck, shortness of breath, sore throat, cough and headache. Occasionally, inflammation of the eye (conjunctivitis), mouth ulcers or low blood pressure may occur.
The symptoms of this allergic reaction can occur at any time during treatment with abacavir. However they usually occur in the first six weeks of treatment. The symptoms worsen with continued treatment and may be life-threatening or even fatal if treatment is continued.

[4] https://www.ema.europa.eu/en/medicines/human/EPAR/ziagen

There is also an **Alert Card** included in each Ziagen 20 mg/ml oral solution, pack to remind the patients´ caregivers and medical staff about abacavir hypersensitivity. The patient should keep this card with him/her at all times.

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

Summary of Prequalification Status for Ziagen 20 mg/ml oral solution

	Initial Acceptance		**Requalification**	
	Date	**Outcome**	**Date**	**Outcome**
Status on PQ list	20 March 2002	listed	27 June 2019	listed
Dossier Evaluation	06 Sept 2001	MR	27 June 2019	requalified

MR: meets requirements

The table represents the status of relevant completed activities only.