WHO Prequalification Programme
WHO PUBLIC ASSESSMENT REPORT (WHOPAR)

Notezine[1]

International Nonproprietary Name (INN):
Diethylcarbamazine (as citrate) 100mg Tablet

Abstract

Notezine, manufactured at Sanofi-Aventis France was submitted to be considered for prequalification in 2011 when the product was licensed / registered in at least one of the ICH regions and subsequently accepted for the WHO list of prequalified products for the large scale preventative chemotherapy interventions for the control of lymphatic filariasis on 06 September 2016.

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.

Notezine contain diethylcarbamazine citrate, a synthetic piperazine derivative with an antihelmintic action. It has the potential to interrupt the parasitic life cycle by destruction of microfilariae which are essential for host to vector transmission of the parasite. There is evidence to suggest that diethylcarbamazine is also macrofilaricidal.
Studies of mass drug administration (MDA) in adults and in children over 2 years of age have shown that diethylcarbamazine citrate, in combination with albendazole, reduced microfilaraemia in endemic populations when administered as a single-dose, once-yearly treatment.
Efficacy and safety of diethylcarbamazine citrate in combination with albendazole in MDA programmes have been shown in a number of clinical studies in different geographical regions, leading to the inclusion of this regimen in the recommendations of the WHO Global Programme to Eliminate Lymphatic Filariasis.
(http://www.who.int/lymphatic_filariasis/elimination-programme/en/)
Note: in the Summary of Product Characteristics, included in this WHOPAR, the posology is expressed in terms of base (3 mg/kg) equivalent to 6 mg/kg in terms of citrate.
For safety reasons diethylcarbamazine citrate must only be used in areas where onchocerciasis is not co-endemic.

In the absence of circulating microfilaraemia, the administration of diethylcarbamazine citrate, when given at the recommended dosage, may cause nausea, vomiting, abdominal pain, diarrhoea, loss of appetite, muscle pain, dizziness, drowsiness, fatigue and headache.

In patients with circulating microfilaraemia adverse reactions may be more common and severe, particularly in patients with a high parasite burden. These are considered allergic reactions due to antigen-antibody reaction caused by dead microfilariae or adult filarial worms. The intensity and the severity of adverse reactions are usually associated with the level of microfilariaemia in the blood prior to treatment.

[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://apps.who.int/prequal/info_general/documents/TRS961/TRS961_Annex10.pdf

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 French "National Agency for the Safety of Medicine and Health Products" (http://www.ansm.sante.fr), 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.

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 package in order to protect from moisture.
The shelf-life at this storage condition is 36 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://agence-prd.ansm.sante.fr/php/ecodex/index.php#result)
The English language version of the Patient Information Leaflet, the Summary of Product Characteristics and the labelling, as certified to be French authorities approved texts, are included in this WHOPAR.

Parts 2a, 2b, 3, 4, 5 and 7 of the WHOPAR for Notezine are included here.

Summary of Prequalification Status for Notezine

	Initial Acceptance			
	Date	**Outcome**	**Date**	**Outcome**
Status on PQ list, i.e. date of listing	06 Sept 2016	listed		
Dossier Evaluation	12 Aug 2016	MR		

MR: meets requirements

The table represents the status of relevant completed activities only.

[3] http://apps.who.int/prequal/info_general/documents/TRS986/TRS986_ANNEX-5_SRA-Guide.pdf