



The Secretary of the WHO Expert Committee on the
Selection and Use of Essential Medicines
Policy, Access and Rational Use
Department of Medicines Policy and Standards
World Health Organization (WHO)
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By email: emlsecretariat@who.int

To whom it may concern:

We are happy to endorse DNDi's application for inclusion of NECT, the co-administration of oral nifurtimox with intravenous eflornithine, for the treatment of stage 2 *T. b. gambiense* sleeping sickness into the WHO Model List of Essential Medicines.

NECT represents a significant improvement over current therapy. At present, patients with stage 2 *T. b. gambiense* infection are treated either with melarsoprol, a toxic organoarsenical drug, or with eflornithine. Eflornithine monotherapy is safer than melarsoprol, but it requires 2 weeks of 4 daily intravenous infusions, which is logistically difficult in the resource-poor settings where sleeping sickness is treated. The NECT regimen reduces the number of infusions and the duration of therapy, so it is less burdensome for patients and health care workers. It also is more cost-effective.

The safety and efficacy data that support the use of NECT were collected in a multicenter clinical trial that conformed to the highest international standards and included remarkably complete patient follow-up. The NECT regimen was well-tolerated, with low mortality and fewer serious adverse events than eflornithine monotherapy. The efficacy of NECT was convincingly shown to be noninferior to the standard eflornithine schedule, and the data actually suggest that it may be more effective.

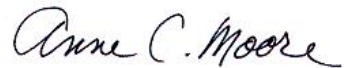
The use of combination therapy might offer some protection against the development of drug resistance. The emergence of resistance to the available anti-trypanosomal drugs is a serious concern because of the limited number of drugs, the 100% case-fatality rate of untreated infection, and the important role of treatment in the control strategies for *T. b. gambiense*. Melarsoprol-refractory *T. b. gambiense* has been reported by various sleeping sickness programs in Sudan and Uganda.

Since 2002, the WHO Collaborating Center for African Trypanosomiasis at CDC has worked with country programs to conduct longitudinal surveillance for sleeping sickness treatment failure at 9 sentinel sites. We have documented melarsoprol treatment failure rates of 45% or higher at 3 sites within Angola and the Democratic Republic of Congo. Currently, most patients who fail melarsoprol can be cured with eflornithine monotherapy. However, eflornithine administered as monotherapy may be particularly vulnerable to the eventual development of resistance because of the drug's short half-life, mode of action (trypanostatic rather than trypanocidal), complex administration, and questionable efficacy in patients co-infected with HIV. Eflornithine is the last effective drug in our

arsenal for stage 2 *T. b. gambiense* infection. Protecting it by use in combination therapy is a high priority for all of us working on sleeping sickness treatment and control.

We urge the WHO's Expert Committee on the Selection and Use of Essential Medicines to adopt NECT into the WHO Model List of Essential Medicines. Its use will have an immediate impact and also may help protect our existing drugs for the future.

Yours sincerely,

A handwritten signature in cursive script that reads "Anne C. Moore".

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Director, WHO Collaborating Center for African Trypanosomiasis Treatment Failure
and Drug Resistance