

Clinical study comparing the nifurtimox-eflornithine combination with the standard eflornithine regimen for the treatment of *Trypanosoma brucei gambiense* human African trypanosomiasis in the meningo-encephalitic phase

The study of the use of the combination of eflornithine administered IV two times a day for seven days plus nifurtimox administered orally three times a day for ten days compared with eflornithine alone administered 4 times a day for 14 days conducted by MSF and DNDi is highly welcome. TDR is conducting a similar study in Uganda (109 patients). The results will be available after the completion of the 18 month follow up (mid 2009). However, the preliminary in-hospital safety data from the TDR study (until day 18 or 22) seem to be consistent with the safety data that DNDi has provided.

The clinical review document provided by DNDi in the website supporting the use of the eflornithine-nifurtimox combination is very encouraging. There is a clear benefit for the patients and the health systems with halving both the number of daily infusions and total treatment duration with eflornithine. This in spite of the fact that the value of adding nifurtimox has not been fully substantiated by neither of these studies - as there was no control arm with eflornithine alone twice daily for 7 days, which was considered ethically not acceptable.

Based on what we know from the use of nifurtimox for Chagas disease, rare adverse events (some of them serious) have been described. Most of these are neurological and some would be difficult to distinguish from the African trypanosomiasis meningo-encephalitic phase symptoms. Fortunately, we did not observe any of these serious events during the studies, but the sample size may not be enough to detect rare events. It would therefore be highly advisable for the product sponsor(s) to develop a risk management and pharmacovigilance plan to monitor and minimize the potential negative safety aspects. An implementation research programme should also be considered to bring the product to full scale use.