19th Expert Committee on the Selection and Use of Essential Medicines
April 8-12 2013

Expert peer review on Nifurtimox-Eflornithine (NECT) combination addition in EMLc

1. Assessment of efficacy
   a. Have all relevant studies on efficacy been included
      Yes
   b. Summarize the data on efficacy, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      NECT or eflornithine monotherapy provide cure or favorable evolution rates of over 94% in both adults and children after 18 to 24 months evaluation.
      NECT combination therapy was placed on the WHO EML for adults in the 16th edition, but
      Eflornithine monotherapy continues to be the official treatment of choice for children because of no comparative test trials in children.
      WHO pharmacovigilance database, MSF cohort studies and DNDi clinical trials involving a total of more than 500 children below 15 years of age show that effectiveness of NECT is not inferior to eflornithine therapy.
   c. Please provide any additional relevant information with reference
      None

2. Assessment of safety
   a. Have all relevant studies on safety been included
      Yes
   b. Summarize the data on safety, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      Both adults and children develop significant adverse effects with use of NECT (up to 86% in some studies) but children fewer and less AEs than adults (Up to 4 times more Alirol et al, MSF)
      The WHO pharmacovigilance study 9 out of 1735 died (fatality of 0.52 %), none was in children, though children may show an annual rate of relapse which is higher than adults.
   c. Please provide any additional relevant information with reference
      None

3. Assessment of cost and availability
   a. Have all relevant data on cost and cost effectiveness been provided?
      Yes
   b. Summarize the data on cost and cost effectiveness, in comparison to what is listed in EML where applicable (limit to 2 to 3 sentences)
      Medicines are supplied free at site through donation organized by the WHO. By using lesser infusion fluids and equipment, lesser staff burden and shorter duration of hospital stay than eflornithine alone, NECT can be deduced to be more cost effective than the current eflornithine monotherapy. In fact the treatment actually arrives at destination at about half the cost of eflornithine alone.
   c. Please provide any additional relevant information with reference
      The increased number of expected patients will actually increase the overall cost to the WHO
   d. Is the product available in several low and middle income countries?
      Yes, thanks to the effort of the WHO.
      The disease exits only in these under-developed countries.
4. Assessment of public health need
a. Please provide the public health need for this product (1-2 sentences)
The tsetse fly, that transmits this disease, exits in 36 countries of Sub-Saharan Africa, representing an enormous population potentially at risk. The DNDi Geneva estimates that the population of children in about 14 countries classed as very high or high risk at about 1.2million.

b. Do guidelines (especially WHO guidelines) recommend this product? If yes, which ones? List 1 or 2 international preferable
The WHO guidelines already in its 16th edition of EML already recommend the product for adults. The WHO guidelines already use both medicines for children separately in the treatment of HAT (eflornithine) and Chaga’s disease (Nifurtimox).

5. Are there special requirements for use or training needed for safe/effective use?
If yes, please provide details in 1-2 sentences
Personnel in treatment centers, which are usually enclave and rural areas, have to be trained in placing IV catheters, calculating doses and managing adverse effects of medicines. This is not necessarily more than it is already being done with administering eflornithine alone.

6. Is the proposed product registered by a stringent regulatory authority?
Yes

7. Any other comments
None

8. What is your recommendation to the committee (please provide the rationale)
I recommend that Nifurtimox +Eflorthinine combination (NECT) be included in the in the 4th WHO model list of Essential medicines for children (EMLc) as first line treatment for second stage T. B Gambiense HAT.
The non-inclusion of this combination when it was granted for adult treatment was because of safety concerns. Even though there have been no randomized control studies in children since then, clinical field trial studies (DNDi), cohort studies (MSF) and pharmacovigilance studies have all shown that the effectiveness is comparable in both adults and children, the occurrence of major adverse effects including fatalities are less in children. NECT therapy is more cost –effective than the present eflornithine monotherapy recommended now and would attract more compliance because of simplification of administering.
All the organizations and NGOs involved in the treatment of T. b. gambiense HAT are of this opinion and many are already doing it even without specific WHO guidelines.