Nifurtimox

Essential medicine status

Section: 6. Anti-infective medicines > 6.5. Antiprotozoal medicines > 6.5.5. Antitrypanosomal medicines > 6.5.5.1. African trypanosomiasis > 6.5.5.1.2. Medicines for the treatment of 2nd stage African trypanosomiasis

EMLc | ATC codes: P01CC01

Indication	African trypanosomiasis ICD11 code: 1F51
INN	Nifurtimox
Medicine type	Chemical agent
List type	Core
Additional notes	Only to be used in combination with eflornithine, for the treatment of Trypanosoma brucei gambiense infection.
Formulations	Oral > Solid: 120 mg
EML status history	First added in 2009 (TRS 958) Changed in 2013 (TRS 985)
Sex	All
Age	Also recommended for children
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Patents have expired in most jurisdictions Read more about patents.
Wikipedia	Nifurtimox
DrugBank	Nifurtimox

Summary of evidence and Expert Committee recommendations

An application for the addition of nifurtimox tablets to the EMLc was submitted by the Drugs for Neglected Diseases initiative (DNDi), Geneva, Switzerland. Human African trypanosomiasis is transmitted by tsetse flies which are present in 36 sub-Saharan African countries. Of those, 13 countries have reported cases of sleeping sickness since 2000, with a declining trend. Treatment strategies have played a major role in this decline. Children account for approximately 25% of the total cases reported. Nifurtimox–eflornithine combination therapy (NECT) is as effective as eflornithine alone for treating second-stage African trypanosomiasis but also has safety advantages and is easier to administer (infusion every 12 hours for 7 days versus every 6 hours for 14 days). Both are listed in the EML. Data from the seven most affected countries show that 59% of adult patients were treated with the combination in 2010 (1) and 86% in 2011. Listing of both medicines in the EML has helped to scale up access to NECT. Eflornithine is already listed in the EMLc for second-stage African trypanosomiasis. Nifurtimox is listed in the EMLc only for American trypanosomiasis, but is listed for both American and African trypanosomiasis in the EML. Additional data are now available on children and hence this application was submitted to include nifurtimox in the EMLc to facilitate the combination therapy for sleeping sickness. There are no randomized controlled trials to assess the combination of nifurtimox and eflornithine specifically in children. A clinical trial (multicentre, open-label, phase IIIb) to assess NECT in field conditions was conducted in six sites in the Democratic Republic of the Congo. Of a total of 629 patients included in the trial, 100 were children below 12 years of age, 14 were pregnant women and 33 were breastfeeding mothers. Ninety-eight percent of the 629 patients were alive and well on discharge (2). With 24-month follow-up, similar cure rates were shown in children and adults, with close to 89% alive and well. A cohort study of patients from Médecins sans Frontières (MSF) treatment centres, including 120 children, also showed good results (3). Adverse reactions were common (60–90%) but severe events were relatively rare. A pharmacovigilance study of NECT reported adverse effects, the commonest being vomiting/nausea and abdominal pain followed by headache, musculoskeletal pains and vertigo.

Adverse events in children were similar to those in adults but the major adverse events were less frequent (4). Both NECT and eflornithine monotherapy have similar health-system requirements, such as the need for intravenous infusion in a hospital setting. Nifurtimox is supplied free of charge according to an agreement with WHO and, in practice, it is less costly to procure the combination than the individual components. Considering the public health need for this combination in the affected countries and the data on effectiveness and safety particularly in children, the Expert Committee recommended that nifurtimox be added to the EMLc. It was noted that this would also help countries to scale up treatment programmes for Trypanosoma brucei gambiense second-stage infection.

1. Simarro PP, Franco J, Diarra A, Postigo JA, Jannin J. Update on field use of the available drugs for the chemotherapy of human African trypanosomiasis. Parasitology. 2012;139(7):842-6. http://dx.doi.org/10.1017/S0031182012000169 PMID:22309684 2. Schmid C, Kuemmerle A, Blum J, Ghabri S, Kande V, Mutombo W, et al. In-hospital safety in field conditions of nifurtimox eflornithine combination therapy (NECT) for T. b. gambiense sleeping sickness. PLoS Negl Trop Dis. 2012;6(11):e1920. http://dx.doi.org/10.1371/journal.pntd.0001920 PMID:23209861 3. Alirol E, Schrumpf D, Amici Heradi J, Riedel A, de Patoul C, Quere M, et al. Nifurtimox-eflornithine combination therapy for second-stage gambiense human African trypanosomiasis: Medecins Sans Frontieres experience in the Democratic Republic of the Congo. Clin Infect Dis. 2013;56(2):195-203. http://dx.doi.org/10.1093/cid/cis886 PMID:23074318 4. Franco J, Simarro P, Diarra A, Ruiz-Postigo J, Samo M, Jannin J. Monitoring the use of nifurtimox-eflornithine combination therapy (NECT) in the treatment of second stage gambiense human African trypanosomiasis. Res Rep Trop Med. 2012;3:93-101. http://dx.doi.org/10.2147/RRTM.S34399