# APPLICATION FOR REVISION OF ANTITRYPANOSOMAL MEDICINES IN WHO MODEL LIST OF ESSENTIAL MEDICINES

The objective of this application is to assure consistency among the antitrypanosomal medicines in the WHO Model list of essential drugs according to their safety and their use in the endemic areas. Therefore, the proposal is to modify the antitrypanosomal section.

There are 2 main parts in this application. The first part deals with the treatment of first stage of Human African Trypanosomiasis (HAT) while the second part deals with the second stage.

In the present Essential drugs list, treatments for HAT are defined as follows:

**Core list**: melarsoprol and suramin
**Complementary list**: eflornithine and pentamidine

## Human African Trypanosomiasis

HAT is transmitted through the bite of tsetse flies. In infected people, the trypanosomes multiply in the blood and lymph glands, it is call first stage or hemolymphatic stage. Later crossing the blood-brain barrier to invade the central nervous system where they provoke major neurological disorders. It is the second stage or so call menigoencephalic stage.

HAT takes two forms, depending on the protozoal parasite involved:

- *Trypanosoma brucei gambiense* (T.b.g.) is found in west and central Africa. This form represents more than 90% of reported cases of sleeping sickness and causes a chronic infection. A person can be infected for months or even years without major signs or symptoms of the disease. When the diagnosis is set up, the patient is often already in an advanced disease stage when the central nervous system is affected.
- *Trypanosoma brucei rhodesiense* (T.b.r.) is found in eastern and southern Africa. This form represents less than 10% of reported cases and causes an acute infection. First signs and symptoms are observed a few months or weeks after infection. The disease develops rapidly and invades the central nervous system.

## 1. Therapy for the first stage of HAT

### 1.1.) Summary statement

Treatment of the first stage is based on pentamidine and suramin. Other drugs as eflornithine or melarsoprol, although effective in the first stage, due to their side effects and their complexity of administration, are not used for the treatment of this stage. They are kept for the treatments of the second stage.

**Pentamidine**

Pentamidine is a positively charged aromatic diamidine introduced in 1937. It is the treatment of choice for the first stage of *T. b. gambiense* infections.

Dosage is 4 mg/kg/day given by intramuscular injection for seven consecutive days.

Pentamidine is concentrated in the cytoplasm of the trypanosome by active transport, and some strains become resistant by suppressing this transport mechanism[1]. Since it produces variable results for *T. b. rhodesiense*[2], this drug is only used for *T. b. gambiense.*

**Suramin**

Suramin is a negatively charged, high-molecular-weight sulfated naphthylamine. Its first used against sleeping sickness was in 1922 It is the preferred treatment for the first stage of *T. b. rhodesiense* infections. Treatment is long in a series of five IV injections at 5–7-day intervals.

## 1.2.) WHO Focal Point for this application.

Dr Pere P. Simarro
Sleeping sickness surveillance and control programme
Innovative and Intensified Disease Management
Neglected Tropical Diseases
World Health Organization
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## 1.3.) Organization supporting the application

- Innovative and Intensified Disease Management
  Neglected Tropical Diseases
  World Health Organization
  Geneva
  Switzerland
- Médecins Sans Frontières
  8, rue Saint Sabin
  75011 Paris

## 1.4.) International Nonproprietary Names (INNs) of medicines included in application.

Pentamidine
Suramine

## 1.5.) Formulations

**Pentamidine** is available in two forms:

- • vials containing 300 mg of pentamidine isethionate (Pentacarinat®) for conditions other than sleeping sickness;
- • vials containing 200 mg of pentamidine isethionate, in the form of powder specifically formulated for sleeping sickness treatment and donated to WHO for distribution free of charge for the treatment of sleeping sickness.

**Suramin** (Germanine®) is available in vials containing 1 g of active compound in the form of powder that is solved in distilled water as a 10% solution immediately prior to injection.

## 1.6.) International availability

Pentamidine is produced and donated by: sanofi-aventis. Suramin is produced and donated by Bayer HealthCare. The drugs are available.
Thanks to an agreement signed by WHO and sanofi-aventis in 2006, the donation and the availability of pentamidine free of charge for endemic countries is guaranteed until 2011.
Thanks to an agreement signed by WHO and Bayer HealthCare in 2001, the donation and the availability of suramin was guaranteed the last five years. A new agreement is planned to be signed in 2007 which will guarantee the availability of suramin free of charge for endemic countries until 2012
Drugs are produced by companies according WHO forecast and shipped to the different users: National Control Programmes, NGOs according their requests.

## 1.7.) Whether application is requested for an individual medicine or therapeutic group.

These drugs are individual medicines.

## 1.8.) Public Health Relevance

**Incidence**
In 2005, 15651 cases of T.b.g. and 727 cases of T.b.r were reported.
36 sub-Saharan African countries are endemic and about 60 millions of persons are considered at risk.
**Prevalence**
The total prevalence of HAT is estimated around 50 to 70,000 persons infected of whom more than 95% are infected by T.b.g.
The rate of disease stage among T.b.g. form treated patients shows is around 50%. This distribution is unknown for T.b.r patients although it is estimated to be the same.

## 1.9.) Treatment details

### 1.9.1. Dosage and duration

**Pentamidine**

Dosage is 4 mg/kg/day given by intramuscular injection for seven consecutive days.

**Suramin**

The recommended dosage is 20 mg/kg/day with a maximum dose of 1 g per injection. The drug is administered intravenously at the rate of one injection per week. The treatment course is 5 weeks for a total of five injections. A test dose of 4-5 mg/kg/ the first day is recommended.

### 1.9.2. Need for special diagnostic or treatment facilities and skills

**Diagnostic**

Both treatments require the same skills for diagnostic.
The usual procedure is to perform a screening test (Card Agglutination Trypanosomiasis Test) and a clinical examination. In case of suspicion (serological or clinical), confirmation must be established with the direct examination of the parasite in the blood, in the lymph nodes or in the cerebrospinal fluid (CSF). Staging is realized with the examination of the CSF (white blood cells count and research of the parasite).

**Treatments**

Both treatments require the same facilities and skills. Suramin treatment, as it is intravenous and longer and discontinuous, requires a more complex management.

## 1.10.) Summary of comparative effectiveness in a variety of clinical settings

**Pentamidine**

Resistance to pentamidine has been induced in laboratory models and also been found in the field but without significant consequence on the treatments for T.b.g[3].

**Suramin**

Suramin is the treatment of choice for *T,b,r* and trypanosomal resistance to suramin has not been a serious problem after 80 years of use in the treatment of HATt.

## 1.11.) Summary of comparative evidence on safety

**Pentamidine**
Pentamidine is usually well tolerated, with hypotension and hypoglycemia as the most important reported side-effects[4]. Nausea and/or vomiting, local reactions at the site of injection include pain, pruritus, rash, tachycardia, are also seen., Hypocalcemia and abnormal findings in liver function have also been reported[3,5].

**Suramin**
Severe side-effects have often been reported, including anaphylactic shocks, severe cutaneous reactions, neurotoxic signs, and cases of renal failure which is the most common problem of suramin monotherapy, although it is usually mild. Polyneuropathy

and stomatitis have also been described. A test dose of 4-5 mg/kg body is recommended to prevent idiosyncratic reactions[3,4,5].

### 1.12.) Summary of available data on comparative cost and cost-effectiveness within the pharmacological class or therapeutic group:

Both drugs are donated to WHO for free distribution by the pharmaceutical companies:

- Pentamidine, is donated by sanofi-aventis
- Suramin is donated by Bayer HealthCare

### 1.13.) Regulatory Status

Pentamidine is used in National treatment policies in T.b.g. endemic countries as treatment for first stage

Suramin is used in National treatment policies in T.b.r. endemic countries as treatment for first stage.

As WHO receives the orders for the different HAT drugs, and provides green light for distribution, it is possible to know how many vials have been ordered and where.

Between 2001 and 2006, 333,064 pentamidine vials and 6,697 suramin vials have been sent to 24 endemic countries. Considering that the treatment is 7 vials of pentamidine or 5 vials of suramin for a 50 kg patient, this amount would correspond to around 48,500 pentamidine treatments and 1,340 suramin treatments.

The Table 1 summarizes the orders of pentamidine and suramin per countries between 2001 and 2006:

**Table 1 Orders of pentamidine and suramin per endemic countries between 2001 and 2006**

| | Vials | | Treatments | |
|---|---|---|---|---|
| **Countries in Africa currently been supplied.** | **Pentamidine** | **Suramin** | **Pentamidine** | **Suramin** |
| Angola | 20,900 | 0 | 2,986 | 0 |
| Benin | 1,050 | 0 | 150 | 0 |
| Burkina-Faso | 120 | 0 | 17 | 0 |
| Cameroon | 660 | 5 | 94 | 1 |
| Central African Republic | 13,200 | 0 | 1,886 | 0 |
| Chad | 15,500 | 0 | 2,214 | 0 |
| Congo Brazzaville | 29,190 | 0 | 4,170 | 0 |
| Cote d'Ivoire | 860 | 0 | 123 | 0 |
| Democratic Republic of Congo | 181,600 | 0 | 25,942 | 0 |
| Equatorial Guinea | 810 | 0 | 116 | 0 |
| Gabon | 1300 | 0 | 186 | 0 |
| Gambia | 7 | 0 | 0 | 0 |
| Ghana | 140 | 60 | 20 | 12 |
| Guinea | 1540 | 0 | 220 | 0 |
| Kenya | 17 | 60 | 2 | 12 |
| Liberia | 0 | 0 | 0 | 0 |
| Malawi | 0 | 1400 | 0 | 280 |
| Mozambique | 0 | 142 | 0 | 29 |
| Nigeria | 300 | 0 | 43 | 0 |
| Rwanda | 0 | 0 | 0 | 0 |
| South-Africa | 0 | 0 | 0 | 0 |
| Sudan | 52,950 | 200 | 7,564 | 40 |
| Tanzania | 0 | 2780 | 0 | 556 |
| Togo | 0 | 0 | 0 | 0 |
| Uganda | 12,170 | 1825 | 1,738 | 365 |
| Yaoundé | 750 | 0 | 0 | 0 |
| Zambia | 0 | 200 | 0 | 40 |
| Zimbabwe | 0 | 30 | 0 | 6 |
| Total | **333,064** | **6,697** | **47,477** | **1341** |

### 1.14.) Pharmacopoeial Standards

Both pentamidine and suramin are part of the essential drugs list but pentamidine, which the most commonly used drug as Table 1 shows, appears in the complementary list.

### 1.15.) Proposed text for WHO Model Formulary.

It is proposed to place the pentamidine in the core list of the WHO essential drugs list.

# 2. Therapy for the second stage of HAT

## 2.1.) Summary statement

Drugs used for the first stage of the disease (pentamidine and suramin) cannot be used in the second stage once the parasites have invaded the central nervous system because these drug does not cross the blood–brain barrier. The available drugs for the treatment of the second stage are

- Melarsoprol
- Eflornithine

**Melarsoprol**

Developed in 1949, Melarsoprol (Arsobal ®) has been for many years the only drug used for the treatment of second stage of HAT. Melarsoprol is an organo-arsenical drug. Several protocols have been developed in an attempt to curb the severe adverse reactions: myocardial damage, hypertension and exfoliative dermatitis and the most serious side-effect: reactive encephalopathy, which occurs in 5–10% of patients treated with melarsoprol with a case fatality ratio (CFR) around 50%[6, 7, 8].

Resistance to melarsoprol has been documented since the 1970s[9, 10, 11].

**Eflornithine**

Eflornithine (difluoromethylornithine [DFMO]), (Ornidyl®) an inhibitor of ornithine decarboxylase originally developed as an anticancer agent in the 1980s, was registered (1990) for the treatment of HAT T.b.g second stage. Different open studies showed its efficacy (studies against placebo were impossible due to ethics) [12, 13, 14, 15, 16, 17, 18]. This drug was initially unavailable due to production problems and high pricing. It is now used for the treatment of *T.b.g*. in several countries where it showed its efficacy and appeared safer than melarsoprol [42] (less side effects and a CFR inferior: 1.7 to 3%).

Resistance to eflornithine has not yet been reported.

## 2.2.) WHO Focal Point for this application.

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Neglected Tropical Diseases
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## 2.3.) Organization supporting the application

- Innovative and Intensified Disease Management
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  World Health Organization
  Geneva
  Switzerland

- Médecins Sans Frontières
  8, rue Saint Sabin
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### 2.4.) International Nonproprietary Names (INNs) of medicines included in application.

Melarsoprol
Eflornithine

### 2.5.) Formulations

Injectable melarsoprol, ampoules of 5 ml; 36 mg/ml (180 mg of active compound).
Injectable eflornithine, bottles of 100 ml; 200 mg/ml (20 g of active compound).

### 2.6.) International availability

Both melarsoprol and eflornithine are produced and donated to WHO by: sanofi-aventis
The drugs are available. Thanks to an agreement signed by WHO and sanofi-aventis the 10th of October 2006, the donation and the availability of melarsoprol and eflornithine free of charge for endemic countries are guaranteed until 2011. Drugs are produced by companies according WHO forecast and shipped to the different users: National Control Programmes, NGOs according their requests.

### 2.7.) Whether application is requested for an individual medicine or therapeutic group.

These drugs are individual medicines.

### 2.8.) Public Health Relevance

**Incidence**
In 2005, 15651 cases of T.b.g. and 727 cases of T.b.r were reported.
36 sub-Saharan African countries are endemic and about 60 millions of persons are considered at risk.
**Prevalence**
The total prevalence of HAT is estimated around 50 to 70,000 persons infected of whom more than 95% are infected by T.b.g.
The rate of disease stage among T.b.g. form treated patients shows is around 50%. This distribution is unknown for T.b.r patients although it is estimated to be the same.

### 2.9.) Treatment details

#### 2.9.1. Dosage and duration

**Melarsoprol**

Although some countries still follow a discontinued 3–4-day series of daily injections 3.6 mg/kg at 7-day intervals. Some protocols use increased doses from 1.2 to 3.6 mg/kg of melarsoprol in each series. The most commonly accepted protocol consisted of 2.2 mg/kg/day for 10 days. This treatment allowed to reduce the total quantity of melarsoprol by 30% and reduce the length of hospitalization by 16 days with comparable efficacy but unfortunately it did not reduce the risk or incidence of encephalopathy[19].

**Eflornithine**

Dosage depends on the weight and age

A. First line

• **Adult** dosage is 400 mg/kg/day administered in four daily slow infusions (lasting approximately 2 hours) during 14 days. Infusions are given every 6 hours, which represents a dose of 100 mg/kg per infusion;
• The recommended dosage for **children** is 150 mg/kg per infusion, following the same protocol as for adults during 14 days.
Each dose should be diluted in 100 cc in adult or 50 cc of sterile water for injection in children .

### 2.9.2. Need for special diagnostic or treatment facilities and skills

**Diagnostic**

Both treatments require the same skills for diagnostic.
The usual procedure is to perform a screening test (Card Agglutination Trypanosomiasis Test) and a clinical examination. In case of suspicion (serological or clinical), confirmation must be established with the direct examination of the parasite in the blood, in the lymph nodes or in the cerebrospinal fluid (CSF). Staging is realized with the examination of the CSF (white blood cells count and research of the parasite).

**Treatments**

**Melarsoprol**
Injections are intravenous and must be given slowly due to the risk of thrombo-phlebitis and necrosis at the injection site if the liquid is injected into the tissues surrounding the vein. Such a reaction generally precludes the use of this site for another injection for an extended period.
Injections must be performed using glass syringes.

**Eflornithine**
As it is administered in 4 infusions per day during 14 days, eflornithine requires complementary equipment and material in addition of skilled medical staff during day and night and therefore its use is difficult in rural remote areas with poor equipment and few human resources where the disease is prevalent.

### 2.10.) Summary of comparative effectiveness in a variety of clinical settings

**Melarsoprol**

Here are summarized some failure rates concerning melarsoprol treatments for T.b.g. and their references:

**Table 2 Melarsoprol treatments efficacy for HAT *(T. b. gambiense) :***

| Country | Year | Number of treated patients | Failure rates(%) | References |
|---|---|---|---|---|
| Cameron | 1951 | 394 | 3,0 | Friedheim, 1951 |
| Zaïre | 1984 | 1809 | 3,0 | Pépin & Milord, 1994 |
| Côte d'Ivoire | 1992 | 350 | 3,7 | Doua & Yapo, 1993 |
| Zaïre | 1994 | 1021 | 6,2 | Pépin *and al.*, 1994 |
| Uganda | 1999 | 428 | 30,4 | Legros *and al.*, 1999 |
| South Sudan | 2000 | 548 | 18,4* | MSF H, (unpublished) |

* After 6 months follow-up

Resistance to melarsoprol has been documented since the 1970s [9] [10] [11] and is now present in some foci in Democratic Republic of Congo, Angola, Sudan and Uganda.

**Eflornithine**

Even if eflornithine is effective in both stages of T.b.g., it is only used for the treatment of the second stage. There is a innate eflornithine-resistance of T.b.r. [10, 20].

Here are summarized some failure rates concerning treatments with eflornithine for T.b.g. Only the treatments with at least 400mg/kg/day were taken into account.

**Table 3 Eflornithine treatments efficacy for HAT *(T. b. gambiense):***

| Country | Year | Number of treated patients | Failure rates(%) | References |
|---|---|---|---|---|
| Uganda | 1993-1998 | 57 | 27% (*) | J Pepin et al. |
| Côte d'Ivoire, Congo & DRC | 1993-1998 | 127 | 3% (*) | J Pepin et al. |
| Sudan | 2001-2002 | 1058 (**) | 4.7% | G. Priotto et al. |
| Sudan | 2002-2005 | 587 | 12.6% | J.R. Franco et al. |

(*) Relapse rate was higher among the children under 12 (treatment was 400 mg/kg/day whatever was the age. Recommendations to treat children under 12 with 600mg/kg/day were introduced later).

(**) 647 patients had a follow-up of at least 12 months

The efficacy of the 14 days regimen varies from 97,1% to 73,4%. Poor results in Uganda contrast with more positive MSF unpublished reports concerning the use of eflornithine in Omugo health centre.

There are only two studies aiming at comparing the safety and the efficacy of melarsoprol and eflornithine. These are non randomized studies in Sudan and in Republic of Congo comparing cohorts of patients treated with various regimen

The study in Sudan [21] compared the characteristics of 708 patients treated with melarsoprol in 2001 and 2002 with characteristics of the 251 patients treated with DFMO in 2003. The rates of patient attendance to post-treatment follow-up visits were 64% at 6 months after treatment and 46% at 12 months after treatment. There were 9 relapses (3.6%) and 1 death (0.4%) in the DFMO group (n=249), and there were 16 relapses (2.3%) and 6 deaths (0.9%) in the melarsoprol group (n=683) during the 12-month follow-up period. Post-treatment relapse and death rates after treatment with DFMO and melarsoprol were statistically comparable[22]

A study in Congo[23] analysed the outcomes of death during treatment and relapse within 1 year of discharge for 288 patients treated with eflornithine, 311 patients treated with the series melarsoprol regimen and 62 patients treated with a short-course (10-day) melarsoprol regimen between April 2001 and April 2005.

Of the 637 patients who survived and could be included in the analysis of relapse rate, 452 (71%) were due for follow-up having been treated more than 1 year before the programme ended. Of these, 434 (96%) attended a follow-up visit within the first year. The cumulated incidence of relapse among those who attended at least one follow-up visit 1 year after discharge was 8.1% (11/136) among those treated with eflornithine, 14% (36/258) among those treated with standard melarsoprol and 15.5% (9/58) among those treated with short-course melarsoprol [24]. The high level of relapse rate was explained by the increase of resistance to melarsoprol.

According to the review of literature, apart in the areas where resistance to melarsoprol has appeared, the efficacy of melarsoprol and eflornithine are comparable.

## 2.11.) Summary of comparative evidence on safety

**Melarsoprol**

Melarsoprol is neurotoxic and the major risk is fatal encephalopathy which is responsible of a mortality ranging between 0.95 and 9,4% ([25], [26]). There have been isolated cases of seizures, peripheral neuropathy, headache, tremor, fever, abdominal pain, chest pain, skin rash with a possible form of Lyell's syndrome, peripheral thrombophlebitis related to i.v. injection, and cardiac, renal and hepatic toxicity as well as possible agranulocytosis [27], [28]. These reactions usually occur with the initial injections but some delayed reactions have also been described, after completion of treatment [29].

Overall fatality varies from 2% [30] to 9.8%[31] for T.b.g. and from 3.4% [32] to 12%[33] for T.b.r. infections. The exact origin of this toxicity is still not known but the solvent (propylene glycol) itself and the detoxifying agent (dimercaprol) included in the compound may contribute to this toxicity[34].

In a large-scale clinical, the concomitant application of prednisolone at 1 mg per kg body weight has been shown to reduce the incidence of encephalopathic syndromes by two thirds.

**Eflornithine**

The side effects vary from one study to another one. Clinical status of the patients and different case definitions may influence the frequencies. The main results are summarized in the

**Table 4** [35], [36], [37], [38], [39], [40], [41], [42].

**Table 4 Eflornithine main side effects**

| Reference | Hardenberg | Milord | Milord | Pépin | Priotto | Chappuis | Franco |
|---|---|---|---|---|---|---|---|
| Number of patients | 324 | 150 | 63 | 163 | 1058 | 139 | 587 |
| Anaemia | 44,4% | 33% | 38% | NR | NR | NR | 0,3% |
| Leukopenia | 26,5% | 43% | NR | NR | NR | NR | NR |
| Thrombocytopenia | 6,8% | NR | NR | NR | NR | NR | NR |
| Bleeding | NR | NR | NR | 1% | NR | 2,2% | 1,2% |
| Diarrhoea | 11,7% | 4% | NR | 16% | 2,4% | 20,9% | 25,9% |
| Abdominal pain | 2,5% | NR | NR | 14% | 2,9% | 38,1% | 37,3% |
| Nausea/Vomiting | NR | NR | NR | 8% | 2,0% | 6,5% | 11,2% |
| Anorexia | 1,2% | NR | NR | NR | NR | NR | NR |
| Convulsions/other encephalopathy signs | 7,4% | 8% | 9,5% | 9,8% | 4,3% | 2,2% | 4,4% |
| Headache | 2,2% | 0% | NR | NR | NR | 52,5% | NR |
| Dizziness | 0,3% | 0% | NR | NR | NR | NR | 4,6% |
| Ototoxicity | NR | NR | NR | 1% | NR | NR | 0,2% |
| Fever | 5,9% | NR | NR | NR | 2,2% | 14,4% | 11,8% |
| Infection | NR | NR | NR | 15% | 4,2% | 2% | 2,6% |
| Oedema/HTA | NR | NR | NR | NR | NR | 5% | NR |
| Alopecia | 1,9% | 0% | NR | NR | 1,1% | NR | 4,3% |
| Death | 5,9% | 2% | NR | 3% | 1,6% | 0,7% | 0,3% |

In the studies above mentioned conducted in Sudan and in DRC, summary of the results is as follows:

In Sudan, patients with second-stage human African trypanosomiasis treated with eflornithine (n=251) in 2003 had an adjusted relative risk of death of 0.2 and experienced significantly fewer cutaneous and neurological adverse effects than did patients who were treated with melarsoprol in 2001 and 2002 (n=708).

In Congo: A total of 1.7% (5/288) of patients treated with eflornithine died compared with 4.8% (15/311) of those treated with series of melarsoprol and 6.5% (4/62) of those treated with short-course melarsoprol.

## 2.12.) Summary of available data on comparative cost and cost-effectiveness within the pharmacological class or therapeutic group:

Both drugs melarsoprol and eflornithine are donated to WHO for free distribution by the sanofi aventis

Eflornithine requires 4 infusions per day during 14 days vs 1 daily IV injection for melarsoprol during 10 days. In addition the solvents and equipment for infusion needed for the use of eflornithine produce additional cost. Therefore eflornithine treatment cost is more important than melarsoprol treatment.

## 2.13.) Regulatory Status of Eflornithine

Eflornithine is currently being adopted by National treatment policies as first line treatment of T:b.g. second stage. WHO is encouraging this policy due to same efficacy and less toxicity, In addition the presence of melarsoprol-resistant foci leads to the increase of the use of eflornithine.

As WHO receives the orders for the different HAT drugs, and provides green light for distribution, it is possible to know how many vials have been ordered and where.

Between 2001 and 2006, 211,410 eflornithine vials and 429,949 melarsoprol vials have been sent to 28 endemic countries. Considering that the treatment is 14 vials of eflornithine or 10 vials of melarsoprol for a 50 kg patient, this amount would correspond to around 15,100 eflornithine treatments and 43,000 melarsoprol treatments.

The table 5 summarizes the orders of melarsoprol and eflornithine per countries between 2001 and 2006:

**Table 5 : orders of eflornithine and melarsoprol between 2001 and 2006**

| Countries in Africa currently been suplied. | Eflornithine | Melarsoprol | Eflornithine | Melarsoprol |
|---|---|---|---|---|
| Angola | 27,482 | 56,515 | 1,963 | 5,652 |
| Benin | | 450 | 0 | 45 |
| Burkina-Faso | 123 | 250 | 9 | 25 |
| Cameroon | 69 | 660 | 5 | 66 |
| Central African Republic | 9,680 | 13,850 | 691 | 1,385 |
| Chad | | 13,500 | 0 | 1,350 |
| Congo Brazaville | 17,436 | 19,300 | 1,245 | 1,930 |
| Cote d' ivoire | 1,040 | 1,000 | 74 | 100 |
| Democratic Republic of Congo | 45,112 | 275,250 | 3,222 | 27,525 |
| Equatorial Guinea | 642 | 300 | 46 | 30 |
| Gabon | 127 | 3,500 | 9 | 350 |
| Gambia | | 10 | 0 | 1 |
| Ghana | 140 | | 10 | 0 |
| Guinea | | 2,100 | 0 | 210 |
| Kenya | 10 | 190 | 1 | 19 |
| Liberia | | | 0 | 0 |
| Malawi | | 1,300 | 0 | 130 |
| Mozambique | | 1,270 | 0 | 127 |
| Nigeria | 300 | 300 | 21 | 30 |
| Rwanda | 4 | 10 | 0 | 1 |
| South-Africa | 19 | 44 | 1 | 4 |
| Sudan | 99,498 | 13,950 | 7,107 | 1,395 |
| Tanzania | | 8,220 | 0 | 822 |
| Togo | | 50 | 0 | 5 |
| Uganda | 9,728 | 17,400 | 695 | 1,740 |
| Yaounde | | 250 | 0 | 25 |
| Zambia | | 210 | 0 | 21 |
| Zimbabwe | | 70 | 0 | 7 |
| Total | **211,410** | **429,949** | **15,099** | **42,995** |

During the same period, around 1,500 eflornithine vials and 2,200 melarsoprol vials were sent to non endemic countries (mainly to treat imported cases): Belgium, France, Germany, Holland, India, Italy, Japan, UK, US, Scotland, Sweden and Switzerland.

## 2.14.) Pharmacopoeial Standards

Eflornithine is not included in the 5th Edition of the International Pharmacopoeia. It is part of the essential drugs list but appears in the complementary list.

## 2.15.) Proposed text for WHO Model Formulary.

It is proposed to place the eflornithine in the core list of the WHO essential drugs list.

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