EDITORIAL

Translated from *Rev Prescrire* **February 2006; 26 (269): 135-136**

Sleeping sickness: a cosmetic solution

Eflornithine was initially tested for the treatment of some forms of cancer in the 1970s but was rapidly abandoned due to a lack of evidence of efficacy in clinical trials (a)(1-3). Its effect on the trypanosome that causes African trypanosomiasis (sleeping sickness) was accidentally discovered in the laboratory and confirmed in 1987 through the "miraculous" cure of a terminally ill patient (1,4).

At that time sleeping sickness was resurgent in most endemic zones, and drugs that had been in use for half a century were no longer effective in some patients (b,c). Melarsoprol, an arsenic derivative (and the only drug effective in the terminal phase of the disease), caused fatal encephalitis in about 5% of patients (5). Eflornithine is also effective at the terminal stage of the disease and lacks the toxicity of melarsoprol. It is therefore clearly a better option than melarsoprol, even if it has to be administered as slow 6-hour infusions every day for 14 days (5).

Patients in need. **Eflornithine proved to be too expensive for the treatment of poor patients and no longer profitable enough for the manufacturer (currently part of the Sanofi Aventis group), which suspended production in 1995 (d)(1). Stocks of eflornithine were rapidly depleted, leaving patients who did not respond to melarsoprol with no alternative. The World Health Organization (WHO) and Médecins Sans Frontières, whose teams are involved in the fight against sleeping sickness, desperately tried to find a way to ensure continued production of eflornithine (1).**

Saved by a cosmetic. **By chance, the commercial success of Vaniqa° cosmetic cream in the United States rekindled interest in the production of eflornithine (see page 102 of this issue).**

In May 2001, Aventis and WHO signed an agreement guaranteeing the production of eflornithine (as well as melarsoprol and pentamidine) (5). Aventis agreed to cover all required therapy up to 2006, free of charge. The total value of this donation was estimated at 5 million US dollars per year, including financial support for a 5-year WHO programme on treatment for sleeping sickness and the search for better treatments. Aventis offered to transfer its technology and know-how if other producers came forward. The long-term availability of treatments for sleeping sickness is still not guaranteed, even if Sanofi Aventis has committed to make eflornithine available until another solution is found (5).

Uncertain future. **Eflornithine represents an improvement over melarsoprol, but its complex mode of administration makes it unsuitable for use in the field. It is therefore crucial to discover new treatments that have positive risk-benefit balances and are easy to administer (preferably orally). Ongoing research is focusing on combinations of existing drugs with the aim of limiting resistance and, at the same time, reducing the necessary dose (and toxicity) (6). New drugs that are potentially active against the trypanosome are in the pipeline but have not yet entered preclinical development (6).**

This story may yet have a positive outcome, but it is hardly a model for the treatment of neglected, common, life-threatening diseases in poor countries.

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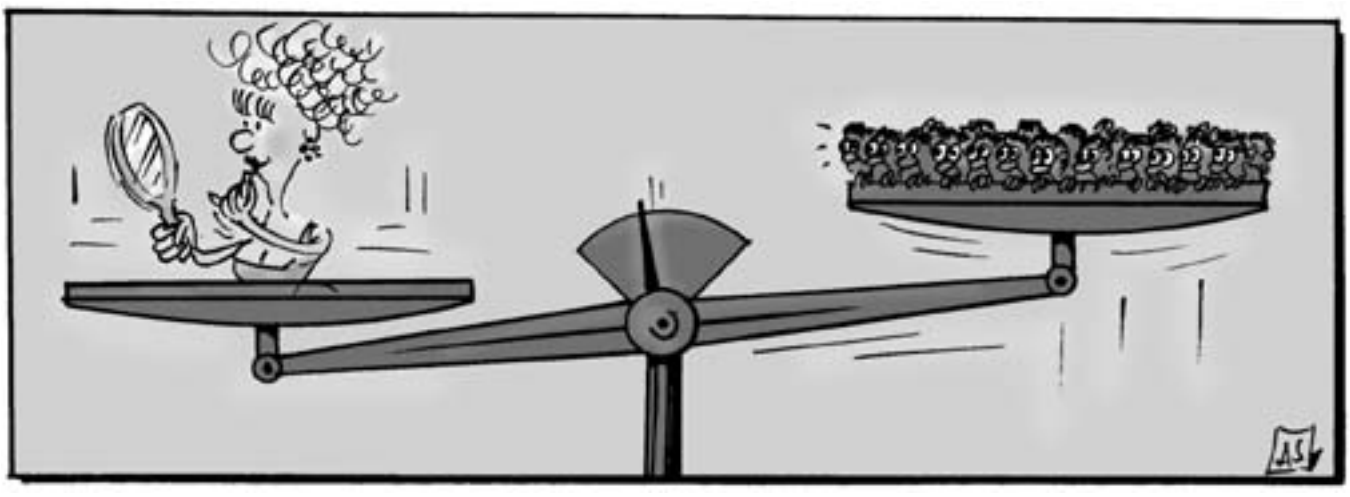

► ***a-*** *Eflornithine was not effective in the treatment of cancer but, like cytotoxic agents, caused hair loss. This effect led to development of Vaniqa° in hirsutism (1).*

b- *The re-emergence of African trypanosomiasis, a disease that had become rare in 1960, resulted from the virtual disappearance of mobile screening and treatment teams, as well as marked economic deterioration and wars in countries such as Congo, Angola and Sudan. According to the World Health Organisation (WHO), 60 million people have been exposed to the infection and about 500 000 are infected and will die if left untreated (6,7).*

c- *Treatment was then based on pentamidine and suramine sodium in the lymphatic-blood phase of the disease, and melarsoprol in the terminal meningoencephalic phase (4,7).*

d- *During the same period, melarsoprol production became unreliable, as did suramine production; the price of pentamidine (reformulated to prevent Pneumocystis carinii pneumonia) rose 10-fold (1,4).*

Selected references from Prescrire's document watch.

1- Wickware P "Resurrecting the resurrection drug" *Nature medicine* 2002; **8** (9): 908-909.
2- "Eflornithine hydrochloride". In "Martindale The complete drug reference" 34th ed, The Pharmaceutical Press, London 2005: 604.
3- Coyne PE "The eflornithine story" *J Am Acad Dermatol* 2001; **45** (5): 784-786.
4- Prescrire Rédaction "Maladie du sommeil cherche sponsor" *Rev Prescrire* 2000; **20** (207): 472-473.
5- "Sleeping sickness" *MSF Fact sheet* MSF campaign for access to essential medicines, May 2004: 4 pages.
6- Legros D et al. "Treatment of human trypanosomiasis - present situation and needs for research and development" *Lancet Infect Dis* 2002; **2**: 437-440.
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ADVERTISING

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"Compliance support programmes": a Trojan horse

● **France may soon legalise company funded "compliance support programmes", using the transposition of a European Directive that does not even mention this issue as a smokescreen. Drug companies' covert goal is simply to increase the use of their products.**

Direct-to-consumer advertising of prescription drugs is permitted in the United States, where public protests led pharmaceutical firms to adopt a specific code of conduct (1). This practice is forbidden in Europe, but drug companies, hand in hand with the European Commission, are continually seeking to "soften up" this prohibition (2).

A Trojan horse. Drug companies use "compliance support" as a key argument in favour of direct-to-consumer advertising (3).

According to a report written for drug company executives, "*Pharma companies have good reason to be concerned that so many patients with chronic conditions are dropping out of therapy prematurely. Not only does that drastically decrease the campaign's potential return on investment, but a commonly used advertising statistic maintains that it costs six times more to gain a new patient than to retain a current one*" (4). Non-compliance is estimated to "cost" companies more than 30 billion dollars per year (5).

Drug companies have already launched compliance support programmes in many countries.

Improper "transposition" of a European Directive in France. Legalisation of "compliance support programmes" was introduced along with a government bill meant to transpose a European Directive, even though the Directive does not even mention these programmes (see page 115 of this issue) (6). In fact, the European Parliament, along with national governments, rejected Commission proposals supporting direct-to-consumer advertising of prescription drugs.

Resist! The draft bill states that drug companies will be able to use physicians to set up individualised tools (telephone reminders, toll-free numbers, tailored patient education, home nursing visits, etc.)" (6). This is nothing more than door-to-door sales, and will further undermine physicians' and pharmacists' relations with the public.

Patients often have good reasons for stopping treatment. How could these company-sponsored measures possibly promote impartial reassessment of a drug's risk-benefit balance? How could they possibly lead to more effective pharmacovigilance? How could they lead to less costly treatments?

While the principle of "compliance support" is an interesting one, how can anyone believe that drug companies, with obvious conflicts of interest, should provide this service?

Budget restrictions are weighing heavily on many sectors of the healthcare system, but pharmaceutical companies still expect society to pick up the tab (through drug refunding) for home visits by nurses whose unstated goal is to increase prescription drug use.

If we fail to take action on this issue, public interests will yet again be given lower priority than making a profit.

Selected references from Prescrire's literature search.

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2- Prescrire Editorial Staff "Medicines in Europe Forum: the most important changes in the new legislation" Website: http://www.prescrire.org/aLaUne/dossierEuropeSynthese2En.php
3- Wosinska M "Advertising to acquire or retain?" *DTC Perspectives* 2003; **2** (3)**:** 22-26. Website http://www.hbs.edu consulted on 1 March 2006.
4- Smith D "DTC's new job: boosting compliance" *Pharmaceutical Executive* 2003. Website http://www.pharmexec.com consulted on 27 February 2006.
5- "Patient compliance is a $30 billion complaint". Website http://www.bioportfolio.com consulted on 27 February 2006.
6- "Projet Ordonnance n° - Rapport au Président de la République" 14 December 2005: 9 pages.