

Fenfluramine does not appear to possess the degree of abuse potential of such abused anorectics as the amphetamines, when tested in animals and humans (see below under *Drug Dependence*).

Under PRECAUTIONS:

Fenfluramine differs in its pharmacologic profile from other "anorectic" drugs with which the prescribing practitioner may be familiar. Correspondingly, there are possible risks not associated with other "anorectics"; such risks include those of diarrhea, sedation, and posttherapeutic depression. The possibility of these hazards should be weighed against the possible advantage of decreased central nervous system stimulation and/or abuse potential.

In addition the consultants reviewed and approved the draft preamble to a policy statement which forms the attachment under Tab B.

The conclusions and recommendations were as follows:

CONCLUSIONS

1. Adult obese subjects instructed in dietary management and treated with "anorectic" drugs on the average tend to lose more weight than those treated with placebo and diet in relatively short-term trials.

2. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial. The possible origins of the increased weight loss due to the various drug effects are not established. The increased weight loss appears to be related to variables other than the drug prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.

3. The magnitude of increased weight loss of drug treated patients over placebo treated patients, was only a fraction of a pound a week. The rate of weight loss, was greatest in the first weeks of therapy for both drug and placebo subjects and tended to decrease in succeeding weeks.

4. The natural history of obesity is measured in years, whereas the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically trivial. The limited usefulness of these agents must be measured against any possible risk factors inherent in their use.

5. The amphetamines including methamphetamine have been widely abused in numerous populations. It is thus in the best interests of the public health to limit the use of amphetamines as far as is compatible with adequate therapy. This is both to minimize the risk of dependence in susceptible patients being treated and to decrease the amount of drugs being distributed, since widespread prescription of a dependence-producing drug inevitably increases the possibility for diversion to non-medical use and abuse.

6. Evidence presented for newer "anorectic" congeners of the amphetamine family and non-amphetamine drugs do not set them apart as having higher benefit or lower risks than older available drugs. The risk potential of Fenfluramine may be an exception to this general statement.

7. There was no evidence in the data reviewed which showed that combination of an "anorectic" agent with other drugs increase the benefits or reduce the risk of the "anorectic" agent.

8. There are no clinical data which support the parenteral use of these drugs in the treatment of obesity. Obesity is not an indication for the parenteral use of these agents.

RECOMMENDATIONS

On the basis of the data reviewed and from all evidence at hand the following actions are therefore recommended:

1. That all "anorectics" reviewed, (d1-amphetamine, d-amphetamine, methamphetamine, benzphetamine, phenfermine, chlorphenfermine, chlortermine, phenmetrazine, phendimetrazine, fenfluramine, mazindol and diethylpropion) with the exception of fenfluramine, be placed on Schedule II on the basis of abuse potential.

2. That combinations of "anorectics" with other drugs be evaluated in accordance with the policy of the FDA on combination drugs, that each constituent of the drug combination contribute to the total effect claimed for the combined drugs, and that the present available and proposed drug combinations be handled in this manner in view of the lack of demonstrated efficacy for each of the constituents of the drug combinations reviewed.

3. That amphetamines prepared for or in a form suitable for parenteral use not be approved for use in the treatment of obesity.