

No formal move has been made to schedule other anorectics, but their absence from the Schedules appears to be one of the significant omissions of the Act. HEW, and by extension FDA, are obligated both scientifically and by the Act, to advise the Justice Department with respect to drugs with abuse potential. Formal recommendations with respect to the abuse potential of marketed and unmarketed anorectics appear overdue.

5. Deadlines

Deadlines and commitments of various kinds exist with respect to the actions implied above. The NDA's both for amphetamines and new entities have now exceeded the statutory review time limit of 180 days. The DESI Notices implementing 8 NAS/NRC recommendations await publication. Efficacy supplements submitted in response to the "possibly effective" Notice for other anorectics have exceeded the 180-day period. An estimate of medical need for amphetamines and phenmetrazine depends upon our conclusions as to efficacy, and is also overdue: upon it will depend manufacturing quotas and industry plans for 1973. In this regard, we were questioned in February 1972, before the House Subcommittee on Public Health and Environment and the Senate Subcommittee on Juvenile Delinquency as to our conclusions on the use of amphetamines in treating obesity, and we projected an answer for July.

SCIENTIFIC BACKGROUND WITH RESPECT TO ANORECTIC DRUGS

1. Efficacy studies

Repeatedly in discussions with consultants and outside experts the question of the results of anorectic trials in general was raised. FDA staff therefore carried out a unique computer-supported review of all controlled anorectic studies on file in FDA. 206 studies with 11 anorectic drugs were analyzed after screening by physician-medical officers. Individual patient data on 9,800 subjects were recorded on 72,000 IBM cards; and programs for tabulation and analyses of the data were developed and applied. The resulting library of data and analyses provides an unparalleled review of the class of drugs.

The analyses generally supported the efficacy of anorectic drugs. Use of the drugs in obese subjects was associated with more weight loss than was diet alone. The degree of extra weight loss was small—a few tenths of a pound a week in many cases—and variations were great. In trials which continued for 12 or 16 weeks, those subjects who remained in the trials lost a significant amount of weight e.g., 25–40% of excess weight, both in the control groups and when on drugs, but they consistently lost more weight on drugs.

2. Morbidity-mortality data

Larger questions of long standing remain unanswered, such as the long-term effect on morbidity and mortality of the use of anorectics. These questions are of basic importance, since the usefulness of the drugs depends in large part upon the assumption that they somehow help prevent the adverse effects of obesity.

3. Evidence of abuse

Evidence of various sorts of abuse is most abundant for the amphetamines. This is particularly so for use in the "street" and in student populations but also was found in a large sample of people of fixed residence in the conventional occupations.

It is reasonably assumed that abuse is also associated with prescriptions for obesity, but there are only minimal studies of this association. In addition to evidence of abuse of amphetamines, evidence also exists in fair quantity for abuse of phenmetrazine and diethylpropion. For other anorectics evidence of abuse is scanty or lacking. Experience with other abusable drugs has shown, however, that documentation of abuse lags markedly behind abuse, and, when it appears, is only the tip of the iceberg.

4. Animal and other studies on the comparability of ONE effects

Pharmacologic data in animals which would permit detailed comparisons of anorectic agents are imperfect or incomplete. Insofar as they exist, they indicate that the drugs are far more similar than dissimilar. The one exception to this statement is fenfluramine, which appears to possess depressant rather than stimulant qualities.

This pharmacologic contrast is based on observations in both animals and humans.