Actions

(Name of drug) is a sympathomimetic amine with CNS stimulant activity. Peripheral actions include elevation of systolic and diastolic blood pressures and weak bronchodilator and respiratory stimulant action. Drugs of this class used in obesity are commonly known as "anorectics" or "anorexigenics". It has not been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects, may be involved, for example.

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

The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The origins of the increased weight loss due to the various possible drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related in part 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.

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 limited.

DRUG DEPENDENCE SECTION OF WARNINGS SECTION

Drug Dependence. (Name of drug) has been extensively abused. Tolerance, extreme psychological dependence, and severe social disability have occurred. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with (name of drug) include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxication is psychosis, often clinically indistinguishable from schizophrenia.

3. *Marketing status.* Marketing of such drugs may be continued under the conditions described in the notice entitled Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study, published in the Federal Register July 14, 1970 (35 FR 11273), as follows:

a. For holders of "deemed approved" new drug applications (i.e., an application which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling and a supplement for updating information, including full manufacturing information with respect to items 7 and 8 of Form FD-356H (§ 314.1(c)), as described in paragraphs (a)(1) (i) and (iii) of the notice of July 14, 1970. For preparations claiming controlled release, such supplement should contain studies comparing blood levels occurring with the controlled release form with blood levels occurring with single units of the conventional form given multiple times. For example, when comparing a 30 mg. controlled release form normally given every 12 hours with a 10 mg. conventional form normally given every 4 hours, the comparison should involve 1 unit of the controlled release form given once and one unit of the 10 mg. form given every 4 hours.

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application as described in paragraph (a)(3)(i) of that notice, except that full manufacturing information with respect to items 7 and 8 of Form FD-356H (§ 314.1(c)) is required. For preparations claiming controlled release such supplement should contain studies comparing blood levels occurring with the controlled release form with blood levels occurring with single units of the conventional form given multiple times. For example, when comparing a 30 mg. controlled release form normally given every 12 hours with a 10 mg. conventional form normally given every 4 hours, the comparison should involve 1 unit of the controlled release form given once and one unit of the 10 mg. form given every 4 hours.