CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83900

DRAFT FINAL PRINTED LABELING

Labeling: ORIG

NDA No: 83-900 Rc'd. 2-24-76

Reviewed by: MA Jacobs 2/26/76

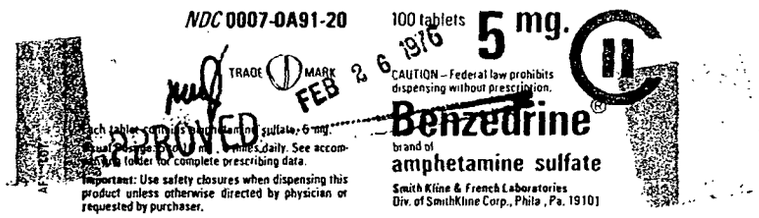
'BENZEDRINE'

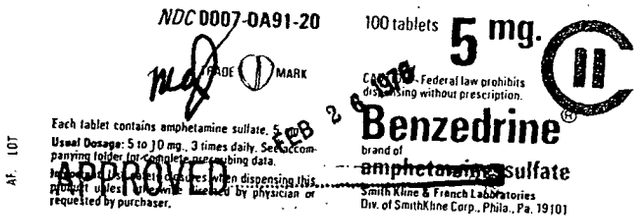
(amphetamine sulfate)

TABLETS

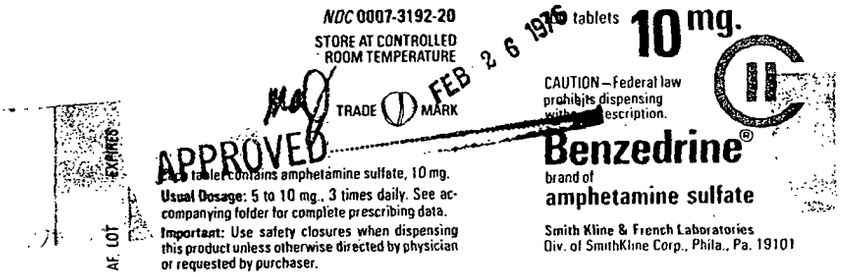
NDA 83-900

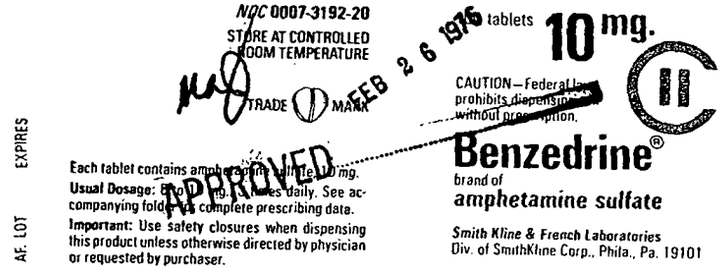
5 mg. - 100's





10 mg. - 100's





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PRESCRIBING INFORMATION

Benzedrine®

brand of **amphetamine sulfate**

Spansule® capsules

brand of sustained release capsules

and Tablets

APPROVED 1976

WARNING

AMPHETAMINES HAVE A HIGH POTENTIAL FOR ABUSE. THEY SHOULD THUS BE TRIED ONLY IN WEIGHT REDUCTION PROGRAMS FOR PATIENTS IN WHOM ALTERNATIVE THERAPY HAS BEEN INEFFECTIVE. ADMINISTRATION OF AMPHETAMINES FOR PROLONGED PERIODS OF TIME IN OBESITY MAY LEAD TO DRUG DEPENDENCE AND MUST BE AVOIDED. PARTICULAR ATTENTION SHOULD BE PAID TO THE POSSIBILITY OF SUBJECTS OBTAINING AMPHETAMINES FOR NON-THERAPEUTIC USE OR DISTRIBUTION TO OTHERS, AND THE DRUGS SHOULD BE PRESCRIBED OR DISPENSED SPARINGLY.

DESCRIPTION

Benzedrine (amphetamine sulfate, SK&F) is a racemic mixture of the dextro and levo isomers of amphetamine sulfate, a sympathomimetic amine of the amphetamine group. Chemically, amphetamine is *dl*-alpha-methylphenethylamine, and is present in all forms of 'Benzedrine' as the neutral sulfate.

Spansule® sustained release capsules—Each 'Spansule' sustained release capsule contains amphetamine sulfate, 15 mg., so prepared that an initial dose is released promptly and the remaining medication is released gradually over a prolonged period.

Tablets—Each tablet contains amphetamine sulfate, 5 mg. or 10 mg.

ACTIONS

Amphetamines are sympathomimetic amines 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 nondrug 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.

'Benzedrine' *Spansule* capsules are formulated to release the active drug substance *in vivo* in a more gradual fashion than the standard formulation, as demonstrated by blood levels. The formulation has not been shown superior in effectiveness over the same dosage of the standard, noncontrolled-release formulations given in divided doses.

INDICATIONS

Narcolepsy.

Minimal Brain Dysfunction in Children, as adjunctive therapy to other remedial measures (psychological, educational, social).

Special Diagnostic Considerations: Special etiology of minimal brain dysfunction (MBD) is unknown, and there is no single diagnostic test. Adequate diagnosis requires the use not only of medical but of special psychological, educational, and social resources.

The characteristic signs most often observed are chronic history of short attention span, distractibility, emotional lability, impulsivity, moderate to severe hyperactivity, minor neurological signs and abnormal EEG.

Learning disabilities may or may not be present. The diagnosis of MBD must be based upon a complete history and evaluation of the child and not solely on the presence of one or more of these signs.

Drug treatment is not indicated for all children with MBD. Appropriate educational placement is essential and psychological or social intervention may be necessary. When remedial measures alone are insufficient, the decision to prescribe stimulant medication will depend upon the physician's assessment of the chronicity and severity of the child's symptoms.

Drug treatment is not intended for use in the child whose hyperactivity is due to environmental factors and/or primary psychiatric disorders.

Exogenous Obesity, as a short-term (a few weeks) adjunct in a regimen of weight reduction based on caloric restriction, for patients refractory to alternative therapy, e.g., repeated diets, group programs, and other drugs. The limited usefulness of amphetamines (see ACTIONS) should be weighed against possible risks inherent in use of the drug, such as those described below.

CONTRAINDICATIONS

Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states.

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crises may result).

WARNINGS

When tolerance to the "anorectic" effect develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued.

Amphetamines may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or vehicles; the patient should therefore be cautioned accordingly.

Drug Dependence: Amphetamines have 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.