

15052 COMPETITIVE PROBLEMS IN THE DRUG INDUSTRY

ANTI-OBESITY DRUGS—GENERAL

MEMORANDUM

FEBRUARY 5, 1964.

To: Ralph C. Smith, M.D., Acting Medical Director.

From: Robert O. Knox, M.D., Medical Officer.

Subject: Drugs or classes of drugs in which there is a particular question of salary or lack of efficacy.

1. There is serious doubt as to the efficacy of the anorexigenic drugs in general in the treatment of obesity. (Ref: JAMA July 9, 1964, Vol. 175, pp. 1131-1135). According to one report, only 2% accomplish a long-term reduction in weight. Most of the reports claiming efficacy are based on short-term studies, and demonstrate only a few pounds of weight loss.

2. There is also serious doubt as to the efficacy of the peripheral vaso-dilator drugs in the treatment of intermittent claudication. Most workers feel that they are of little benefit, and there are reports of an actual decrease of blood flow to the muscle, coupled with the danger of hypertension due to cutaneous vaso-dilation.

MEMORANDUM

JULY 28, 1967.

To: Merle L. Gibson, M.D., Acting Director, Division of Neuropharmacological Drugs.

From: Robert O. Knox, M.D., Medical Officer, Division of Neuropharmacological Drugs.

Subject: The need to improve the present package inserts for the "Anorexigenic" drugs.

1. Despite much evidence attesting to the relative ineffectiveness of these, or any other compounds, in the treatment of obesity, numerous preparations are widely distributed and represented to be effective agents.

2. It appears advisable at this time to revise the present package inserts (and thereby the advertising) for these drugs including those already on the market to reflect more accurately the true situation.

3. Attached is a rough draft of a tentative package insert which may serve as a basis for further discussion. It would seem advisable to invite representatives from Drug Surveillance to discuss this matter with us so that we may arrive at a consensus. Several attempts have already been made to accomplish this, but frequent changes in staff have prevented any definitive step being taken.

MEMORANDUM

MAY 19, 1969.

To: Merle L. Gibson, M.D., Director, Division of Neuropharmacological Drugs.

From: Robert O. Knox, M.D., Division of Neuropharmacological Drugs.

Subject: Establishment of an FDA policy regarding anorexigenics.

1. During 1969, the NAS/NRC panels have evaluated various sympathomimetic amines used in the treatment of obesity. For example, phentermine and a phenmetrazine preparation were evaluated as "Effective, but . . ." by the panel on Psychiatric Drugs. A minority of two of the panel members evaluated the sympathomimetic stimulants as "probably effective." The documentation appended to their opinions consist of four references: (a) The first by J. F. Fazekas which discusses various concepts in therapy using anorexigenic agents, but has no actual clinical data. (b) The second is a 1947 article in the AMA by Harris, Ivy, and Searle using Dexedrine. However, there were only seven obese subjects used in two separate four-week periods during which the dose of the drug was progressively increased. The second experiments concerned ten volunteer medical students of normal weight. (c) The third article by Kinard et al. has to do with the use of d-amphetamine in patients on reserpine therapy. (d) The fourth reference is to Harrison's text book of Internal Medicine which of course contains no actual raw data.

2. On November 20, 1968, the Council of the British Medical Association forwarded a report to the Interdepartmental Standing Advisory Committee on drug dependence which contained the following recommendations: