to have a generally short-term anorectic action. They are not a treatment of obesity in themselves and should be used only as an adjunct to a total program of weight reduction. Further, the anorectic effect often plateaus or diminishes after a few weeks.

The DESI announcement for these drugs has been delayed pending completion of a comprehensive study of the efficacy and abuse potential of the entire class of drugs used an anorectic agents. The recommendations resulting from that study were forwarded to you in a memorandum dated October 6, 1972, a copy of which is enclosed for background information (Tab B). As that memorandum with its attachments pointed out, our staff carried out a computer-supported review of all controlled anorectic studies on file in FDA. The analyses generally supported the efficacy of anorectic drugs in that use of the drugs in obese subjects was associated with more weight loss than was diet alone, although the degree of extra weight loss was small and variations were great.

The proposed announcement, therefore, represents our conclusion that these drugs, in conventional dosage form, are effective in the management of exogenous obesity as a short term (a few weeks) adjunct in a regimen of weight reduction based on caloric resrtictions. The limited usefulness of the drugs must be weighed by the physician against possible risk factors.

The enclosed announcement covers the following drugs: Phentermine Hydrochloride; Phendimetrazine Tartrate; Benzphetamine Hydrochloride; Diethylpropion Hydrochloride—all in convention, oral dosage form, and Phenmetrazine Hydrochloride in conventional and prolonged action oral dosage forms.

The claim for prolonged action (phenmetrazine hydrochloride) is classified as possibly effective. Geigy markets this drug as Preludin in a 25 mg. conventional tablet (NDA 10-460) and in a 75 mg. prolonged action tablet (NDA 11-752). The prolonged action product was the one Geigy submitted for Academy review, claiming that a supplement approval after 1962 for the 25 mg. tablet constituted an efficacy determination. However, the Academy's report deals with the basic drug, not with any prolonged action claims. The DESI announcement pertains to both.

Action

The announcement classifies the drugs as effective in conventional dosage form for their only indication and sets forth the lanuage to be used for that indication, as well as for the "Actions" section of the labeling and for a drug-dependence warning. The prolonged action drug is rated possibly effective with respect to its claim for prolonged action. Abbreviated NDAs will be accepted for the effective drugs; however, full manufacturing information is required. Bioavailability data will not be required at the present time.

Impact

The subject document is one of several proposed documents which will impact on the entire class of drugs used for obesity. The others are: A revised policy statement on amphetamines; a proposal to withdraw approval of NDA for parenteral methamphetamine; a DESI follow-up notice proposing to withdraw approval of NDAs providing for anorectic drugs in combination with sedatives or tranquilizers (initially classified as possible effective in DESI 5378, August 8, 1970—Tab C); and a DESI follow-up notice which will elevate certain single-entity drugs previously published as possibly effective (Tab C), to effective (except for sustained-action claims).

Other preparations which contain the active constituent of drugs in the subject document are as follows:

1. Phentermine in a resin complex offered for prolonged release (NDA 11-613 Ionamin Capsules) is in DESI 5378 (Tab C).

2. Diethylpropion HCl in sustained or prolonged release form. Tenuate Dospon Tablets (NDA 12-546) are included in DESI 5378 (Tab C). Marketed as Tepanil Ten-Tabs (provided for in a supplement to NDA 11-673 (Tepanil)), it was not reviewed by the Academy; however, that product will be subject to the follow-up notice applicable to Tenuate Dospan.

Diethylpropion HCl in combination with vitamins (NDA 12-261—Natorexic has been discontinued and NDA approval, withdrawn.

3. Phenmetrazine in combination with minerals and vitamins (Geigy's Preluvite, NDA 12-371) has been discontinued. It was handled in DESI 5378 (Tab C).

Tenuate was among the leading 100 drugs prescribed in 1970 and Preludin was among the leading 150.