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CORRESPONDENCE **About Orlistat**

Sir,

Orlistat is an expensive drug which is claimed to promote weight loss by reducing fat absorption.

Its marketing is mainly backed by two large placebo-controlled, double-blind studies in severely overweight subjects receiving a controlled-energy diet plus orlistat or placebo. During the first year, orlistat-treated subjects lost more weight than placebo-treated subjects. The differences were 3.9 kg in the European study (1) and 2.9 kg in the American study (2). These modest differences are statistically significant because of the high number of subjects, but can hardly be regarded as clinically or cosmetically significant in such overweight subjects.

Moreover the placebo design was biased. The authors seem to have underestimated the potential and significant bias linked to the high prevalence of specific gastrointestinal effects in the orlistat-treated group: in the American study, at least one gastrointestinal effect was experienced by 79% of subjects in the orlistat group [flatulence with discharge (40.1%), oily spotting (37.2%), faecal urgency (29.7%), fatty/oily stool (19.8%), oily evacuation (14.3%), faecal incontinence (11.8%), and increased defecation (11.1%)]. In the European study, one or more gastrointestinal effects were experienced by 94% of subjects in the orlistat group. The prevalence of specific adverse events was also common [fatty/oily stool (31%), oily spotting (18%), oily evacuation (6%)]. As the American authors noted, these effects may well have made some of the orlistat-treated subjects suspect they were taking the active product. It is even probable that most of them were convinced of this and the double-blind design was thus seriously impaired. A

simple check, namely asking the subjects if they believed that they had received the placebo or orlistat, would have avoided this pitfall. In the absence of this check, and in view of the modest results of orlistat on weight loss, its real efficacy seems doubtful.

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