In the United States District Court for the District of New Jersey

Criminal No. 391–66 Bill of Particulars

UNITED STATES OF AMERICA *v.* CIBA PHARMACEUTICAL COMPANY, DIVISION OF CIBA CORPORATION

Now comes the United States of America by David M. Satz, Jr., United States Attorney, and Matthew J. Scola, Assistant United States Attorney for the District of New Jersey, and pursuant to Order of the Court, under Rule 7(f) of the Federal Rules of Criminal Procedure, provides the following Bill of Particulars:

COUNT I

1. The mailing piece referred to was not substantially the same as the labeling authorized by the approved new drug application effective with respect to the drug Esidrix-K in the following respects:

(a) Taken as a whole, the mailing piece would leave the prescribing physician with a different interpretation of the effects of the drug than he would have by reading the authorized labeling, in that the mailing piece implies that the drug would protect all patients against potassium electrolyte imbalance.

(b) The mailing piece omits the caution statement: "Combined therapy: When necessary, other hypertensive agents may be added cautiously. Since this drug potentiates the antihypertensive effect of other agents, such additions should be gradual. Dosages of ganglionic blockers in particular should be halved."

(c) The mailing piece omits these factors which predispose to hypokelemia (hypopotassemia): "intensive and prolonged diuretic therapy," "restricted sodium chloride intake" and "corticosteroid therapy."

(d) The mailing piece omits the information expressed in the approved labeling: "Since these tablets may not provide all the potassium required by some patients, a diet rich in this element will help obviate depletion."

(e) The mailing piece misleadingly claims that the drug affords "protection" by the following two statements: "Nearly twice the potassium protection offered by any other combination tablets for edema/hypertension" and that the drug "provides the most potassium protection", thereby inviting unwarranted reliance in the use of the drug, by leading the reader to believe that Esidrix-K, in recommended dosage, can prevent or correct potassium electrolyte imbalance in all patients, whereas there are some patients who require much more potassium than can be supplied by the upper range of the usual dose of Esidrix-K recommended (1.048 grams of potassium, or 2 grams of potassium chloride in two tablets), and, therefore, some patients who may not be protected at all from potassium imbalance by the highest recommended daily dose of this drug.

(f) The mailing piece states that the drug provides an "amount [of potassium] well within recommended prophylactic range (1–3 Gm.)," which statement is misleading and at variance with the approved labeling in that only the higher recommended maintenance daily dose of two tablets of Esidrix-K 1000 supplies sufficient potassium (1.048 Gm.) to be within the lower part of this prophylactic range. The statement is further misleading and at variance with the approved labeling because even 1.048 Gm. of potassium daily would not protect all patients against potassium electrolyte imbalance.

(g) The mailing piece states, as one reason for the claim that Esidrix-K provides the most potassium protection, that the 50/1000 tablet "dissolves completely and consistently in the upper intestine within 17 to 20 minutes, facilitating rapid absorption and full therapeutic benefits," which statement has not been approved for package insert labeling, and is contrary to fact, since the work described in the new drug application to which the statement refers was on simulated intestinal fluid *in vitro* and not in the actual upper intestine of men or animals.

(h) The mailing piece distorts the scientific article of R. E. Ray (Reference No. 6) to an extent that it implies approval of a more prolonged administration of the drug than the author in fact gave it, in that the article is quoted incompletely to imply that Ray gave Esidrix-K, with good results and without untoward reactions, to 45 women with obesity and cyclic edema