

(c) Until the results of compatibility studies are evaluated, a large volume parenteral drug product for intravenous use in humans that is packaged in a plastic immediate container on or after April 16, 1979, is misbranded unless its labeling contains a warning that includes the following information:

(1) A statement that additives may be incompatible.

(2) A statement that, if additive drugs are introduced into the parenteral system, aseptic techniques should be used and the solution should be thoroughly mixed.

(3) A statement that a solution containing an additive drug should not be stored.

(d) This section does not apply to a biological product licensed under the Public Health Service Act of July 1, 1944 (42 U.S.C. 201).

[62 FR 12084, Mar. 14, 1997]

§310.515 Patient package inserts for estrogens.

(a) *Requirement for a patient package insert.* FDA concludes that the safe and effective use of drug products containing estrogens requires that patients be fully informed of the benefits and risks involved in the use of these drugs. Accordingly, except as provided in paragraph (e) of this section, each estrogen drug product restricted to prescription distribution, including products containing estrogens in fixed combinations with other drugs, shall be dispensed to patients with a patient package insert containing information concerning the drug's benefits and risks. An estrogen drug product that does not comply with the requirements of this section is misbranded under section 502(a) of the Federal Food, Drug, and Cosmetic Act.

(b) *Distribution requirements.* (1) For estrogen drug products, the manufacturer and distributor shall provide a patient package insert in or with each package of the drug product that the manufacturer or distributor intends to be dispensed to a patient.

(2) In the case of estrogen drug products in bulk packages intended for multiple dispensing, and in the case of injectables in multiple-dose vials, a sufficient number of patient labeling

pieces shall be included in or with each package to assure that one piece can be included with each package or dose dispensed or administered to every patient. Each bulk package shall be labeled with instructions to the dispenser to include one patient labeling piece with each package dispensed or, in the case of injectables, with each dose administered to the patient. This section does not preclude the manufacturer or labeler from distributing additional patient labeling pieces to the dispenser.

(3) Patient package inserts for estrogens dispensed in acute-care hospitals or long-term care facilities will be considered to have been provided in accordance with this section if provided to the patient before administration of the first estrogen and every 30 days thereafter, as long as the therapy continues.

(c) *Patient package insert contents.* A patient package insert for an estrogen drug product is required to contain the following information:

(1) The name of the drug.

(2) The name and place of business of the manufacturer, packer, or distributor.

(3) A statement regarding the benefits and proper uses of estrogens.

(4) The contraindications to use, i.e., when estrogens should not be used.

(5) A description of the most serious risks associated with the use of estrogens.

(6) A brief summary of other side effects of estrogens.

(7) Instructions on how a patient may reduce the risks of estrogen use.

(8) The date, identified as such, of the most recent revision of the patient package insert.

(d) *Guidance language.* The Food and Drug Administration issues informal labeling guidance texts under §10.90(b)(9) of this chapter to provide assistance in meeting the requirements of paragraph (c) of this section. Requests for a copy of the guidance text should be directed to the Center for Drug Evaluation and Research, Division of Metabolism and Endocrine Drug Products (HFD-510), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

(e) *Exemptions.* This section does not apply to estrogen-progestogen oral contraceptives. Labeling requirements for these products are set forth in §310.501.

(f) *Requirement to supplement approved application.* Holders of approved applications for estrogen drug products that are subject to the requirements of this section must submit supplements under §314.70(c) of this chapter to provide for the labeling required by paragraph (a) of this section. Such labeling may be put into use without advance approval by the Food and Drug Administration.

[55 FR 18723, May 4, 1990]

§310.516 Progestational drug products; labeling directed to the patient.

(a) The Commissioner of Food and Drugs concludes that the safe and effective use of any progestational drug product requires that patients be informed that there is an increased risk of birth defects in children whose mothers have taken this drug during the first 4 months of pregnancy. Accordingly, except as provided by paragraph (d) of this section, any progestational drug product that is the subject of a new drug application approved either before or after October 9, 1962 and all identical, related, or similar drug products as defined in §310.6, whether or not the subject of an approved new drug application, shall be dispensed to patients with labeling in lay language containing such a warning. The patient labeling shall be provided as a separate printed leaflet independent of any additional materials.

(b) The patient labeling shall specifically include the following:

- (1) Name of the drug.
- (2) Name and place of business of the manufacturer, packer, or distributor.
- (3) A warning that there is an increased risk of birth defects in children whose mothers take this drug during the first 4 months of pregnancy.
- (4) A brief discussion of the nature of the risks of birth defects resulting from the use of these drugs during the first 4 months of pregnancy.
- (5) A brief statement that these drugs are no longer considered safe as a test for pregnancy.

(6) A statement that the patient should inform her physician as soon as possible if she discovers that she was pregnant when she took the drug.

(c) The patient labeling shall be printed in accordance with the following specifications:

(1) The minimum letter size shall be one-sixteenth of an inch in height.

(2) Letter heights pertain to the lower-case letter "o" or its equivalent that shall meet the minimum height standard.

(3) Type used shall conform to the minimum letter height. The body copy shall contain 1-point leading, noncondensed type, and shall not contain any light-face type or small capital letters.

(d) This section does not apply to a progestogen-containing product intended for contraception, which shall be labeled according to the requirements of §310.501.

(e)(1) Patient labeling for each progestational drug product shall be provided in or with each package intended to be dispensed to the patient. Patient labeling for drug products dispensed in acute-care hospitals or long-term care facilities will be considered to have been provided in accordance with this section if provided to the patient before first administration of the drug and every 30 days thereafter, as long as the therapy continues.

(2) In the case of progestational drug products in bulk packages intended for multiple dispensing, a sufficient number of patient-labeling pieces shall be included in or shall accompany each bulk package to assure that one can be included with each package dispensed to every patient. Each bulk package shall be labeled with instructions to the dispenser to include one patient-labeling piece with each package dispensed to the patient. This section does not preclude the manufacturer or labeler from distributing additional patient-labeling pieces to the dispenser.

(3) In the case of progestational drug products for injection, each package shall include a sufficient number of patient-labeling pieces for the volume of the vial, and instructions to the practitioner administering the drug to give one patient-labeling piece to each premenopausal woman, except those in