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of phenindione. Patients should be instructed to report promptly prodromal symptoms such as marked fatigue, chill, fever, and sore throat. Periodic blood studies and liver function tests should be performed. Use of the drug should be discontinued if leukopenia occurs or if evidence of hypersensitivity, such as dermatitis or fever, appears.''

(b) Regulatory action may be initiated with respect to preparations of phenindione intended for use by man found within the jurisdiction of the act on or after November 25, 1961, unless such preparations are labeled in accordance with paragraph (a) of this section.

§ 201.311 [Reserved]

§ 201.312 Magnesium sulfate heptahydrate; label declaration on drug products.

Magnesium sulfate heptahydrate should be listed on the label of a drug product as epsom salt, which is its common or usual name.

§ 201.313 Estradiol labeling.

The article presently recognized in The National Formulary under the heading ''Estradiol'' and which is said to be ''17-cis-beta estradiol'' is the same substance formerly recognized in the United States Pharmacopeia under the designation ''Alpha Estradiol.'' The substance should no longer be referred to in drug labeling as ''Alpha Estradiol.'' The Food and Drug Administration would not object to label references to the article as simply ''Estradiol''; nor would it object if the label of a preparation containing this substance referred to the presence of ''Estradiol (formerly known as Alpha Estradiol).''

§ 201.314 Labeling of drug preparations containing salicylates.

(a) The label of any oral drug preparation intended for sale without prescription and which contains any salicylate ingredient (including aspirin, salicylamide, other salicylates, and combinations) must conspicuously bear, on a clearly contrasting background, the warning statement: ''Keep out of reach of children [highlighted in bold type]. In case of overdose, get medical help or contact a Poison Control Center right away,'' or ''Keep out of reach of children [highlighted in bold type],'' except that if the article is an aspirin preparation, it shall bear the first of these warning statements. Such a warning statement is required for compliance with section 502(f)(2) of the Federal Food, Drug, and Cosmetic Act and is intended to guard against accidental poisonings. Safety closures that prevent access to the drug by young children are also recommended to guard against accidental poisonings.

(b) Effervescent preparations and preparations containing para-aminosalicylate as the only salicylate ingredient are exempted from this labeling requirement.

(c) Aspirin tablets sold as such and containing no other active ingredients, except tablets which cannot be readily subdivided into a child's dose because of their coating or size, should always bear dosage directions for each age group down to 3 years of age, with a statement such as ''For children under 3 years of age, consult your physician.'' It is recommended that:

(1) Aspirin tablets especially made for pediatric use be produced only in 1¼-grain size to reduce the hazard of errors in dosage;

(2) By June 1, 1967, manufacturers and distributors of 1¼-grain size aspirin tablets discontinue the distribution of such tablets in retail containers containing more than 36 tablets, to reduce the hazard of accidental poisoning;

(3) The flavoring of 5-grain aspirin tablets or other ''adult aspirin tablets'' be discontinued; and

(4) Labeling giving undue emphasis to the pleasant flavor of flavored aspirin tablets be discontinued.

(d) Salicylate preparations other than aspirin tablets sold as such may, at the option of the distributor, be labeled for use by adults only. If their labeling and advertising clearly offer them for administration to adults only.

(e)(1) It is the obligation of the distributor who labels a salicylate preparation for administration to children to make certain that the article is suitable for such use and labeled with adequate directions for use in the age group for which it is offered, but in no

case should such an article bear directions for use in children under 3 years of age. If the directions provide for administration to children as young as 3 years of age, the label should bear the statement, ''For children under 3 years of age consult your physician.'' However, if the directions provide for administration to children only of an age greater than 3 years (for example, the dosage instructions provide for administration of the article to children only down to age 6), the label should bear a statement such as, ''For younger children consult your physician.''

(2) A statement such as, ''For children under 3 years of age consult your physician'' or ''For younger children consult your physician'' is not required on the label of an article clearly offered for administration to adults only.

(f) If the labeling or advertising of a salicylate preparation offers it for use in arthritis or rheumatism, the label and labeling should clearly state that the beneficial effects claimed are limited to: ''For the temporary relief of minor aches and pains of arthritis and rheumatism.'' The qualifying phrase ''for the temporary relief of minor aches and pains'' should appear with the same degree of prominence and conspicuousness as the phrase ''arthritis and rheumatism''. The label and labeling should bear in juxtaposition with such directions for use conspicuous warning statements to the effect: ''Caution: If pain persists for more than 10 days, or redness is present, or in conditions affecting children under 12 years of age, consult a physician immediately.'' The salicylate dosage should not exceed 60 grains in a 24-hour period or 10 grains in a 4-hour period. If the article contains other analgesics, the salicylate dosage should be appropriately reduced.

(g)(1) The label of any drug containing more than 5 percent methyl salicylate (wintergreen oil) should bear a conspicuous warning such as: ''Do not use otherwise than as directed.'' These drug products must also include the ''Keep out of reach of children'' warning and the accidental ingestion warning as required in § 330.1(g) of this chapter.

(2) If the preparation is a counterirritant or rubefacient, it should also bear a caution such as, ''Caution: Discontinue use if excessive irritation of the skin develops. Avoid getting into the eyes or on mucous membranes.'' (See also § 201.303.)

(h)(1) The labeling of orally or rectally administered over-the-counter aspirin and aspirin-containing drug products subject to this paragraph is required to prominently bear a warning. The warning shall be as follows: ''Children and teenagers should not use this medicine for chicken pox or flu symptoms before a doctor is consulted about Reye syndrome, a rare but serious illness reported to be associated with aspirin.''

(2) This warning statement shall appear on the immediate container labeling. In cases where the immediate container is not the retail package, the retail package also must bear the warning statement. In addition, the warning statement shall appear on any labeling that contains warnings and, in such cases, the warning statement shall be the first warning statement under the heading ''Warnings.''

(3) Over-the-counter drug products subject to this paragraph and labeled solely for use by children (pediatric products) shall not recommend the product for use in treating flu or chicken pox.

(4) Any product subject to this paragraph that is not labeled as required by this paragraph and that is initially introduced or initially delivered for introduction into interstate commerce after June 5, 1986, is misbranded under sections 201(n) and 502 (a) and (f) of the Federal Food, Drug, and Cosmetic Act.

[40 FR 13998, Mar. 27, 1985, as amended at 51 FR 8182, Mar. 7, 1986; 53 FR 21637, June 9, 1988; 53 FR 24830, June 30, 1988; 64 FR 13291, Mar. 17, 1999]

EFFECTIVE DATE NOTE: At 64 FR 13291, Mar. 17, 1999, § 201.314 was amended by revising the first two sentences in paragraph (a) and by revising paragraphs (g)(1) and (h)(1), effective Apr. 16, 1999. For the convenience of the user the superseded text is set forth as follows:

§ 201.314 Labeling of drug preparations containing salicylates.

(a) The label of any oral drug preparation intended for sale without prescription and which contains any salicylate ingredient (including aspirin, salicylamide, other salicylates, and combinations) must bear a