

## § 355.10

treatment of dental cavities (decay, caries).

(d) *Dental caries*. A disease of calcified tissues of teeth characterized by demineralization of the inorganic portion and destruction of the organic matrix.

(e) *Dentifrice*. An abrasive-containing dosage form (gel, paste, or powder) for delivering an anticaries drug to the teeth.

(f) *Fluoride*. The inorganic form of the chemical element fluorine in combination with other elements.

(g) *Fluoride ion*. The negatively charged atom of the chemical element fluorine.

(h) *Fluoride supplement*. A special treatment rinse dosage form that is intended to be swallowed, and is promoted to health professionals for use in areas where the water supply contains 0 to 0.7 parts per million (ppm) fluoride ion.

(i) *Preventive treatment gel*. A dosage form for delivering an anticaries drug to the teeth. Preventive treatment gels are formulated in an anhydrous glycerin base with suitable thickening agents included to adjust viscosity. Preventive treatment gels do not contain abrasives.

(j) *Treatment rinse*. A liquid dosage form for delivering an anticaries drug to the teeth.

(k) *Treatment rinse concentrated solution*. A fluoride treatment rinse in a concentrated form to be mixed with water before using to result in the appropriate fluoride concentration specified in the monograph.

(l) *Treatment rinse effervescent tablets*. A fluoride treatment rinse prepared by adding an effervescent tablet (a concentrated solid dosage form) to water before using to result in the appropriate fluoride concentration specified in the monograph.

(m) *Treatment rinse powder*. A fluoride treatment rinse prepared by adding the powder (a concentrated solid dosage form) to water before using to result in the appropriate fluoride concentration specified in the monograph.

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## 21 CFR Ch. I (4-1-11 Edition)

### Subpart B—Active Ingredients

#### § 355.10 Anticaries active ingredients.

The active ingredient of the product consists of any of the following when used in the concentration and dosage form established for each ingredient:

(a) *Sodium fluoride*—(1) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a gel or paste dosage form*. Sodium fluoride 0.188 to 0.254 percent with an available fluoride ion concentration  $\geq$  650 parts per million (ppm).

(2) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a powdered dosage form*. Sodium fluoride 0.188 to 0.254 percent with an available fluoride ion concentration of  $\geq$  850 ppm for products containing the abrasive sodium bicarbonate and a poured-bulk density of 1.0 to 1.2 grams per milliliter.

(3) *Treatment rinses*. (i) An aqueous solution of acidulated phosphate fluoride derived from sodium fluoride acidulated with a mixture of sodium phosphate, monobasic, and phosphoric acid to a level of 0.1 molar phosphate ion and a pH of 3.0 to 4.5 and which yields an effective fluoride ion concentration of 0.02 percent.

(ii) An aqueous solution of acidulated phosphate fluoride derived from sodium fluoride acidulated with a mixture of sodium phosphate, dibasic, and phosphoric acid to a pH of 3.5 and which yields an effective fluoride ion concentration of 0.01 percent.

(iii) Sodium fluoride 0.02 percent aqueous solution with a pH of approximately 7.

(iv) Sodium fluoride 0.05 percent aqueous solution with a pH of approximately 7.

(v) Sodium fluoride concentrate containing adequate directions for mixing with water before using to result in a 0.02-percent or 0.05-percent aqueous solution with a pH of approximately 7.

(b) *Sodium monofluorophosphate*—(1) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a gel or paste dosage form*. Sodium monofluorophosphate 0.654 to 0.884 percent with an available fluoride ion concentration (consisting of  $\text{PO}_3\text{F}^-$  and  $\text{F}^-$  combined)  $\geq$  800 ppm.

(2) *Dentifrices containing 1,500 ppm theoretical total fluorine in a gel or paste*

*dosage form.* Sodium monofluorophosphate 1.153 percent with an available fluoride ion concentration (consisting of PO<sub>3</sub>, F<sup>=</sup> and F<sup>-</sup> combined) ≥ 1,275 ppm.

(c) *Stannous fluoride*—(1) *Dentifrices containing 850 to 1,150 ppm theoretical total fluorine in a gel or paste dosage form.* (i) Stannous fluoride 0.351 to 0.474 percent with an available fluoride ion concentration ≥ 700 ppm for products containing abrasives other than calcium pyrophosphate.

(ii) Stannous fluoride 0.351 to 0.474 percent with an available fluoride ion concentration ≥ 290 ppm for products containing the abrasive calcium pyrophosphate.

(2) *Preventive treatment gel.* Stannous fluoride 0.4 percent in an anhydrous glycerin gel, made from anhydrous glycerin and the addition of suitable thickening agents to adjust viscosity.

(3) *Treatment rinse.* Stannous fluoride concentrate marketed in a stable form and containing adequate directions for mixing with water immediately before using to result in a 0.1-percent aqueous solution.

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### § 355.20 Packaging conditions.

(a) *Package size limitation.* Due to the toxicity associated with fluoride active ingredients, the following package size limitations are required for anticaries drug products:

(1) *Dentifrices.* Dentifrice (toothpastes and tooth powders) packages shall not contain more than 276 milligrams (mg) total fluorine per package.

(2) *Preventive treatment gels and treatment rinses.* Preventive treatment gel and treatment rinse packages shall not contain more than 120 mg total fluorine per package.

(3) *Exception.* Package size limitations do not apply to anticaries drug products marketed for professional office use only and labeled in accord with § 355.60.

(b) *Tight container packaging.* To minimize moisture contamination, all fluoride powdered dentifrices shall be packaged in a tight container as defined as a container that protects the contents from contamination by extraneous liquids, solids, or vapors, from loss of the

article, and from efflorescence, deliquescence, or evaporation under the ordinary or customary conditions of handling, shipment, storage, and distribution, and is capable of tight reclosure.

## Subpart C—Labeling

### § 355.50 Labeling of anticaries drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as: (select one or both of the following: ‘anticavity’ or ‘fluoride’) (select one of the following as appropriate: “dentifrice,” “toothpaste,” “tooth polish,” “tooth powder;” (optional: “dental”) “preventive treatment gel;” or (optional: “treatment” or “dental”)) (select one of the following: “rinse,” “concentrated solution,” “rinse powder,” or “rinse effervescent tablets”). The word “mouthwash” may be substituted for the word “rinse” in this statement of identity if the product also has a cosmetic use, as defined in section 201(i) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(i)).

(b) *Indication.* The labeling of the product states, under the heading “Indication,” the following: “Aids in the prevention of dental (select one of the following: “cavities,” “decay,” “caries (decay),” or “caries (cavities)”). Other truthful and nonmisleading statements, describing only the indication for use that has been established and listed in this paragraph (b), may also be used, as provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(c) *Warning.* The labeling of the product contains the following warning under the heading “Warning”:

(1) *For all fluoride dentifrice (gel, paste, and powder) products.* “Keep out of reach of children under 6 years of age. [highlighted in bold type] If more than used for brushing is accidentally swallowed, get medical help or contact a