

§ 343.20 [Reserved]

§ 343.22 Permitted combinations of active ingredients for cardiovascular-rheumatologic use.

Combinations containing aspirin must meet the standards of an acceptable dissolution test, as set forth in § 343.90. The following combinations are permitted: Aspirin identified in §§ 343.12 and 343.13 may be combined with any antacid ingredient identified in § 331.11 of this chapter or any combination of antacids permitted in accordance with § 331.10(a) of this chapter provided that the finished product meets the requirements of § 331.10 of this chapter and is marketed in a form intended for ingestion as a solution.

Subpart C—Labeling

§§ 343.50–343.60 [Reserved]

§ 343.80 Professional labeling.

The labeling of an over-the-counter drug product written for health professionals (but not for the general public) shall consist of the following:

(a) *For products containing aspirin identified in §§ 343.12 and 343.13 or permitted combinations identified in § 343.22.* (These products must meet United States Pharmacopeia (USP) standards for dissolution or drug release in § 343.90.)

(1) The labeling contains the following prescribing information under the heading “Comprehensive Prescribing Information” and the subheadings “Description,” “Clinical Pharmacology,” “Clinical Studies,” “Animal Toxicology,” “Indications and Usage,” “Contraindications,” “Warnings,” “Precautions,” “Adverse Reactions,” “Drug Abuse and Dependence,” “Overdosage,” “Dosage and Administration,” and “How Supplied” in the exact language and the exact order provided as follows:

COMPREHENSIVE PRESCRIBING
INFORMATION

DESCRIPTION

(Insert the proprietary name and the established name (if any) of the drug, type of dosage form (followed by the phrase “for oral administration”), the established name(s) and quantity of the active ingredient(s) per dosage unit, the

total sodium content in milligrams per dosage unit if the sodium content of a single recommended dose is 5 milligrams or more, the established name(s) (in alphabetical order) of any inactive ingredient(s) which may cause an allergic hypersensitivity reaction, the pharmacological or therapeutic class of the drug, and the chemical name(s) and structural formula(s) of the drug.) Aspirin is an odorless white, needle-like crystalline or powdery substance. When exposed to moisture, aspirin hydrolyzes into salicylic and acetic acids, and gives off a vinegary-odor. It is highly lipid soluble and slightly soluble in water.

CLINICAL PHARMACOLOGY

Mechanism of Action: Aspirin is a more potent inhibitor of both prostaglandin synthesis and platelet aggregation than other salicylic acid derivatives. The differences in activity between aspirin and salicylic acid are thought to be due to the acetyl group on the aspirin molecule. This acetyl group is responsible for the inactivation of cyclooxygenase via acetylation.

PHARMACOKINETICS

Absorption: In general, immediate release aspirin is well and completely absorbed from the gastrointestinal (GI) tract. Following absorption, aspirin is hydrolyzed to salicylic acid with peak plasma levels of salicylic acid occurring within 1–2 hours of dosing (see PHARMACOKINETICS—*Metabolism*). The rate of absorption from the GI tract is dependent upon the dosage form, the presence or absence of food, gastric pH (the presence or absence of GI antacids or buffering agents), and other physiologic factors. Enteric coated aspirin products are erratically absorbed from the GI tract.

Distribution: Salicylic acid is widely distributed to all tissues and fluids in the body including the central nervous system (CNS), breast milk, and fetal tissues. The highest concentrations are found in the plasma, liver, renal cortex, heart, and lungs. The protein binding of salicylate is concentration-dependent, *i.e.*, nonlinear. At low concentrations (<100 micrograms/milliliter (µg/mL)), approximately 90 percent of plasma salicylate is bound to albumin while at higher concentrations (>400 µg/mL), only about 75 percent is bound. The early signs of salicylic overdose (salicylism), including tinnitus (ringing in the ears), occur at plasma concentrations approximating 200 µg/mL. Severe toxic effects are associated with levels >400 µg/mL. (See ADVERSE REACTIONS and OVER-DOSAGE.)

Metabolism: Aspirin is rapidly hydrolyzed in the plasma to salicylic acid such that plasma levels of aspirin are essentially undetectable 1–2 hours after dosing. Salicylic acid is primarily conjugated in the liver to