Nursing Mothers

Nursing mothers should avoid using aspirin because salicylate is excreted in breast milk. Use of high doses may lead to rashes, platelet abnormalities, and bleeding in nursing infants.

Pediatric Use

Pediatric dosing recommendations for juvenile rheumatoid arthritis are based on well-controlled clinical studies. An initial dose of 90–130 mg/kg/day in divided doses, with an increase as needed for anti-inflammatory efficacy (target plasma salicylate levels of 150–300 µg/mL) are effective. At high doses (i.e., plasma levels of greater than 200 µg/mL), the incidence of toxicity increases.

ADVERSE REACTIONS

Many adverse reactions due to aspirin ingestion are dose-related. The following is a list of adverse reactions that have been reported in the literature. (See **Warnings**.)

Body as a Whole: Fever, hypothermia, thirst.

Cardiovascular: Dysrhythmias, hypotension, tachycardia.

Central Nervous System: Agitation, cerebral edema, coma, confusion, dizziness, headache, subdural or intracranial hemorrhage, lethargy, seizures.

Fluid and Electrolyte: Dehydration, hyperkalemia, metabolic acidosis, respiratory alkalosis.

Gastrointestinal: Dyspepsia, GI bleeding, ulceration and perforation, nausea, vomiting, transient elevations of hepatic enzymes, hepatitis, Reye's Syndrome, pancreatitis.

Hematologic: Prolongation of the prothrombin time, disseminated intravascular coagulation, coagulopathy, thrombocytopenia.

Hypersensitivity: Acute anaphylaxis, angioedema, asthma, bronchospasm, laryngeal edema, urticaria.

Musculoskeletal: Rhabdomyolysis.

Metabolism: Hypoglycemia (in children), hyperglycemia.

Reproductive: Prolonged pregnancy and labor, stillbirths, lower birth weight infants, antepartum and postpartum bleeding.

Respiratory: Hyperpnea, pulmonary edema, tachypnea.

Special Senses: Hearing loss, tinnitus. Patients with high frequency hearing loss may have difficulty perceiving tinnitus. In these patients, tinnitus cannot be used as a clinical indicator of salicylism.

Urogenital: Interstitial nephritis, papillary necrosis, proteinuria, renal insufficiency and failure.

DRUG ABUSE AND DEPENDENCE

Aspirin is nonnarcotic. There is no known potential for addiction associated with the use of aspirin.

OVERDOSAGE

Salicylate toxicity may result from acute ingestion (overdose) or chronic intoxication. The early signs of salicylic overdose (salicylism), including tinnitus (ringing in the ears), occur at plasma concentrations approaching 200 µg/mL. Plasma concentrations of aspirin above 300 µg/mL are clearly toxic. Severe toxic effects are associated with levels above 400 µg/mL. (See **Clinical Pharmacology**.) A single lethal dose of aspirin in adults is not known with certainty but death may be expected at 30 g. For real or suspected overdose, a Poison Control Center should be contacted immediately. Careful medical management is essential.

Signs and Symptoms: In acute overdose, severe acid-base and electrolyte disturbances may occur and are complicated by hyperthermia and dehydration. Respiratory alkalosis occurs early while hyperventilation is present, but is quickly followed by metabolic acidosis.

Treatment: Treatment consists primarily of supporting vital functions, increasing salicylate elimination, and correcting the acid-base disturbance. Gastric emptying and/or lavage is recommended as soon as possible after ingestion, even if the patient has vomited spontaneously. After lavage and/or emesis, administration of activated charcoal, as a slurry, is beneficial, if less than 3 hours have passed since ingestion. Charcoal adsorption should not be employed prior to emesis and lavage.

Severity of aspirin intoxication is determined by measuring the blood salicylate level. Acid-base status should be closely followed with serial blood gas and serum pH measurements. Fluid and electrolyte balance should also be maintained.

In severe cases, hyperthermia and hypovolemia are the major immediate threats to life. Children should be sponged with tepid water. Replacement fluid should be administered intravenously and augmented with correction of acidosis. Plasma electrolytes and pH should be monitored to promote alkaline diuresis of salicylate if renal function is normal. Infusion of glucose may be required to control hypoglycemia.

Hemodialysis and peritoneal dialysis can be performed to reduce the body drug content. In patients with renal insufficiency or in cases of life-threatening intoxication, dialysis is usually required. Exchange transfusion may be indicated in infants and young children.

DOSAGE AND ADMINISTRATION

Each dose of aspirin should be taken with a full glass of water unless patient is fluid restricted. Anti-inflammatory and analgesic dosages should be individualized. When aspirin is used in high doses, the development of tinnitus may be used as a clinical sign of elevated plasma salicylate levels except in patients with high frequency hearing loss.

Ischemic Stroke and TIA: 50–325 mg once a day. Continue therapy indefinitely.

Suspected Acute MI: The initial dose of 160–162.5 mg is administered as soon as an MI is suspected. The maintenance dose of 160–162.5 mg a day is continued for 30 days post-infarction. After 30 days, consider further therapy based on dosage and administration for prevention of recurrent MI.

Prevention of Recurrent MI: 75–325 mg once a day. Continue therapy indefinitely.

Unstable Angina Pectoris: 75–325 mg once a day. Continue therapy indefinitely.

Chronic Stable Angina Pectoris: 75–325 mg once a day. Continue therapy indefinitely.

CABG: 325 mg daily starting 6 hours post-procedure. Continue therapy for 1 year post-procedure.

PTCA: The initial dose of 325 mg should be given 2 hours pre-surgery. Maintenance dose is 160–325 mg daily. Continue therapy indefinitely.

Carotid Endarterectomy: Doses of 80 mg once daily to 650 mg twice daily, started presurgery, are recommended. Continue therapy indefinitely.

Rheumatoid Arthritis: The initial dose is 3 g a day in divided doses. Increase as needed for anti-inflammatory efficacy with target plasma salicylate levels of 150–300 µg/mL. At high doses (i.e., plasma levels of greater than 200 µg/mL), the incidence of toxicity increases.

Juvenile Rheumatoid Arthritis: Initial dose is 90–130 mg/kg/day in divided doses. Increase as needed for anti-inflammatory efficacy with target plasma salicylate levels of 150–300 µg/mL. At high doses (i.e., plasma levels of greater than 200 µg/mL), the incidence of toxicity increases.

Spondyloarthropathies: Up to 4 g per day in divided doses.

Osteoarthritis: Up to 3 g per day in divided doses.

Arthritis and Pleurisy of SLE: The initial dose is 3 g a day in divided doses. Increase as needed for anti-inflammatory efficacy with target plasma salicylate levels of 150–300 µg/mL. At high doses (i.e., plasma levels of greater than 200 mµ/mL), the incidence of toxicity increases.

HOW SUPPLIED

(*Insert specific information regarding, strength of dosage form, units in which the dosage form is generally available, and information to facilitate identification of the dosage form as required under § 201.57(k)(1), (k)(2), and (k)(3).) Store in a tight container at 25* °C (77 °F); excursions permitted to 15–30 °C (59–86 °F).

REV: October 23, 1998.

Dated: September 7, 1999.

Margaret M. Dotzel,

Acting Associate Commissioner for Policy.

[FR Doc. 99–23684 Filed 9–13–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 558

New Animal Drugs for Use in Animal Feeds; Lasalocid and Virginiamycin

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations to reflect approval of a new animal drug application (NADA) filed by Roche Vitamins, Inc. The NADA provides for

use of approved lasalocid and virginiamycin Type A medicated articles to make Type C medicated feeds used for prevention of coccidiosis and for increased rate of weight gain and improved feed efficiency in growing turkeys.

EFFECTIVE DATE: September 14, 1999.

FOR FURTHER INFORMATION CONTACT: Charles J. Andres, Center for Veterinary Medicine (HFV–128), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–827–1600.

SUPPLEMENTARY INFORMATION: Roche Vitamins, Inc., 45 Waterview Blvd., Parsippany, NJ 07054–1298, filed NADA 141–150 that provides for use of Avatec® (90.7 grams per pound (g/lb) of lasalocid as lasalocid sodium) and Stafac® (20 or 227 g/lb of virginiamycin) Type A medicated articles to make Type C medicated feeds for growing turkeys. The Type C medicated feeds are used for prevention of coccidiosis caused by *Eimeria meleagrimitis*, *E. gallopavonis*, and *E. adenoeides*, and for increased rate of weight gain and improved feed efficiency in growing turkeys. The NADA is approved as of August 6, 1999, and the regulations are amended in 21 CFR 558.311 to reflect the approval. The basis of approval is discussed in the freedom of information summary.

In accordance with the freedom of information provisions of 21 CFR part 20 and 514.11(e)(2)(ii), a summary of safety and effectiveness data and information submitted to support approval of this application may be seen in the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, between 9 a.m. and 4 p.m., Monday through Friday.

The agency has determined under 21 CFR 25.33(a)(2) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

This rule does not meet the definition of ''rule'' in 5 U.S.C. 804(3)(A) because it is a rule of ''particular applicability.'' Therefore, it is not subject to the congressional review requirements in 5 U.S.C. 801–808.

List of Subjects in 21 CFR Part 558

Animal drugs, Animal feeds.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under the authority delegated to the Commissioner of Food and Drugs and redelegated to the Center for Veterinary Medicine, 21 CFR part 558 is amended as follows:

PART 558—NEW ANIMAL DRUGS FOR USE IN ANIMAL FEEDS

1. The authority citation for 21 CFR part 558 continues to read as follows:

Authority: 21 U.S.C. 360b, 371.

2. Section 558.311 is amended in the table in paragraph (e)(1)(xiv), under the ''Combination in grams per ton'' column, by alphabetically adding an entry for ''Virginiamycin 10 to 20'' to read as follows:

§ 558.311 Lasalocid.

* * * * *

(e)(1) * * *

Lasalocid sodium activity in grams per ton	Combination in grams per ton	Indications for use	Limitations	Sponsor
* *	*	*	* *	*
(xiv) 68 (0.0075 pct) to 113 (0.0125 pct).		* * *	* * *	* * *
* *	*	*	* *	*
	Virginiamycin 10 to 20	Growing turkeys; for prevention of coccidiosis caused by *E. meleagrimitis*, *E. gallopavonis*, and *E. adenoeides*, and for increased rate of weight gain and improved feed efficiency.	Feed continuously as sole ration. As lasalocid sodium provided by 063238 and virginiamycin provided by 000069.	063238
* *	*	*	* *	*

* * * * *

Dated: August 30, 1999.

Stephen F. Sundlof,

Director, Center for Veterinary Medicine.

[FR Doc. 99–23970 Filed 9–13–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HOUSING AND URBAN DEVELOPMENT

24 CFR Part 982

[Docket No. FR–4428–C–03]

RIN 2577–AB91

Section 8 Tenant-Based Assistance Programs Statutory Merger of Section 8 Certificate and Voucher Programs; Correction

AGENCY: Office of the Assistant Secretary for Public and Indian Housing, HUD.

ACTION: Correction.

SUMMARY: This document makes various corrections to HUD's May 14, 1999 interim rule amending the regulations for the Section 8 tenant-based rental voucher program. The interim rule implemented most of the Section 8 tenant-based program provisions contained in the Quality Housing and Work Responsibility Act of 1998 (the ''Public Housing Reform Act''). Of particular significance, the May 14, 1999 interim rule implemented section 545 of the Public Housing Reform Act. Section 545 provides for the complete merger of the Section 8 tenant-based Certificate and Voucher programs. The purpose of this document is to make