CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 75-988

Name: Prednisolone Sodium Phosphate Oral Solution 5 mg (base) / 5 mL

Sponsor: Paddock Laboratories, Inc.

Approval Date: May 25, 2004

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Approvable Letter(s)	
Approved Labeling	X
Labeling Review(s)	X
Medical Review(s)	
Chemistry Review(s)	X
Bioequivalence Review(s)	X
Statistical Review(s)	
Microbiology Review(s)	
Administrative Document(s)	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

APPROVAL LETTER

ANDA 75-988

MAY 25 2004

Paddock Laboratories, Inc.
Attention: David Rosenberg
3940 Quebec Avenue North
Minneapolis, MN 55427

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated September 14, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Prednisolone Sodium Phosphate Oral Solution, 5 mg (base)/5 mL.

Reference is also made to your amendments dated October 16, 2002; August 25, 2003; and February 17, 2004.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Prednisolone Sodium Phosphate Oral Solution, 5 mg (base)/5 mL to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Pediapred® Oral Solution, 5 mg (base)/5 mL, of Celltech Pharmaceuticals, Inc.).

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

We request that you submit, in duplicate, any proposed advertising or promotional copy that you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print.

Submit both copies together with a copy of the final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FDA 2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FDA 2253 at the time of their initial use.

Sincerely yours,

Robert Lee Lest/for 5/25/2004

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-988
Division File
Field Copy
HFD-610/R. West
HFD-330
HFD-205
HFD-610/Orange Book Staff

Endorsements:
HFD-623/N.Takiar/ N. Takiar 3/8/04
HFD-623/D.Gill/ DSGill 3-8-04
HFD-617/S.Park S. Park 3/9/04
HFD-613/R.Wu/ RWu 3/10/04
HFD-613/J.Grace/ 3/10/04

Robert Lee Lost 3/25/04
pending acceptable EER

V:\FIRMSNZ\PADDOCK\LTRS&REV\75988.ap.doc

F/T by: EW 3/8/04

APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

APPROVED LABELING

Prednisolone Sodium Phosphate Oral Solution

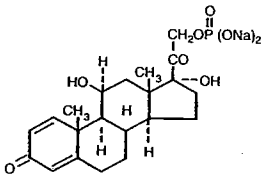
(prednisolone sodium phosphate, USP)
5 mg (base)/ 5 mL*
Rx only

***DESCRIPTION:**

Prednisolone Sodium Phosphate (prednisolone sodium phosphate, USP) Oral Solution is a dye free, colorless to light straw colored, bubblegum flavored solution. Each 5 mL (teaspoonful) of Prednisolone Sodium Phosphate Oral Solution contains 6.7 mg prednisolone sodium phosphate (5 mg prednisolone base) in a palatable, aqueous vehicle.

Prednisolone Sodium Phosphate Oral Solution also contains dibasic sodium phosphate, edetate disodium, methylparaben, purified water, sodium biphosphate, sorbitol, and bubblegum flavor.

Prednisolone sodium phosphate occurs as white or slightly yellow, friable granules or powder. It is freely soluble in water; soluble in methanol; slightly soluble in alcohol and in chloroform; and very slightly soluble in acetone and in dioxane. The chemical name of prednisolone sodium phosphate is pregna- 1,4-diene-3,20- dione, 11,17-dihydroxy-21-(phosphonooxy)-, disodium salt, (11β)-. The empirical formula is $C_{21}H_{27}Na_2O_8P$; the molecular weight is 484.39. Its chemical structure is:



Pharmacological Category: Glucocorticoid

CLINICAL PHARMACOLOGY:

Naturally occurring glucocorticoids (hydrocortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Prednisolone is a synthetic adrenocortical steroid drug with predominantly glucocorticoid properties. Some of these properties reproduce the physiological actions of endogenous glucocorticosteroids, but others do not necessarily reflect any of the adrenal hormones' normal functions; they are seen only after administration of large therapeutic doses of the drug. The pharmacological effects of prednisolone which are due to its glucocorticoid properties include: promotion of gluconeogenesis; increased deposition of glycogen in the liver; inhibition of the utilization of glucose; anti-insulin activity; increased catabolism of protein; increased lipolysis; stimulation of fat synthesis and storage; increased glomerular filtration rate and resulting increase in urinary excretion of urate (creatinine excretion remains unchanged); and increased calcium excretion.

Depressed production of eosinophils and lymphocytes occurs, but erythropoiesis and production of polymorphonuclear leukocytes are stimulated. Inflammatory processes (edema, fibrin deposition, capillary dilatation, migration of leukocytes and phagocytosis) and the later stages of wound healing (capillary proliferation, deposition of collagen, cicatrization) are inhibited.

Prednisolone can stimulate secretion of various components of gastric juice. Suppression of the production of corticotropin may lead to suppression of endogenous corticosteroids. Prednisolone has slight mineralocorticoid activity, whereby entry of sodium into cells and loss of intracellular potassium is stimulated. This is particularly evident in the kidney, where rapid ion exchange leads to sodium retention and hypertension.

Prednisolone is rapidly and well absorbed from the gastrointestinal tract following oral administration. Prednisolone sodium phosphate oral solution produces a 14% higher peak plasma level of prednisolone which occurs 20% faster than that seen with tablets. Prednisolone is 70-90% protein-bound in the plasma and it is eliminated from the plasma with a half-life of 2 to 4 hours. It is metabolized mainly in the liver and excreted in the urine as sulfate and glucuronide conjugates.

INDICATIONS AND USAGE:

Prednisolone Sodium Phosphate Oral Solution is indicated in the following conditions:

1. **Endocrine Disorders**

   Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance); congenital adrenal hyperplasia; hypercalcemia associated with cancer; nonsuppurative thyroiditis.

2. **Rheumatic Disorders**

   As adjunctive therapy for short term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low dose maintenance therapy); ankylosing spondylitis; acute and subacute bursitis; acute nonspecific tenosynovitis; acute gouty arthritis; epicondylitis. For the treatment of systemic lupus erythematosus, dermatomyositis (polymyositis), polymyalgia rheumatica, Sjogren's syndrome, relapsing polychondritis, and certain cases of vasculitis.

3. **Dermatologic Diseases**

   Pemphigus; bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-Johnson syndrome); exfoliative erythroderma; mycosis fungoides.

4. **Allergic States**

   Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in adult and pediatric populations with: seasonal or perennial allergic rhinitis; asthma; contact dermatitis, atopic dermatitis, serum sickness; drug hypersensitivity reactions.

5. **Ophthalmic Diseases**

   Uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids; temporal arteritis; sympathetic ophthalmia.

6. **Respiratory Diseases**

   Symptomatic sarcoidosis; idiopathic eosinophilic pneumonias; fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy; asthma (as distinct from allergic asthma listed above under "Allergic States"), hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, acute exacerbations of chronic obstructive pulmonary disease (COPD), and Pneumocystis carinii pneumonia (PCP) associated with hypoxemia occurring in an HIV (+) individual who is also under treatment with appropriate anti-PCP antibiotics. Studies support the efficacy of systemic corticosteroids for the treatment of these conditions: allergic bronchopulmonary aspergillosis, idiopathic bronchiolitis obliterans with organizing pneumonia.

7. **Hematologic Disorders**

   Idiopathic thrombocytopenic purpura in adults; selected cases of secondary thrombocytopenia; acquired (autoimmune) hemolytic anemia; pure red cell aplasia; Diamond-Blackfan anemia.

8. **Neoplastic Diseases**

   For the treatment of acute leukemia and aggressive lymphomas in adults and children.

9. **Edematous States**

   To induce diuresis or remission of proteinuria in nephrotic syndrome in adults with lupus erythematosus and in adults and pediatric populations, with idiopathic nephrotic syndrome, without uremia.

10. **Gastrointestinal Diseases**

    To tide the patient over a critical period of the disease in: ulcerative colitis; regional enteritis.

11. **Nervous System**

    Acute exacerbations of multiple sclerosis.

12. **Miscellaneous**

    Tuberculous meningitis with subarachnoid block or impending block, tuberculosis with enlarged mediastinal lymph nodes causing respiratory difficulty, and tuberculosis with pleural or pericardial effusion (appropriate antituberculous chemotherapy must be used concurrently when treating any tuberculosis complications); Trichinosis with neurologic or myocardial involvement; acute or chronic solid organ rejection (with or without other agents).

ENLARGED TO 110% BY FDA STAFF

CONTRAINDICATIONS:

Systemic fungal infections.
Hypersensitivity to the drug or any of its components.

WARNINGS:

General:

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

Endocrine:

Corticosteroids can produce reversible hypothalamic-pituitary adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment.

Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Infections (general):

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. There may be decreased resistance and inability to localize infection when corticosteroids are used. Infection with any pathogen including viral, bacterial, fungal, protozoan or helminthic infection, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect humoral or cellular immunity, or neutrophil function. These infections may be mild to severe, and, with increasing doses of corticosteroids, the rate of occurance of infectious complications increases. Corticosteroids may also mask some signs of infection after it has already started.

Viral infections:

Chicken pox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information). If chicken pox develops, treatment with antiviral agents should be considered.

Special pathogens:

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Candida, Mycobacterium, Ameba, Toxoplasma, Pneumocystis, Cryptococus, Nocardia, etc.

Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea.

Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Corticosteroids should not be used in cerebral malaria.

Tuberculosis:

The use of prednisolone in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy these patients should receive chemoprophylaxis.

Vaccination:

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered, however, the response to such vaccines can not be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease.

Ophthalmic:

Use of corticosteroids may produce posterior subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to bacteria, fungi or viruses. The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes. Corticosteroids should not be used in active ocular herpes simplex.

Cardio-renal:

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

PRECAUTIONS:

General:

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy, most often for chronic conditions. Discontinuation of corticosteroids may result in clinical improvement.

Endocrine:

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Ophthalmic:

Intraocular pressure may become elevated in some individuals. If steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored.

Neuro-psychiatric: Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis, they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION)

An acute myopathy has been observed with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevation of creatinine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Gastrointestinal:

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending

perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer.

Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent.

Cardio-renal:

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with hypertension, congestive heart failure, or renal insufficiency.

Musculoskeletal:

Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (i.e. decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in the protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in children and adolescents and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy.

Information for Patients:

Patients should be warned not to discontinue the use of Prednisolone Sodium Phosphate Oral Solution abruptly or without medical supervision, to advise any medical attendants that they are taking Prednisolone Sodium Phosphate Oral Solution and to seek medical advice at once should they develop fever or other signs of infection.

Persons who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chicken pox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

Drug Interactions:

Drugs such as barbiturates, phenytoin, ephedrine, and rifampin, which induce hepatic microsomal drug metabolizing enzyme activity may enhance metabolism of prednisolone and require that the dosage of Prednisolone Sodium Phosphate Oral Solution be increased.

Increased activity of both cyclosporin and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

Estrogens may decrease the hepatic metabolism of certain corticosteroids thereby increasing their effect.

Ketoconazole have been reported to decrease the metabolism of certain corticosteroids by up to 60% leading to an increased risk of corticosteroid side effects.

Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.

Concomitant use of aspirin (or other non-steroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.

When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., diuretics, amphotericin-B), patients should be observed closely for development of hypokalemia. Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.

Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

Due to inhibition of antibody response, patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. If possible, routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued.

Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.

Corticosteroids may suppress reactions to skin tests.

Pregnancy: Teratogenic effects: Pregnancy Category C. Prednisolone has been shown to be teratogenic in many species when given in doses equivalent to the human dose. Animal studies in which prednisolone has been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. There are no adequate and well-controlled studies in pregnant women. Prednisolone Sodium Phosphate Oral Solution should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Mothers:

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Prednisolone Sodium Phosphate Oral Solution is administered to a nursing woman.

Pediatric Use:

The efficacy and safety of prednisolone in the pediatric population are based on the well-established course of effect of corticosteroids which is similar in pediatric and adult populations. Published studies provide evidence of efficacy and safety in pediatric patients for the treatment of nephrotic syndrome (>2 years of age), and aggressive lymphomas and leukemias (>1 month of age). However, some of these conclusions and other indications for pediatric use of corticosteroids, e.g., severe asthma and wheezing, are based on adequate and well-controlled trials conducted in adults, on the premises that the course of the diseases and their pathophysiology are considered to be substantially similar in both populations.

The adverse effects of prednisolone in pediatric patients are similar to those in adults (see ADVERSE REACTIONS). Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis. Children who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity. This negative impact of corticosteroids on growth has been observed at low systemic doses and in the absence of laboratory evidence of HPA axis suppression (i.e., cosyntropin stimulation and basal cortisol plasma levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in children than some commonly used tests of HPA axis function. The linear growth of children treated with corticosteroids by any route should be monitored, and the potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of other treatment alternatives. In order to minimize the potential growth effects of corticosteroids, children should be titrated to the lowest effective dose.

ADVERSE REACTIONS (listed alphabetically under each subsection):

Fluid and Electrolyte Disturbances: Congestive heart failure in susceptible patients; fluid retention; hypertension; hypokalemic alkalosis; potassium loss; sodium retention.

Cardiovascular: Hypertrophic cardiomyopathy in premature infants.

Musculoskeletal: Aseptic necrosis of femoral and humeral heads; loss of muscle mass; muscle weakness; osteoporosis; pathologic fracture of long bones; steroid myopathy; tendon rupture; vertebral compression fractures.

Gastrointestinal: Abdominal distention; elevation in serum liver enzyme levels (usually reversible upon discontinuation); pancreatitis; peptic ulcer with possible perforation and hemorrhage; ulcerative esophagitis.

Dermatologic: Facial erythema; increased sweating; impaired wound healing; may suppress reactions to skin tests; petechiae and ecchymoses; thin fragile skin; urticaria; edema.

Metabolic: Negative nitrogen balance due to protein catabolism.

Neurological: Convulsions; headache; increased intracranial pressure with papilledema (pseudotumor cerebri), usually following discontinuation of treatment; psychic disorders; vertigo.

Endocrine: Decreased carbohydrate tolerance; development of cushingoid state; hirsutism; increased requirements for insulin or oral hypoglycemic agents in diabetes; manifestations of latent diabetes mellitus; menstrual irregularities; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; suppression of growth in children.

Opthalmic: Exophthalmos; glaucoma; increased intraocular pressure; posterior subcapsular cataracts.

Other: Increased appetite; malaise; nausea; weight gain.

OVERDOSAGE:

The effects of accidental ingestion of large quantities of prednisolone over a very short period of time have not been reported, but prolonged use of the drug can produce mental symptoms, moon face, abnormal fat deposits, fluid retention, excessive appetite, weight gain, hypertrichosis, acne, striae, ecchymosis, increased sweating, pigmentation, dry scaly skin, thinning scalp hair, increased blood pressure, tachycardia, thrombophlebitis, decreased resistance to infection, negative nitrogen balance with delayed bone and wound healing, headache, weakness, menstrual disorders, accentuated menopausal symptoms, neuropathy, fractures, osteoporosis, peptic ulcer, decreased glucose tolerance, hypokalemia, and adrenal insufficiency. Hepatomegaly and abdominal distention have been observed in children.

Treatment of acute overdosage is by immediate gastric lavage or emesis followed by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy the dosage of prednisolone may be reduced only temporarily, or alternate day treatment may be introduced.

DOSAGE AND ADMINISTRATION:

The initial dosage of Prednisolone Sodium Phosphate Oral Solution may vary from 5 mL to 60 mL (5 to 60 mg prednisolone base) per day depending on the specific disease entity being treated. In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time, there is a lack of satisfactory clinical response, Prednisolone Sodium Phosphate Oral Solution should be discontinued and the patient placed on other appropriate therapy. **IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.** After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of Prednisolone Sodium Phosphate Oral Solution for a period of time consistent with the patient's condition. If after long term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

In the treatment of acute exacerbations of multiple sclerosis, daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day or 4 to 8 mg dexamethasone every other day for one month have been shown to be effective.

In pediatric patients, the initial dose of Prednisolone Sodium Phosphate Oral Solution may vary depending on the specific disease entity being treated. The range of initial doses is 0.14 to 2 mg/kg/day in three or four divided doses (4 to 60 mg/m2bsa/day).

The standard regimen used to treat nephrotic syndrome in pediatric patients is 60 mg/m2/day given in three divided doses for 4 weeks, followed by 4 weeks of single dose alternate-day therapy at 40 mg/m2/day.

The National Heart, Lung, and Blood Institute (NHLBI) recommended dosing for systemic *prednisone, prednisolone or methylprednisolone* in children whose asthma is uncontrolled by inhaled corticosteroids and long-acting bronchodilators is 1-2 mg/kg/day in single or divided doses. It is further recommended that short course, or "burst" therapy, be continued until a child achieves a peak expiratory flow rate of 80% of his or her personal best or symptoms resolve. This usually requires 3 to 10 days of treatment, although it can take longer. There is no evidence that tapering the dose after improvement will prevent a relapse.

For the purpose of comparison, the following is the equivalent milligram dosage of the various glucocorticoids:

Cortisone, 25	*Triamcinolone, 4*
Hydrocortisone, 20	*Paramethasone, 2*
Prednisolone, 5	*Betamethasone, 0.75*
Prednisone, 5	*Dexamethasone, 0.75*
Methylprednisolone, 4	

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intramuscularly or into joint spaces, their relative properties may be greatly altered.

HOW SUPPLIED:

Prednisolone Sodium Phosphate (prednisolone sodium phosphate, USP) Oral Solution is a colorless to light straw colored solution containing 6.7 mg prednisolone sodium phosphate (5 mg prednisolone base) per 5 mL (teaspoonful).

NDC 0574-0148-04 120 mL bottle

Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

Paddock Laboratories, Inc.
Minneapolis, MN 55427

Paddock Laboratories, Inc.

2122671 (06-02B)

NDC 0574-0148-04

Prednisolone Sodium Phosphate Oral Solution (Prednisolone Sodium Phosphate, USP)

Rx only

Bubble Gum Flavor

ORAL SOLUTION
5 mg (base)/5 mL*

ALCOHOL FREE, DYE FREE, SUGAR FREE

120 mL (4 fl. oz.)

DOSAGE: For complete dosage information please consult package insert.

***DESCRIPTION:** Each 5 mL (teaspoonful) contains prednisolone sodium phosphate 6.7 mg (5 mg prednisolone base) in a bubble gum flavored solution.

NOTE: See package insert for full prescribing information, including contraindications, warnings and precautions.

Store at 4°- 25°C (39°- 77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

Paddock Laboratories, Inc.
Minneapolis, MN 55427

Paddock Laboratories, Inc.

2122671 (06-028)

Paddock Laboratories, Inc.

ANDA 75-988: Prednisolone Sodium Phosphate, USP
Minor Amendment

0022

NDC 0574-0148-04

Prednisolone Sodium Phosphate Oral Solution (Prednisolone Sodium Phosphate, USP)

Rx only

Bubble Gum Flavor

APPROVED MAY 25 2004

ORAL SOLUTION
5 mg (base)/5 mL*

ALCOHOL FREE, DYE FREE, SUGAR FREE

120 mL (4 fl. oz.)

Paddock Laboratories, Inc.

3 05740 14804 4

NDC 0574-0148-04

Prednisolone Sodium Phosphate Oral Solution (Prednisolone Sodium Phosphate, USP)

Rx only

Bubble Gum Flavor

APPROVED MAY 25 2004

ORAL SOLUTION
5 mg (base)/5 mL*

ALCOHOL FREE, DYE FREE, SUGAR FREE

120 mL (4 fl. oz.)

Paddock Laboratories, Inc.

DOSAGE: For complete dosage information please consult package insert.

***DESCRIPTION:** Each 5 mL (teaspoonful) contains prednisolone sodium phosphate 6.7 mg (5 mg prednisolone base) in a bubble gum flavored solution.

NOTE: See package insert for full prescribing information, including contraindications, warnings and precautions.

Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

Paddock Laboratories, Inc.
Minneapolis, MN 55427

2170074 (06-02B)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

LABELING REVIEW(S)

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-988
Date of Submission: September 14, 2000
Applicant's Name: Paddock Laboratories, Inc.
Established Name: Prednisolone Sodium Phosphate Oral Solution, 5 mg (base)/5 mL
Proposed Proprietary Name: [redacted]

Labeling Deficiencies:

1. **GENERAL COMMENTS**
   Your proposed proprietary name "[redacted] is under review. We defer comment on the proposed name at this time.

2. **CONTAINER** – 120mL bottles

   a. Front Panel
      i. See GENERAL COMMENTS above.

      ii. 5 mg (base)/5 mL*

      iii. Revise to "quantity statement" to read as follows

      120 mL (4 fl. oz.)

   b. Side Panel
      *DESCRIPTION: Each 5 mL (teaspoonful)...

3. **CARTONS** – for 120 mL bottles

   See comments listed under 2(a.) and 2. (b.) above.

4. **PACKAGE INSERT**

   a. See GENERAL COMMENTS listed above.

   b. See comment under 2.(a.)ii. listed above

Please revise your labels and labeling, as instructed above, and submit in final print.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm. Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECK LIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23 (See FTR)		x	
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? **Waiting for response from ODS.**			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	X		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x

Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			X
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?			x
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		x	
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. **MODEL LABELING**
   The most recently labeling for **Pediapred** ® Oral Solution (NDA 19-157/S-011, 012 & 013; approved December 17, 1998)
   Prednisolone Sodium Phosphate is listed in the USP 24, but "Prednisolone Sodium Phosphate Oral Solution" is not subject to USP 24 monograph.
2. **This drug product CONTAINS NO ALCOHOL.**
3. The manufacturing will be done by Paddock Laboratories Inc. (B. 1.1 page 358)
4. INACTIVE INGREDIENTS
   The listing of inactive ingredients in the DESCRIPTION section of the package insert **DOES NOT** appear to be consistent with the listing of inactive ingredients found in the statement of components and composition appearing on vol. B. 1.1, page 315.
5. PATENTS/EXCLUSIVITIES

Patent Data – NDA 19-157

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
4448774	December 22, 2002	None		IV	None

Exclusivity Data– NDA 19-157

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

The firms statement is accurate.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
NDA - CONTAINER: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

INSERT: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

ANDA - CONTAINER: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

INSERT: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

7. PACKAGING CONFIGURATIONS
NDA - 120 mL
ANDA – 120 mL bottles in — bottles with a CRC closure.

8. CONTAINER/CLOSURE SYSTEM
Container: Amber '— bottles
Closure - 120 mL bottles in — bottles with a CRC closure.(See page 536 vol. B. 1.2)

Date of Review: March 11, 2002 Date of Submission: September 14, 2000 (Draft)

Primary Reviewer: Date: 3/14/02

Team Leader: John Grace Date: 3/14/2002

---

cc:

ANDA: 75-988
DUP/DIVISION FILE
HFD-613/JBforDCatterson/JGrace (no cc)
V:\FIRMSNZ\PADDOCK\LTRS&REV\75988na1.l
Review

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 75-988
Date of Submission: October 16, 2002 (FPL)
Applicant's Name: Paddock Laboratories, Inc.
Established Name: Prednisolone Sodium Phosphate Oral Solution, 5 mg (base)/5 mL

APPROVAL SUMMARY

Do you have 12 Final Printed Labels and Labeling? Yes.

CONTAINER – bottles containing 120 mL
Satisfactory in **final print** as of the October 16, 2002 submission, Rev. 06-02B, Vol. A4.1

CARTON – bottles containing 120 mL
Satisfactory in **final print** as of the October 16, 2002 submission, Rev. 06-02B, Vol. A4.1

PACKAGE INSERT
Satisfactory in **final print** as of the October 16, 2002 submission; Rev. 06-02B, Vol. A4.1

Revisions needed post-approval: No

PATENTS/EXCLUSIVITIES

Patent Data – NDA 19-157

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
4448774	December 22, 2002	None	Steroid formulation	III	None

Exclusivity Data– NDA 19-157

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

BASIS OF APPROVAL:
Was this approval based upon a petition? No.
What is the RLD on the 356(h) form: Pediapred®
NDA Number: 19-157
NDA Drug Name: Pediapred® (prednisolone sodium phosphate oral solution)
NDA Firm: Celltech Pharmaceuticals, Inc.
Date of Approval of NDA Insert and supplement: December 17, 1998; 19-157/ S-011, S-012, S-013, S-015
Has this been verified by the MIS system for the NDA? Yes.
Was this approval based upon an OGD labeling guidance? No.
Basis of Approval for the Container Labels: Most recently approved labeling of the reference listed drug.
Basis of Approval for the Carton Labeling: Most recently approved labeling of the reference listed drug.

REVIEW OF PROFESSIONAL LABELING CHECK LIST

(The following comments are from the previous reviewer, except those bold and italics)

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		x	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 23 (See FTR)		x	
Is this name different than that used in the Orange Book?		x	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.	X		
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present? **Waiting for response from ODS.** ***Name denied by DMETS. Firm withdrew the name in the 10/16/02 amendment.***			
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?	X		
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.	X		
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		x	
Does the package proposed have any safety and/or regulatory concerns?		x	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		x	
Is the strength and/or concentration of the product unsupported by the insert labeling?		x	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		x	
Are there any other safety concerns?		x	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		x	
Has applicant failed to clearly differentiate multiple product strengths?		X	
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	

Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?			x
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			x
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?			x
Has the firm failed to describe the scoring in the HOW SUPPLIED section?			x
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			X
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		x	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?			x
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			x
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)			x
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?		x	
Does USP have labeling recommendations? If any, does ANDA meet them?			x
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		x	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.		x	
Bioequivalence Issues: (Compare bioeqivalency values: insert to study. List Cmax, Tmax, T 2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		x	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		x	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. **MODEL LABELING**
   The most recently labeling for **Pediapred** ® Oral Solution (NDA 19-157/S-011, 012 & 013; approved December 17, 1998)
   Prednisolone Sodium Phosphate is listed in the USP 24, but "Prednisolone Sodium Phosphate Oral Solution" is not subject to USP 24 monograph.

(The following comments are from the previous reviewer, except those bolded and italicized)

2. **This drug product CONTAINS NO ALCOHOL.**
3. The manufacturing will be done by Paddock Laboratories Inc. (B. 1.1 page 358)
4. ***INACTIVE INGREDIENTS***
   The listing of inactive ingredients in the DESCRIPTION section of the package insert DOES appear to be consistent with the listing of inactive ingredients found in the

statement of components and composition appearing on pg. 3 of the April 25, 2002 submission vol. A. 4.1. Note: The inactive ingredient "sodium biphosphate" that appears on the PI is the same as "sodium phosphate monobasic" that appears on the CC statement (according to the chemist, John Franolic, on 1/24/02).

5. PATENTS/EXCLUSIVITIES

Patent Data – NDA 19-157

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
4448774	December 22, 2002	None		III	None

Exclusivity Data– NDA 19-157

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

The firms statement is accurate.

6. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON

NDA - CONTAINER: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

INSERT: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

ANDA - CONTAINER: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

INSERT: Store at 4°-25°C (39°-77°F). May be refrigerated. Keep tightly closed and out of the reach of children.

7. PACKAGING CONFIGURATIONS

NDA - 120 mL

ANDA – 120 mL bottles in — bottles with a CRC closure.

8. CONTAINER/CLOSURE SYSTEM

Container: Amber — bottles

Closure - 120 mL bottles in — bottles with a CRC closure.(See page 536 vol. B. 1.2)

9. PROPRIETARY NAME

The name "———— ' was denied by DMETS. In the October 16, 2002 amendment, the firm requested to withdraw the name.

Date of Review: December 26, 2002 **Date of Submission: October 16, 2002**

Primary Reviewer: Ruby Wu RWu **Date:** 12/26/02

Team Leader: John Grace John J Grace **Date:** 2/21/2003

cc:

ANDA: 75-988
DUP/DIVISION FILE
HFD-613/RWu/JGrace (no cc)
V:\FIRMSNZ\PADDOCK\LTRS&REV\75988.ap.L.doc
Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

CHEMISTRY REVIEW(S)