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

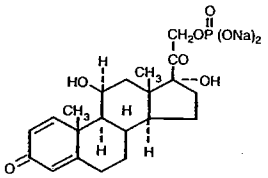
(prednisolone sodium phosphate, USP)
5 mg (base)/ 5 mL*
Rx only

***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)

OFFICE OF GENERIC DRUGS

ABBREVIATED NEW DRUG APPLICATION
CHEMISTRY, MANUFACTURING AND CONTROLS REVIEW

1. **CHEMIST'S REVIEW NO.#** 1

2. **ANDA #** 75-988

3. **NAME AND ADDRESS OF APPLICANT:**
Paddock Laboratories, Inc.
Att. Carol Subialka
3940 Quebec Avenue North
Minneapolis, MN 55427

4. **LEGAL BASIS OF SUBMISSION:**
Reference Listed Drug: **Pediapred® (prednisolone sodium phosphate, USP) oral solution**
Manufacturer: Medeva Pharmaceuticals, Inc. , NDA # 19-157
The applicant has certified that in their opinion and to the best of their knowledge, there is one patent that claims the listed drug referred to in the application. The patent (PIII certification), Patent No. 4448774, will expire on December 22, 2002. The applicant further certifies that it does not intend to market Prednisolone Sodium Phosphate, USP Oral Solution until Patent No. 4448774 has expired.
According to information published in the list of Approved Drug Products 20th edition, Pediapred (prednisolone sodium phosphate, USP) oral solution is not entitled to marketing exclusivity under section 505(j)(4)(D) of the Act.

5. **SUPPLEMENT(s):** N/A

6. **PROPRIETARY NAME:** ————

7. **NONPROPRIETARY NAME:** Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 mL

8. **SUPPLEMENT(s) PROVIDE(s) FOR:** N/A

9. **AMENDMENTS AND OTHER DATES:**

Firm:

09-14-2000	Original submission date
11-02-2000	Additional information - qualitative and quantitative breakdown of the raw materials in the bubble gum flavor
11-13-2000	New correspondence - revised form 356h and additional copies of finished drug product specifications and analytical methods with USP designation removed from product name
11-29-2000	New correspondence- response to teleconference (11/22/00): copies of method validation package

FDA:

10-30-2000	Teleconference -request for qualitative and quantitative breakdown of bubble gum flavor
11-09-2000	Teleconference - request for new form 356h and new copies of the methods validation and specifications with USP designation removed from the product name
11-09-2000	ANDA acceptance letter
11-22-2000	Teleconference - request for 2 copies of analytical methods pages 628-1205

10. **PHARMACOLOGICAL CATEGORY**: Glucocorticoid

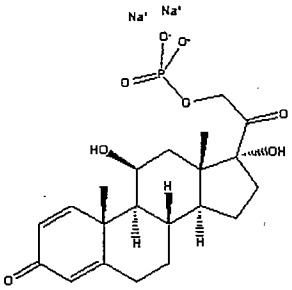
11. **Rx or OTC**: Rx

12. **RELATED IND/NDA/DMF(s)**: Approved NDA # 19-157 for innovator; DMFs: see DMF checklist

13. **DOSAGE FORM**: Solution

14. **STRENGTH**: 5 mg/5mL

15. **CHEMICAL NAME, STRUCTURE AND PHYSICAL PROPERTIES**:
Prednisolone sodium phosphate. Pregna-1,4-diene-3,20-dione,11,17-dihydroxy-21-(phosphonooxy)-,disodium salt, (11β)-. $C_{21}H_{27}Na_2O_8P$. 484.39. [125-02-0]. Glucocorticoid.



16. **COMMENTS**:
The following sections are *NOT SATISFACTORY*
    20. Components and Composition
    23. Raw Material Controls
    26. Manufacturing and Processing
    27. Container/Closure
    29. Laboratory controls
    30. Stability
    31. Samples and Results

17. **CONCLUSIONS AND RECOMMENDATIONS**:
The application is not approvable. A NA MAJOR will issue.

18. **RECORDS AND REPORTS**: N/A

19. **REVIEWER**: John D. Franolic, Ph.D. **DATE COMPLETED**: 02/16/2001
Endorsed by D. Gill, Ph.D.

Redacted 27 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #1

cc: ANDA 75-988
Field Copy
Division File

Endorsements:

HFD-623/J. Franolic/02/16/01 J. Franolic 2/20/01
HFD-623/S. Sherken for D.Gill, Ph.D./02/20/01 S. Sherken 2/23/01
HFD-619/R.Yu/02/21/01 RYu 2/23/01
F/T by: gp/02/21/01
V:\FIRMSNZ\PADDOCK\LTRS&REV\75988.CR1.DOC

A NA MAJOR will issue.

ANDA 75-988

Prednisolone Sodium Phosphate Oral Solution, 5 mg/5mL

Paddock Laboratories, Inc.

John D. Franolic, Ph.D.
Office of Generic Drugs, Division of Chemistry I

Table of Contents

Table of Contents 2

Chemistry Review Data Sheet 3

The Executive Summary 7

I. Recommendations 7

A. Recommendation and Conclusion on Approvability 7

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 7

II. Summary of Chemistry Assessments 7

A. Description of the Drug Product(s) and Drug Substance(s) 7

B. Description of How the Drug Product is Intended to be Used 8

C. Basis for Approvability or Not-Approval Recommendation 8

III. Administrative 9

A. Reviewer's Signature 9

B. Endorsement Block 9

C. CC Block 9

Chemistry Assessment 10

I. Review Of Common Technical Document-Quality (Ctd-Q) Module 3.2: Body Of Data ..... N/A

S DRUG SUBSTANCE [Name, Manufacturer] ..... N/A

P DRUG PRODUCT [Name, Dosage form] ..... N/A

A APPENDICES ..... N/A

R REGIONAL INFORMATION ..... N/A

II. Review Of Common Technical Document-Quality (Ctd-Q) Module 1 ..... N/A

A. Labeling & Package Insert ..... N/A

B. Environmental Assessment Or Claim Of Categorical Exclusion ..... N/A

III. List Of Deficiencies To Be Communicated 37

Chemistry Review Data Sheet

1. ANDA 75-988

2. REVIEW #2

3. REVIEW DATE: 12-Sept-2002

4. REVIEWER: John D. Franolic, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Firm:	
Original Submission	14-Sep-2000
Additional Information (bubble gum flavor)	02-Nov-2000
New Correspondence (356h and revised specs)	13-Nov-2000
New Correspondence (response to 11/22/00 t-con)	29-Nov-2000
FDA:	
T-con (request for bubble gum components)	30-Oct-2000
T-con (request for revised 356h and specs)	09-Nov-2000
Acceptable for filing letter	09-Nov-2000
T-con (request for analytical methods package)	22-Nov-2000
Bioequivalence acceptable	22-Dec-2000
Deficiency Letter (NA MAJOR)	28-Feb-2001

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Major Amendment	25-Apr-2002

7. NAME & ADDRESS OF APPLICANT:

Chemistry Review Data Sheet

Name:	Paddock Laboratories, Inc.
Address:	3940 Quebec Avenue North Minneapolis, MN 55427
Representative:	Paul Bulger
Telephone:	(763) 546-4676

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: ———

b) Non-Proprietary Name (USAN): Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL

9. LEGAL BASIS FOR SUBMISSION:

The basis for the proposed ANDA 75-988 for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, is the approved reference listed drug Pediapred®, the subject of application NDA #19-157 held by Medeva Pharmaceuticals, Inc.

The applicant has certified that in their opinion and to the best of their knowledge, there is one patent that claims the listed drug referred to in the application. The patent (PIII certification), Patent No. 4448774, will expire on December 22, 2002. The applicant further certifies that it does not intend to market Prednisolone Sodium Phosphate, USP Oral Solution until Patent No. 4448774 has expired. According to information published in the list of Approved Drug Products 20th edition, Pediapred (prednisolone sodium phosphate, USP) oral solution is not entitled to marketing exclusivity under section 505(j)(4)(D) of the Act.

10. PHARMACOL. CATEGORY: Glucocorticoid

11. DOSAGE FORM: Solution

12. STRENGTH/POTENCY: 5 mg/5 mL

13. ROUTE OF ADMINISTRATION: Oral

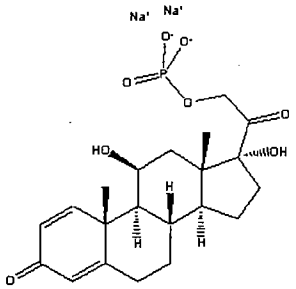
14. Rx/OTC DISPENSED: __X__ Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed
___X__Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name:
Pregna-1,4-diene-3,20-dione,11,17-dihydroxy-21-(phosphonooxy)-,disodium salt, (11β)-.
Molecular Formula: $C_{21}H_{27}Na_2O_8P$
Molecular Weight: 484.39
Structural Formula:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	II			1	Adequate	13-Sep-2002	Reviewed by John Franolic.
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

[1] Action codes for DMF Table:
1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	13-Nov-2001	
Methods Validation	Acceptable (w/comments)	19-Sep-2001	Pacific Regional NW Lab
Labeling	Pending		
Bioequivalence	Iv-vivo study waiver	22-Dec-2000	D. Connor
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

Redacted 32 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #2

cc: ANDA 75-988
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-623/John D. Franolic, Ph.D./09-27-2002 John D. Franolic 10/10/02

HFD-623 /Dave Gill, Ph,D./ N. Taliercio for 10/10/02

HFD-617 /S.Kim, Pharm D./ S. Li 10/10/02

F/T by:

V:\FIRMSNZ\PADDOCK\LTRS&REV\75988.CR2.DOC

TYPE OF LETTER: NOT APPROVABLE – MINOR

#3

CHEMISTRY REVIEW

ANDA 75-988

Prednisolone Sodium Phosphate Oral Solution, 5 mg/5mL

Paddock Laboratories, Inc.

Neeru B. Takiar
Office of Generic Drugs, Division of Chemistry I

Table of Contents

Table of Contents **2**

Chemistry Review Data Sheet **3**

The Executive Summary **7**

I. Recommendations 7

A. Recommendation and Conclusion on Approvability 7

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 7

II. Summary of Chemistry Assessments 7

A. Description of the Drug Product(s) and Drug Substance(s) 7

B. Description of How the Drug Product is Intended to be Used 8

C. Basis for Approvability or Not-Approval Recommendation 8

III. Administrative 9

A. Reviewer's Signature 9

B. Endorsement Block 9

C. CC Block 9

Chemistry Assessment **10**

Chemistry Review Data Sheet

1. ANDA 75-988

2. REVIEW #3

3. REVIEW DATE: July 31, 2003

4. REVIEWER: Neeru B. Takiar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Firm:	
Original Submission	14-Sep-2000
Additional Information (bubble gum flavor)	02-Nov-2000
New Correspondence (356h and revised specs)	13-Nov-2000
New Correspondence (response to 11/22/00 t-con)	29-Nov-2000
Major Amendment (Response to NA letter)	25-Apr-2002
FDA:	
T-con (request for bubble gum components)	30-Oct-2000
T-con (request for revised 356h and specs)	09-Nov-2000
Acceptable for filing letter	09-Nov-2000
T-con (request for analytical methods package)	22-Nov-2000
Bioequivalence acceptable	22-Dec-2000
Deficiency Letter (NA MAJOR)	28-Feb-2001
Deficiency Letter (NA MINOR)	18-Oct-2002

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Ist Minor Amendment	16-Jan-2003
Telephone Amendment	9-May-2003
Telephone Amendment	10-July-2003

7. NAME & ADDRESS OF APPLICANT:

Name: Paddock Laboratories, Inc.

Address: 3940 Quebec Avenue North
Minneapolis, MN 55427

Chemistry Review Data Sheet

Representative: David Rosenburg

Telephone: (763) 732-0297

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: ———
b) Non-Proprietary Name (USAN): Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL

9. LEGAL BASIS FOR SUBMISSION:

The basis for the proposed ANDA 75-988 for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, is the approved reference listed drug Pediapred®, the subject of application NDA #19-157 held by Medeva Pharmaceuticals, Inc.

The applicant has certified that in their opinion and to the best of their knowledge, there is one patent that claims the listed drug referred to in the application. The patent (PIII certification), Patent No. 4448774, will expire on December 22, 2002. The applicant further certifies that it does not intend to market Prednisolone Sodium Phosphate, USP Oral Solution until Patent No. 4448774 has expired. According to information published in the list of Approved Drug Products 20th edition, Pediapred (prednisolone sodium phosphate, USP) oral solution is not entitled to marketing exclusivity under section 505(j)(4)(D) of the Act.

10. PHARMACOL. CATEGORY: Glucocorticoid

11. DOSAGE FORM: Solution

12. STRENGTH/POTENCY: 5 mg/5 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __X__ Rx ___OTC

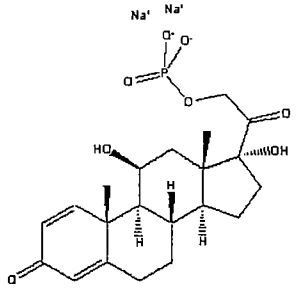
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed
___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name:
Pregna-1,4-diene-3,20-dione,11,17-dihydroxy-21-(phosphonooxy)-,disodium salt, (11β)-.
Molecular Formula: $C_{21}H_{27}Na_2O_8P$

Molecular Weight: 484.39
Structural Formula:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	II			1	Inadequate	7-30-2003	Annual Update reviewed by N. Takiar
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	13-Nov-2001	
Methods Validation	Acceptable (w/comments)	19-Sep-2001	Pacific Regional NW Lab
Labeling	Acceptable	03-21-2003	R.WU/John Grace
Bioequivalence	Iv-vivo study waiver	22-Dec-2000	S. Pradan/D. Connor
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __X__ Yes ____ No If no, explain reason(s) below:

APPEARS THIS WAY
ON ORIGINAL

Redacted 19 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #3

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-988 **APPLICANT:** Paddock Laboratories, Inc.

DRUG PRODUCT: Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 mL

The deficiency presented below represent a MINOR deficiency.

A. Deficiency:

Please note that DMF [redacted] is currently inadequate. The DMF holder, [redacted] has been notified.

Sincerely yours,

Rashmikant M. Patel, Ph. D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-988
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-623/Neeru B. Takiar/07-31-2003; Revised 08-04-2003 N. Takiar 8/14/03

HFD-623 /Dave Gill, Ph,D./8/4/03 DSG. 8-18-03

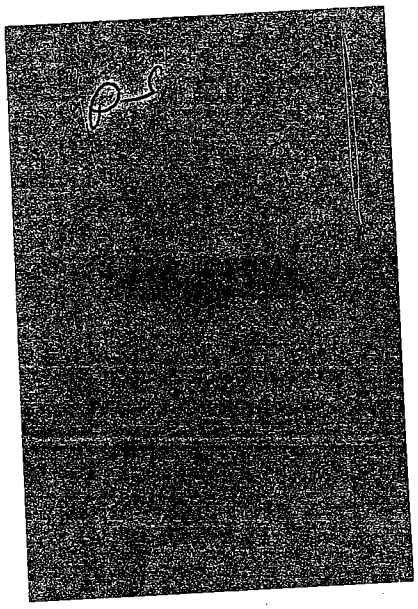
HFD-617 /S.Kim, Pharm D./8/13/03 S. K - 8/18/03

F/T by:ard/8/13/03

V:\FIRMSNZ\PADDOCK\LTRS&REV\75988CR3.doc

TYPE OF LETTER: NOT APPROVABLE (NA Minor – DMF Deficient)

APPEARS THIS WAY
ON ORIGINAL



ANDA 75-988

Prednisolone Sodium Phosphate Oral Solution, 5 mg/5mL

Paddock Laboratories, Inc.

Neeru B. Takiar
Office of Generic Drugs, Division of Chemistry III

Table of Contents

Table of Contents 2

Chemistry Review Data Sheet 3

The Executive Summary 7

I. Recommendations 7

A. Recommendation and Conclusion on Approvability 7

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 7

II. Summary of Chemistry Assessments 7

A. Description of the Drug Product(s) and Drug Substance(s) 7

B. Description of How the Drug Product is Intended to be Used 8

C. Basis for Approvability or Not-Approval Recommendation 8

III. Administrative 8

A. Reviewer's Signature 8

B. Endorsement Block 8

C. CC Block 9

Chemistry Assessment 10

Chemistry Review Data Sheet

1. ANDA 75-988

2. REVIEW #4

3. REVIEW DATE: February 9, 2004

4. REVIEWER: Neeru B. Takiar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Firm:	
Original Submission	14-Sep-2000
Additional Information (bubble gum flavor)	02-Nov-2000
New Correspondence (356h and revised specs)	13-Nov-2000
New Correspondence (response to 11/22/00 t-con)	29-Nov-2000
New Correspondence (response to 6/20/04 t-con)	16-Jul-2001
Major Amendment (Response to NA letter)	25-Apr-2002
Ist Minor Amendment	16-Jan-2003
Telephone Amendment	9-May-2003
Telephone Amendment	10-July-2003
FDA:	
T-con (request for bubble gum components)	30-Oct-2000
T-con (request for revised 356h and specs)	09-Nov-2000
Acceptable for filing letter	09-Nov-2000
T-con (request for analytical methods package)	22-Nov-2000
Bioequivalence acceptable	22-Dec-2000
Deficiency Letter (NA MAJOR)	28-Feb-2001
T-con (firm's request)	20-Jun-2001
Deficiency Letter (NA MINOR)	18-Oct-2002
Minor Amendment (2^{nd})	19-Aug-2003

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Minor Amendment	25-August-2003

7. NAME & ADDRESS OF APPLICANT:

Chemistry Review Data Sheet

Name: Paddock Laboratories, Inc.

Address: 3940 Quebec Avenue North
Minneapolis, MN 55427

Representative: David Rosenburg

Telephone: (763) 732-0297

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: NA
b) Non-Proprietary Name (USAN): Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL

9. LEGAL BASIS FOR SUBMISSION:

The basis for the proposed ANDA 75-988 for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, is the approved reference listed drug Pediapred®, the subject of application NDA #19-157 held by Celltech Pharmaceuticals, Inc.(formerly Medeva Pharmaceuticals, Inc.).

The applicant has certified that in their opinion and to the best of their knowledge, there is one patent that claims the listed drug referred to in the application. The patent (PIII certification), Patent No. 4448774, will expire on December 22, 2002. The applicant further certifies that it does not intend to market Prednisolone Sodium Phosphate, USP Oral Solution until Patent No. 4448774 has expired. According to information published in the list of Approved Drug Products 20th edition, Pediapred (prednisolone sodium phosphate, USP) oral solution is not entitled to marketing exclusivity under section 505(j)(4)(D) of the Act.

10. PHARMACOL. CATEGORY: Glucocorticoid

11. DOSAGE FORM: Solution

12. STRENGTH/POTENCY: 5 mg/5 mL

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __X__ Rx ___OTC

15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed
___X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

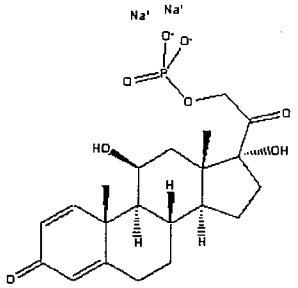
Chemical Name:

Pregna-1,4-diene-3,20-dione,11,17-dihydroxy-21-(phosphonooxy)-,disodium salt, (11β)-.

Molecular Formula: $C_{21}H_{27}Na_2O_8P$

Molecular Weight: 484.39

Structural Formula:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
	II			1	Aadequate	2-09-2004	Reviewed by N. Takiar
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		
	III			4	N/A		

[1] Action codes for DMF Table:

1 – DMF Reviewed.

Other codes indicate why the DMF was not reviewed, as follows:

2 –Type 1 DMF

3 – Reviewed previously and no revision since last review

4 – Sufficient information in application

5 – Authority to reference not granted

6 – DMF not available

7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending	05-Mar-2004	
Methods Validation	Acceptable	19-Sep-2001	Pacific Regional NW Lab
Labeling	Acceptable	03-21-2003	R.WU/John Grace
Bioequivalence	Iv-vivo study waiver	22-Dec-2000	S. Pradan/D. Connor
EA	N/A		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. _X_ Yes ____ No If no, explain reason(s) below:

APPEARS THIS WAY
ON ORIGINAL

Redacted 10 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #4

cc: ANDA 75-988
ANDA DUP
DIV FILE
Field Copy

Endorsements (Draft and Final with Dates):

HFD-623/N. Takiar/02-09-2004 N. Takiar 3/8/04
HFD-623 /D. Gill, Ph.D., TL/2-10-04 DS Gill 3-8-04
HFD-617 /S. Park, PM/3/5/04 S. Park 3/9/04
V:\FIRMSNZ\PADDOCK\LTRS&REV\75988.CR4.doc
F/T by: EW 3/8/04

TYPE OF LETTER: APPROVABLE; EES pending

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

BIOEQUIVALENCE REVIEW(S)

Prednisolone Sodium Phosphate, USP
Oral Solution, 5 mg/5 ml
ANDA #75-988
Reviewer: Sikta Pradhan
v:\firmsnz\Paddock\ltrs&rev\75988w.900

Paddock Laboratories, Inc.
Minneapolis, MN
Submission Date:
September 14, 2000

REVIEW OF A WAIVER REQUEST

I. Background

1. The firm has requested a waiver of an in vivo bioequivalence study requirement for its proposed product, Prednisolone Sodium Phosphate Oral solution, 5 mg/5 ml, manufactured by Paddock Laboratories, Inc. The reference listed product is Pediapred[R] oral liquid, 5 mg/5 ml, marketed by Medeva Pharmaceutical, Inc.

II. Formulation Comparison (Not to be released through FOI)

The test and reference formulations are compared as shown below:

Ingredient	Prednisolone Sodium Phosphate, Oral Liquid Test Product	Pediapred[R] Oral Liquid Ref. Product
	Amount per 5 mL	
Prednisolone sodium phosphate,	6.7 mg (5 mg prednisolone base)	6.7 mg (5 mg prednisolone base)
Dibasic sodium phosphate, USP		
Monobasic sodium phosphate, USP		
Methylparaben		
Edetate disodium		
Sorbitol, USP		
Bubble Gum Flavor		
Purified water		

III. Comments:

1. The test product, Prednisolone Oral Solution, 5 mg/5 ml, contains the same active ingredient in the same concentration and dosage form as the reference product. With the exception of the flavoring, the test formulation does not contain any inactive ingredients known to significantly affect absorption of the active ingredient or drug moieties.

2. Both the test and reference products are dye free oral solution.

3. As per the Agency request, the firm has provided (dated November 2,2000) the qualitative and quantitative formulations for the bubble gum flavoring used in the test formulation. The composition of the bubble gum flavoring (attached herewith) indicates that none of the components are present at the level greater than ←——————————→ . However, the amount of ——————————, present in the flavoring meets the Agency IIG requirements. Therefore, according to the Agency current policy, no safety evaluation is necessary for the bubble gum flavoring present in the test product.

4. Therefore, there are no other safety issues concerning the test formulation because it does not differ from the reference listed drug regarding inactive ingredients, except as indicated. Hence, the waiver of in vivo bioequivalence study may be granted under 21 CFR 320.22 (b)(3).

APPEARS THIS WAY
ON ORIGINAL

IV. Recommendation:

The Division of Bioequivalence agrees that the information submitted by Paddock Laboratories, Inc. on its drug product, Prednisolone Sodium Phosphate Oral Solution, 5 mg (base)/ 5ml, falls under 21 CFR section 320.22 (b) (3) of the Bioavailability/Bioequivalence Regulations. The waiver of an in vivo bioequivalence study for the drug is granted. The Division of Bioequivalence deems the test product, Prednisolone Sodium Phosphate Oral

Solution, 5 mg (base)/ 5ml, bioequivalent to the reference product, Pediapred[R] Oral Solution, 5 mg (base)/5 ml, manufactured by Medeva Pharmaceutical, Inc.

Sikta Pradhan

Sikta Pradhan, Ph.D.
Division of Bioequivalence
Review Branch I

RD INITIALED YCHUANG
FT INITIALED YCHUANG ---------- 12/18/2000

Concur: Barbara M. Davit Date: 12/22/00
for Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

cc: ANDA # 75988W.900 (Original, duplicate), HFD-652 (Huang, Pradhan), HFD-650 (Director), Drug File, Division File

Draft Date: 12/11/00
Final: 12/13/00

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

BIOEQUIVALENCE REVIEW ATTACHMENT

CC: ANDA #75-988
ANDA DUPLICATE
DIVISION FILE
BIO DRUG FILE
FIELD COPY

Endorsements: (Final with Dates)
HFD-652/ S. Pradhan
HFD-650/ Y. Huang 12/18/2000
HFD-617/ K. Scardina
HFD-650/ D. Conner 12/22/00

Printed in final on

V:\firmsnz\Paddock\ltrs&rev\75988W.900

1. Waiver (WAI) 5mg (base)/5 mL Submission date: 09-14-00

Outcome AC

OUTCOME DECISIONS: AC - Acceptable

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-988 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Prednisolone Sodium Phosphate, USP Oral solution, 5 mg (base)/5 ml

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Barbara M Saint

for Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 75-988 SPONSOR: Paddock Lab. Inc.

DRUG AND DOSAGE FORM: Prednisolone Sodium Phosphate, USP Oral Solution

STRENGTH(S): 5 mg / 5 ml

TYPES OF STUDIES: waiver

CLINICAL STUDY SITE(S): N/A

ANALYTICAL SITE(S): N/A

STUDY SUMMARY: please see review

DISSOLUTION: N/A

DSI INSPECTION STATUS

Inspection needed: YES / (NO)	Inspection status:	Inspection results:
First Generic No	Inspection requested: (date)	
New facility ____	Inspection completed: (date)	
For cause ____		
other ____		

PRIMARY REVIEWER: (NAME) BRANCH:

INITIAL: Sirata Radhan DATE: 12.18.00

TEAM LEADER: (NAME) BRANCH:

INITIAL: [illegible] DATE: 12/18/2000

for DIRECTOR, DIVISION OF BIOEQUIVALENCE: DALE P. CONNER, Pharm. D.

INITIAL: BNC DATE: 12/22/00

V:\division\bio\signoff.doc

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

ADMINISTRATIVE DOCUMENTS

Telecon Record

Date: **November 9, 2000**

ANDA: **75988**

Firm: **Paddock Laboratories, Inc.**

Drug: **Prednisolone Sodium Phosphate Oral Solution, 5mg/5ml**

FDA Participants: Martin Shimer

Industry Participants: **Carol Anding(voice mail)**

Phone #: **763-546-4676**

Agenda: **Marty called Carol to ask her to submit a new 356h leaving out the USP nomenclature for Prednisolone Sodium Phosphate Oral Solution, 5mg/5ml. Also since the chemistry will not follow a USP monograph Marty asked Carol to provide 2 additional copies of the methods validation.**

Telecon Record

Date: **November 22, 2000**

ANDA: **75988**

Firm: **Paddock Laboratories**

Drug: **Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 ml**

FDA Participants: Martin Shimer

Industry Participants: **Carol Anding**

Phone #: **763-546-4676**

Agenda: **Marty called Carol Anding at Paddock to ask her to submit 2 copies of the analytical methods pages 628-1205.**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date . APR 18 2001

From Acting Branch Chief, Investigations &
Preapproval Compliance Branch/DMPQ (HFD-324)

Subject Concurrence with District Withhold Recommendation,
ANDA 75-988 Prednisolone Sodium Phosphate
Oral Solution 5mg/5ml

To Pat Beers-Block, Chief
Review Support Branch, HFD-632

Applicant/Manufacturer: Paddock Laboratories, Inc.
3940 Quebec Avenue North
New Hope, MN 55427
CFN 2127022

Division of Manufacturing and Product Quality (DMPQ) has completed a review of an EIR for the subject ANDA. An inspection was conducted at the applicant's manufacturing facility on various dates between December 13, 2000 and January 17, 2001. This inspection included Pre-approval coverage of the oral solution manufacturing operation at this site and in particular, product specific coverage for the subject ANDA.

DMPQ concurs with the District's recommendation to withhold approval of this ANDA. A warning letter was issued by MIN-DO to Paddock Laboratories on March 6, 2001. The warning letter cites global cGMP deficiencies observed in the chemistry and microbiology laboratories that may effect the pending application. Although, Paddock has committed to corrections and hired a consultant, a reinspection should be conducted to verify compliance.

A copy of the EIR and exhibits are attached for your review. If you have questions, please contact me at (301)-827-0062.

Bruce Hartman

Attachments - EIR and Exhibits

cc:
HFD-324 R/F
HFR-CE800 DD
HFR-CE850 MFadden
HFD-324 BHartman
concur: JDietrick 4/18/00
a:\anda75.988

APPEARS THIS WAY
ON ORIGINAL

RECORD OF TELEPHONE CONVERSATION

Reference is made to the firms faxed dated June 18, 2001 requesting clarification on the February 28, 2001 deficiency letter.

Deficiency A.9

[redacted]. If differences are observed, the firm commits to perform further investigation.

The firm asked if this will be requested for other drug product. Dr. Franolic said this will be determined case by case.

Deficiency A.18

The document room never received the copies sent in November 2000. The firm will provide 2 separately bound copies of the methods validation package and the specifications to the attention of the document room.

DATE
June 20, 2001

APPLICATION NUMBER
75-988

TELECON

FDA PARTICIPANTS
Dave Gill
John Franolic
Ruby Yu

PRODUCT NAME
Prednisolone Sodium Phosphate Oral Solution

FIRM NAME
PADDOCK

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Carol Subialka, Mary Beth Erstead, Brad Costello, Jenny Yu, Paul Walter

TELEPHONE NUMBER
763-546-4676 x229

SIGNATURE
Dave Gill DSGill 6/20/01
John Franolic 6/20/01
Ruby Yu 6/20/01

Cc: Division Folder
ANDA
V:\FIRMSNZ\PADDOCK\TELECONS\75988.tc.062001.doc

RECORD OF TELEPHONE CONVERSATION

Reference is made to the unapproved ANDA 75-988. The following deficiencies/comments were communicated to the firm. 1. Reference is made to comments from the Methods Validation Lab. Please provide ——————————————— 2. Please provide stability data to support the storage temperatures stated in the Labeling (Store at 4-25°C). Alternately, please change the storage conditions to USP conditions. FDA asked if the firm performs freeze-thaw cycle studies. The firm stated that they will check whether they conducted these studies. The firm's response may be submitted as a telephone amendment.	**DATE:** April 16 2003 **ANDA NUMBER:** 75-988 **INITIATED BY:** FDA **PRODUCT NAME:** Prednisolone Sodium Phosphate Oral Solution 5 mg/5 mL **FIRM NAME:** Paddock Laboratories, Inc. **FIRM REPRESENTATIVE:** Mary Beth Erstad Maureen Rath Janine Kelly Patrick Johnson David Rosenberg Fred Kostial **PHONE NUMBER:** 763-732-0393 **FDA REPRESENTATIVE:** Dave Gill Neeru Takiar Sarah Kim **SIGNATURES:** Dave Gill DG Neeru Takiar NT 5/1/03 Sarah Kim S.K. 5/1/03

CC: ~~ANDA 75-988~~
Chem. I Telecon Binder
V:\FIRMSNZ\PADDOCK\TELECONS\75988.tc.041603.doc

RECORD OF TELEPHONE CONVERSATION

Reference is made to the unapproved ANDA 75-988.
The following deficiencies/comments were communicated to the firm.

1. [redacted]

2. Please provide supporting data to support the current labeled storage conditions. Also, please provide the freeze-thaw cycling data, which is required for refrigerated conditions (thaw: 25°C; freezing: -20°C to -10°C)

3. Please confirm the expiration date at the storage conditions.
   The firm stated that the expiration date should be [redacted] months for refrigerated storage conditions.

The firm's response may be submitted as a telephone amendment.

DATE:
June 23, 2003

ANDA NUMBER:
75-988

INITIATED BY:
FDA

PRODUCT NAME:
Prednisolone Sodium Phosphate Oral Solution
5 mg/5 mL

FIRM NAME:
Paddock Laboratories, Inc.

FIRM REPRESENTATIVE:
Mary Beth Erstad
Maureen Rath
Janine Kelly
Patrick Johnson
David Rosenberg
Fred Kostial

PHONE NUMBER:
763-732-0393

FDA REPRESENTATIVE:
Dave Gill DJG.JG
Neeru Takiar
Sarah Kim

SIGNATURES:
Dave Gill
Neeru Takiar NT/7/25/03
Sarah Kim 7/24/03

CC: ANDA 75-988
Chem. I Telecon Binder
V:\FIRMSNZ\PADDOCK\TELECONS\75988.tc.062303.doc

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 75-988

CORRESPONDENCE

75-988

Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

505(b)(2)(A) OK!
09-Nov-2000

September 14, 2000

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North
7500 Standish Place, Room 150
Rockville, MD 20855

Re: Abbreviated New Drug Application
for Prednisolone Sodium Phosphate, USP Oral Solution, 5 mg/5 mL

Dear Staff:

Paddock Laboratories, Inc. (Paddock Laboratories) is submitting this original abbreviated new drug application (ANDA), pursuant to Section 507 of the Federal Food, Drug and Cosmetic Act, seeking approval to market Paddock Laboratories' Prednisolone Sodium Phosphate, USP Oral Solution, 5 mg/5 mL. Paddock Laboratories' Prednisolone Sodium Phosphate, USP Oral Solution, 5 mg/5 mL is therapeutically equivalent to the listed drug, Pediapred® (prednisolone sodium phosphate, USP) Oral Solution, 5 mg/5 mL, manufactured by Medeva Pharmaceuticals, Inc., pursuant to NDA 19-157, in that there are no known or suspected bioequivalence problems.

This ANDA consists of three volumes. Paddock Laboratories is filing an archival copy (in blue folders) of the ANDA that contains all the information required in the ANDA, and a technical review copy (in red folders), that contains all the information in the archival copy. A separate copy of the Bioequivalence section (containing Sections I. through VII.) is provided in an orange folder.

We certify that, concurrently with filing this ANDA, a true copy of the technical sections of the ANDA (including a copy of the Form FDA 356h and a certification that its contents are a true copy of those filed with the Office of Generic Drugs) was sent to the local district office. This "field copy" was contained in burgundy folders.

3940 Quebec Avenue North, Minneapolis, MN 55427 • 763.546.4676 • FAX: 763.546.4842 • 800.328.5113

Please direct any written, telephone or fax communication regarding this ANDA to the following individual:

Carol Subialka, Regulatory Affairs Analyst
Paddock Laboratories, Inc.
3940 Quebec Avenue North
Minneapolis, Minnesota 55427
Phone: 763-546-4676
Fax: 763-546-4842

Thank you.

Sincerely,
Paddock Laboratories, Inc.

Carol Anding

Carol Anding
Regulatory Affairs Manager

enclosure

ANDA 75-988

Paddock Laboratories, Inc.
Attention: Carol Anding
3940 Quebec Avenue North
Minneapolis, Minnesota 55427

NOV 9 2000

Dear Madam:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated October 30, 2000 and your correspondence dated November 2, 2000.

NAME OF DRUG: Prednisolone Sodium Phosphate, USP Oral Solution, 5mg/5ml

DATE OF APPLICATION: September 14, 2000

DATE (RECEIVED) ACCEPTABLE FOR FILING: September 15, 2000

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

APPEARS THIS WAY
ON ORIGINAL

Should you have questions concerning this application, contact:

Ruby Yu
Project Manager
(301) 827-5848

Sincerely yours,

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

ANDA 75988
cc: DUP/Jacket
Division File
Field Copy
HFD-610/R.West
HFD-610/P.Rickman
HFD-92
HFD-615/M.Bennett
HFD-600/

Endorsement: HFD-615/NMahmud, Chief, RSB _____ date 09-Nov-2000
HFD-615/MShimer, CSO _____ date 11/03/2000
Word File V:\Firmnz\Paddock\Ltrs&rev.75988ack
F/T
ANDA Acknowledgment Letter!

Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

November 13, 2000

NEW CORRESP
NC

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

Re: **Revised Form FDA 356h and additional copies of specifications and analytical methods for finished drug product in response to telephone request of November 9, 2000 for ANDA 75-988 for Prednislone Sodium Phosphate Oral Solution, 5 mg/5 mL**

Dear Staff:

Please accept this revised Form FDA 356h and additional copies of the finished drug product specifications and analytical methods per a telephone request from Martin Shimer, OGD/CDER, on November 9, 2000.

We are providing a revised Form FDA 356h to replace the September 14, 2000 Form FDA 356h included with our original ANDA submission. The USP designation has been removed from the product name since the finished drug product is a non-compendial item. We are also providing two additional sets of the finished drug product specifications and analytical methods for use by the FDA District Laboratory. The enclosed specifications and methods are the same as those provided in our ANDA submission.

Please call me at 763-546-4676 if you have any questions or need further information.

Sincerely,
Paddock Laboratories, Inc.

Carol Subialka
Regulatory Affairs Analyst

Enclosure

CENTER FOR DRUG
REC'D
NOV 14 2000
OGD
EVALUATION AND RESEARCH

3940 Quebec Avenue North, Minneapolis, MN 55427 • 763.546.4676 • FAX: 763.546.4842 • 800.328.5113

MAJOR AMENDMENT

ANDA 75-988

FEB 28 2001

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Paddock Laboratories, Inc.

TEL: 763-546-4676

ATTN: Carol Subialka

FAX: 763-546-4842

FROM: Ruby Yu

PROJECT MANAGER: 301-827-5848

Dear Madam:

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

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (4 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance

SPECIAL INSTRUCTIONS:

Chemistry and Bioequivalency comments provided. Labeling comments, if any, will be provided when the review is completed.

Ryu 2-28-01

FEB 8 [illegible]

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-988 APPLICANT: Paddock Laboratories, Inc.

DRUG PRODUCT: Prednisolone Sodium Phosphate, USP Oral solution, 5 mg (base)/5 ml

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Barbara M Davit

for Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

Redacted 3 page(s)

of trade secret and/or

confidential commercial

information from

2/28/2001 FDA FAX

Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

July 16, 2001

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

NEW CORRESP
NC

Re: ANDA 75-988 for Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 mL: Response to June 20, 2001, telephone request for additional copies of finished drug product specifications and the methods validation package

Dear Staff:

Please accept these two separately bound copies of the finished drug product specifications and analytical method validation package per a telephone request from Dr. John Franolic, OGD/CDER, on June 20, 2001.

Paddock previously submitted the finished drug product specifications on November 13, 2000, in response to a telephone request from Martin Shimmer, OGD/CDER, on November 9, 2000. Paddock also previously submitted the method validation package on November 29, 2000. This was submitted in response to a telephone request from Martin Shimmer on November 22, 2000. During the telephone discussion on June 20, 2001, Dr, John Franolic confirmed the documents are not on file with OGD/CDER and requested submittal of two separately bound copies.

We are providing two additional sets of the finished drug product specifications and method validation package for use by the FDA District Laboratory. The enclosed specifications and methods are the same as those provided in our ANDA submission. The two separately bound copies contain the finished drug product specifications (Section XIV, page 583 and pages 556 through 580) and the methods validation package (Section XV, pages 628 through 1205) that were included in our original ANDA submission dated September 14, 2000.

Please call me at 763-546-4676, ext. 297 if you have any questions or need further information.

Sincerely,

Carol Subialka
Regulatory Affairs Analyst

CENTER FOR DRUG
RECD
JUL 17 2001
OGD
EVALUATION AND RESEARCH

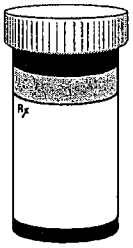
Enclosure

3940 Quebec Avenue North, Minneapolis, MN 55427 • 612.546.4676 • FAX: 612.546.4842 • 800.328.5113

NM 7/27

NW 7/25/01

Fax Cover Sheet



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Rockville, Maryland

To: Mr Shah

Fax: 763-546-4842 **Phone:**

From: Jim Barlow
Fax: 301-443-3847 **Phone:** 301-827-5846

Number of Pages (including cover sheet): 3 **Date:** 3/14/02

Comments:

Dear Mr Shah

Here is the copy of the labeling review for your prednisolone sodium phosphate oral solution application (ANDA 75-988). Please revise accordingly. If you have any questions please feel free to call me.

Sincerely,
Jim Barlow

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

APPEARS THIS WAY
ON ORIGINAL

ANDA 75-988

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

Paddock Laboratories, Inc.
Attention: Mary Beth Erstad
3940 Quebec Avenue North
Minneapolis, MN 55427

MAR 18 2002

Dear Madam:

This letter 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 for Prednisolone Sodium Phosphate USP, Oral Solution, 5 mg/5 mL.

We refer you to our "Not Approvable" letter dated February 28, 2001, which detailed the deficiencies identified during our review of your ANDA. The Agency may consider an ANDA applicant's failure to respond to a "Not Approvable" letter within 180 days to be a request by the applicant to withdraw the ANDA under 314.120(b). Your amendment to the application is overdue. You must amend your application within 10 days of receipt of this letter. Otherwise, an action to withdraw the application will be initiated per 21 CFR 314.99.

If you do not wish to pursue approval of this application at this time, you should request withdrawal in accord with 21 CFR 314.65. A decision to withdraw the application would be without prejudice to refiling.

If you have further questions you may contact Saundra T. Middleton, Project Manager, Regulatory Support Branch, at (301) 827-5862.

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

S. Middleton for

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

cc: ANDA # 75-988
DUP/Division File
HFD-610/PRickman
Endorsement:
HFD-617/GDavis, Chief, RSB, S. Middleton for date 3/18/02
HFD-617/SMiddleton, CSO, S. Middleton date 3/18/02
Word File
V:\FIRMSNZ\PADDOCK\LTRS&REV\75988.OTH
F/T by EEH 03/15/02
10 DAY LETTER!

Paddock
Laboratories, Inc.

Pharmaceuticals for Medicine, Pharmacy and Science

April 25, 2002

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AC

Re: MAJOR AMENDMENT to ANDA 75-988
and Response to Deficiency Letter dated February 28, 2001
for Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 mL

Dear Staff:

Please accept this Major Amendment to Paddock Laboratories, Inc. pending abbreviated new drug application for Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 mL, ANDA 75-988, dated September 14, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act. This amendment is in response to the February 28, 2001, deficiency letter.

In addition to providing a response to the February 28, 2001 deficiency letter, we propose to amend our application with the following changes and updated information:

1. [redacted]

RECEIVED
APR 29 2002
OGD / CDER

3940 Quebec Avenue North, Minneapolis, MN 55427 • 763.546.4676 • FAX: 763.546.4842 • 800.328.5113

Redacted 10 page(s)

of trade secret and/or

confidential commercial

information from

4/25/2002 PADDOCK LETTER

FP

October 16, 2002

ORIG AMENDMENT
NIAP

NEW CORRESP
NC

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: Minor Amendment to ANDA 75-988
for Prednisolone Sodium Phosphate, USP Oral Solution, 5 mg/5 mL
Deficiency Response, Trade Name Withdrawal and Final Printed Labeling

Dear Staff:

Please accept this Minor Amendment Paddock Laboratories' pending ANDA 75-988 for Prednisolone Sodium Phosphate, USP Oral Solution, 5 mg/5 mL. This Minor Amendment:

- provides our response to labeling deficiencies cited in the FDA facsimile dated March 14, 2002,
- withdraws the trade name ————and
- provides proposed final printed labeling.

Kindly notify the Office of Postmarketing Drug Risk Assessment (OPDRA) regarding our decision to withdraw the trade name.

Attachment 1 contains a copy of the FDA facsimile of March 14, 2002 with the stated labeling deficiencies. Attachment 2 provides our response to these labeling deficiencies. Attachment 3 contains the final printed labeling, using the generic name "Prednisolone Sodium Phosphate Oral Solution" (Prednisolone Sodium Phosphate, USP).

Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., certifies that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)]. Please contact me at 763-546-4676 or 763-546-4842 (facsimile) if you have any questions or need additional information. Thank you.

Sincerely,

Frank B. Freedman, Ph.D.
Regulatory Affairs Analyst

Attachments

RECEIVED
OCT 18 2002
OGD / CDER

3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

MINOR AMENDMENT

ANDA 75-988

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

OCT 18 2002

TO: APPLICANT: Paddock Laboratories, Inc.

TEL: ~~763-546-4676~~ 763-732-0297

ATTN: ~~Paul Bulger~~ David Rosenberg.

FAX: ~~763-546-4842~~ 763-546-4842.

FROM: Sarah Kim

PROJECT MANAGER: 301-827-5848

Dear Sir:

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

Reference is also made to your amendment(s) dated: April 25, 2002.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (2 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided. Labeling comments will be provided under separate cover.

SKim
10/18/02

Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

10/18/2002 FDA FAX

January 16, 2003

ORIG AMENDMENT

N|AM

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: MINOR AMENDMENT to ANDA 75-988 in Response to the Deficiency Letter dated October 18 2002 for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL

Dear Staff:

Please accept this Minor Amendment to Paddock Laboratories' pending abbreviated new drug application for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, ANDA 75-988, dated September 14, 2000, submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act. This amendment provides our responses to the October 18, 2002 deficiency letter.

Review and archival copies are included in this submission. A third copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

A copy of the deficiency letter, dated Oct 18 2002, is attached.

Please contact me at 763-732-0297 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,

David Rosenberg

David Rosenberg
Regulatory Affairs Analyst
email: drosenberg@paddocklabs.com

ORIG AMENDMENT

May 9, 2003

N/Am

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: TELEPHONE AMENDMENT
ANDA 75-988 Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL
in Response to Telephone Deficiency communicated April 16, 2003

Dear Ms. Kim:

Please accept this Telephone Amendment to Paddock Laboratories' pending abbreviated new drug application for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, ANDA 75-988, submitted September 14, 2000, pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act. This amendment provides our responses to the information requested during an April 16, 2003 telephone conference call. Included, as listed in the Table of Contents are a revised stability protocol listing refrigerated samples, stability reports for the refrigerated samples, a technical report discussing ——————————— prednisolone sodium phosphate oral solution, and referenced analytical procedures

This response is initially being sent via facsimile, hard copies (original, archival, and review) will be mailed the following business day. A copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please contact me at 763-732-0297 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,

David Rosenberg

David Rosenberg
Regulatory Affairs Analyst

RECEIVED
MAY 14 2003
OGD / CDER

3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com

July 10, 2003

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AM

Re: TELEPHONE AMENDMENT
ANDA 75-988 Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL
in Response to Telephone Deficiency communicated June 23, 2003

Dear Ms. Kim:

Please accept this Telephone Amendment to Paddock Laboratories' pending abbreviated new drug application for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, ANDA 75-988, submitted September 14, 2000, pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act. This amendment provides our responses to the information requested during a June 23, 2003 telephone conference call. Included, as listed in the Table of Contents are a stability reports for Thermal Cycling studies and a technical report discussing our [redacted] for prednisolone sodium phosphate oral solution.

This response is initially being sent via facsimile, hard copies (original and review) will be mailed the same business day. A copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please contact me directly at 763-732-0297 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information. Our general number is listed in the footer.

Sincerely,

David Rosenberg

David Rosenberg
Regulatory Affairs Analyst

RECEIVED
JUL 1 4 2003
OGD/CDER

MINOR AMENDMENT

ANDA 75-988

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

AUG 19 2003

TO: APPLICANT: Paddock Laboratories, Inc. TEL: 763-732-0297

ATTN: David Rosenberg FAX: 763-546-4842

FROM: Sarah Kim PROJECT MANAGER: 301-827-5848

Dear Sir:

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

Reference is also made to your amendment(s) dated: January 16, May 9, and July 10, 2003.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (__1__ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided.

8/19/03

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-988 **APPLICANT:** Paddock Laboratories, Inc.

DRUG PRODUCT: Prednisolone Sodium Phosphate Oral Solution, 5 mg/5 mL

The deficiency presented below represent a MINOR deficiency.

A. Deficiency:

Please note that DMF ____ for _____ _____ is currently inadequate. The DMF holder, _____ has been notified.

Sincerely yours,

DSGill

for Rashmikant M. Patel, Ph. D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

August 25, 2003

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II, HFD-600
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT
N/AM

Re: MINOR AMENDMENT
ANDA 75-988 Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL
in Response to Minor Deficiency Letter dated August 19, 2003

Dear Ms. Kim:

Please accept this Minor Amendment to Paddock Laboratories' pending abbreviated new drug application for Prednisolone Sodium Phosphate Oral Solution, 5mg/5mL, ANDA 75-988, submitted September 14, 2000, pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act. This amendment provides our response to the information requested in a August 19, 2003 minor deficiency letter.

Attached is a letter referencing an amendment to DMF ——————————————— responding to a set of questions in your August 14 letter. Also referenced is Paddock Laboratories, Inc. ANDA 75-988 which is under review, the approval of which is contingent upon the satisfactory review of DMF ———

By attachment of the above referenced amendment to DMF ——, this is Paddock Laboratories, Inc. response to the August 19, 2003 minor deficiency letter. Original(archive) and review copies are included. A copy has been sent to the Minneapolis District Office (field copy). Paddock Laboratories, Inc., does hereby certify that the submitted field copy is a true copy of the technical section of this application [21 CFR 314.94(d)(5)].

Please contact me directly at 763-546-4676 (telephone) or 763-546-4842 (fax) if you have any questions or need additional information.

Sincerely,

David Rosenberg

David Rosenberg
Regulatory Affairs Analyst

RECEIVED
AUG 2 6 2003
OGD/CDER

MW 9-9-03

3940 Quebec Avenue N, Minneapolis, MN 55427 • 800.328.5113 • 763.546.4676 • Fax:763.546.4842 • www.paddocklabs.com