CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

Application Number 40192

Trade Name Prednisolone Syrup USP 15mg/5ml

Generic Name Prednisolone Syrup USP 15mg/5ml

Sponsor WE Pharmaceuticals, Inc.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION 40192

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CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 40192

APPROVAL LETTER

ANDA 40-192

MAY 28 1998

WE Pharmaceuticals, Inc.
Attention: Craig H. Wheeler
1142 D Street
P.O. Box 1142
Ramona, CA 92065

Dear Sir:

This is in reference to your abbreviated new drug application dated June 7, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Prednisolone Syrup USP, 15 mg/5 mL.

Reference is also made to your amendments dated January 16, March 18, May 6, May 8, and May 28, 1998.

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 Syrup USP, 15 mg/5 mL, to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Prelone® Syrup 15 mg/5 mL, of Muro Pharmaceutical, Inc.).

Under 21 CFR 314.70, 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. 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 which 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 proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-240). Please do not use Form FD-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-040) with a completed Form FD-2253 at the time of their initial use.

Sincerely yours,

5/28/98

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 40192

FINAL PRINTED LABELING

NDC 59196-010-24

PRE-PRED™ SYRUP

APPROVED

(PREDNISOLONE SYRUP, USP)

15 mg per 5 mL

240 mL

MAY 28 1998

WE PHARMACEUTICALS, INC.

USUAL DOSAGE: See accompanying circular.

"Rx only"

STORE AT CONTROLLED ROOM TEMPERATURE 15° to 30°C (59° to 86°F)

Dispense in tight, light-resistant and child-resistant containers as defined in USP.

PHARMACIST: Dispense with a suitably calibrated Measuring Device.

3 59196 01024 0

DESCRIPTION: PRE-PRED™ contains 15 mg PREDNISOLONE in each 5 mL (teaspoonful) and alcohol 5%(v/v). Benzoic acid 0.1% added as a preservative.

Manufactured for:
WE PHARMACEUTICALS, INC.
Ramona, California 92065

Manufactured by:
KIEL LABORATORIES, INC.
Gainesville, Georgia 30504

OPEN ALONG PERFORATION

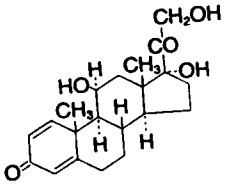
Lot No.:

Exp. Date:

PRE-PRED™ Syrup
(Prednisolone Syrup, USP 15 mg per 5 mL)

DESCRIPTION: PRE-PRED™ Syrup contains prednisolone which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Prednisolone is a white to practically white, odorless, crystalline powder. It is very slightly soluble in water, slightly soluble in alcohol, in chloroform, in dioxane, and in methanol.

The chemical name for Prednisolone is 11β,17,21-trihydroxypregna-1,4-diene-3,20-dione (anhydrous). Prednisolone's molecular weight is 360.45. The molecular formula is $C_{21}H_{28}O_5$ and the structural formula is:



PRE-PRED™ Syrup, for oral administration, contains 15 mg of prednisolone in each 5 mL and alcohol 5% (v/v). Benzoic acid, 0.1% is added as a preservative. It also contains artificial cherry flavor, citric acid, edetate disodium, FD&C red #40, glycerin, propylene glycol, sodium saccharin, sucrose, and purified water. The pH of Prednisolone Syrup is 3.0 to 4.5.

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

Glucocorticoids such as prednisolone cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND USAGE: PRE-PRED™ Syrup 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
- Nonsuppurative thyroiditis
- Hypercalcemia associated with cancer

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
- Post-traumatic osteoarthritis
- Synovitis of osteoarthritis
- Epicondylitis

3. Collagen Diseases
During an exacerbation or as maintenance therapy in selected cases of:
- Systemic lupus erythematosus
- Acute rheumatic carditis

4. Dermatologic Diseases
- Pemphigus
- Bullous dermatitis herpetiforms
- Severe erythema multiform (Stevens-Johnson syndrome)
- Exfoliative dermatitis
- Mycosis fungoides
- Severe psoriasis
- Severe seborrheic dermatitis

5. Allergic States
Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment:
- Seasonal or perennial allergic rhinitis
- Bronchial asthma
- Contact dermatitis
- Atopic dermatitis
- Serum sickness
- Drug hypersensitivity reactions

6. Ophthalmic Diseases
Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
- [illegible]rginal ulcers

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Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
Allergic corneal marginal ulcers
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Diffuse posterior uveitis and choroiditis
Sympathetic ophthalmia
Allergic conjunctivitis
Keratitis
Chorioretinitis
Optic neuritis
Iritis and iridocyclitis

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Symptomatic sarcoidosis
Loeffler's syndrome not manageable by other means
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Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
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Idiopathic thrombocytopenic purpura in adults
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To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

11. Gastrointestinal Diseases
To tide the patient over a critical period of the disease in:
Ulcerative colitis
Regional enteritis

12. Miscellaneous
Tuberculous meningitis with subarachnoid block or impending block used concurrently with appropriate antituberculous chemotherapy. Trichinosis with neurologic or myocardial involvement.

In addition to the above indications **PRE-PRED™ Syrup** is indicated for systemic dermatomyositis (polymyositis).

CONTRAINDICATIONS: Systemic fungal infections.

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

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.

Prolonged 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 fungi or viruses.

Use in pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancies, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

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.

While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

Children who are on drugs which suppress the immune system are more susceptible to infections than healthy children. Chickenpox 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

before, during, and after the stressful situation is indicated.

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The use of **PRE-PRED™ Syrup** 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.

PRECAUTIONS:

Information for patients: Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

General: Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of the 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.

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

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

The lowest possible dose of corticosteroid should be used to control

the condition under treatment, and when reduction in the dosage is possible, the reduction should be gradual.

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.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Steroids should be used with caution in nonspecific Ulcerative Colitis, if there is a probability of impending perforation, abscess or other pyogenic infections: diverticulitis; fresh intestinal anastomoses; active or a latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbation of multiple sclerosis, they do not show that corticosteroids affect the ultimate outcome of 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.)

ADVERSE REACTIONS:

Fluid and Electrolyte Disturbances
- Sodium retention
- Fluid retention
- Congestive heart failure in susceptible patients
- Potassium loss
- Hypokalemic alkalosis
- Hypertension

Musculoskeletal
- Muscle weakness
- Steroid myopathy
- Loss of muscle mass
- Osteoporosis
- Vertebral compression fractures
- Aseptic necrosis of femoral and humeral heads
- Pathologic fracture of long bones

Gastrointestinal
- Peptic ulcer with possible perforation and hemorrhage
- Pancreatitis
- Abdominal distention
- Ulcerative esophagitis

Dermatologic
- Impaired wound healing
- Thin fragile skin
- Petechiae and ecchymoses
- Facial erythema
- Increased sweating
- May suppress reactions to skin tests

Neurological
- Convulsions
- Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment
- Vertigo
- Headache

Endocrine
- Menstrual irregularities
- Development of Cushingoid state
- Suppression of growth in children
- Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness.
- Decreased carbohydrate tolerance
- Manifestations of latent diabetes mellitus
- Increased requirements for insulin or oral hypoglycemic agents in diabetics

Ophthalmic
- Posterior subcapsular cataracts
- Increased intraocular pressure
- Glaucoma
- Exophthalmos

Metabolic
- Negative nitrogen balance due to protein catabolism

DOSAGE AND ADMINISTRATION: Dosage of **PRE-PRED™ Syrup** should be individualized according to the severity of the disease and the response of the patient. For infants and children, the recommended dosage should be governed by the same considerations rather than strict adherence to the ratio indicated by age or body weight.

Hormone therapy is an adjunct to and not a replacement for conventional therapy.

Dosage should be decreased or discontinued [illegible]

rather than strict adherence to the ratio indicated by age or body weight.

Hormone therapy is an adjunct to and not a replacement for conventional therapy.

Dosage should be decreased or discontinued gradually when the drug has been administered for more than a few days.

The severity, prognosis, expected duration of the disease, and the reaction of the patient to medication are primary factors in determining the dosage.

If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Blood pressure, body weight, routine laboratory studies, including two-hour postprandial blood glucose and serum potassium, and chest X-ray should be obtained at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with known or suspected peptic ulcer disease.

The initial dosage of **PRE-PRED™ Syrup** may vary from 5 mg to 60 mg 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, **PRE-PRED™ Syrup** should be discontinued and the patient transferred to 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 **PRE-PRED™ Syrup** 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.

HOW SUPPLIED: PRE-PRED™ Syrup is a cherry flavored red liquid containing 15 mg of Prednisolone in each 5 mL (teaspoonful) and is supplied in 240 mL bottles (NDC 59196-010-24) and 480 mL bottles (NDC 59196-010-48).

Pharmacist: Dispense with a suitably calibrated measuring device to assure proper measuring of dose.

Dose/Volume Chart

15 mg prednisolone = 1 teaspoonful
10 mg prednisolone = 2/3 teaspoonful
7.5 mg prednisolone = 1/2 teaspoonful
5 mg prednisolone = 1/3 teaspoonful

Dispense in tight, light resistant and child-resistant containers as defined in USP/NF.

Store at controlled room temperature 15° - 30°C (59° - 86°F). Do Not Refrigerate.

CAUTION: Federal law prohibits dispensing without prescription.

Manufactured by:
Kiel Laboratories, Inc.
Gainesville, GA. 30504

Distributed by:
WE Pharmaceuticals, Inc.
Ramona, CA 92065

01/98

NDC 59196-010-48

PRE-PRED™ SYRUP

(PREDNISOLONE SYRUP, USP)

5 mg per 5 mL

480 mL

WE PHARMACEUTICALS, INC.

APPROVED
MAY 28 1998

USUAL DOSAGE: See accompanying circular.

"Rx only"

STORE AT CONTROLLED ROOM TEMPERATURE 15° to 30°C (59° to 86°F)

Dispense in tight, light-resistant and child-resistant containers as defined in USP.

PHARMACIST: Dispense with a suitably calibrated Measuring Device.

DESCRIPTION: PRE-PRED™ contains 15 mg PREDNISOLONE in each 5 mL (teaspoonful) and alcohol 5%(v/v). Benzoic acid 0.1% added as a preservative.

3 59196 01048 6

Manufactured for:
WE PHARMACEUTICALS, INC.
Ramona, California 92065

Manufactured by:
KIEL LABORATORIES, INC.
Gainesville, Georgia 30504

Lot No.: Exp. Date:

OPEN ALONG PERFORATION

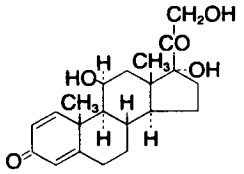
PRE-PRED™ Syrup

(Prednisolone Syrup, USP 15 mg per 5 mL)

2

DESCRIPTION: PRE-PRED™ Syrup contains prednisolone which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Prednisolone is a white to practically white, odorless, crystalline powder. It is very slightly soluble in water, slightly soluble in alcohol, in chloroform, in dioxane, and in methanol.

The chemical name for Prednisolone is 11β,17,21-trihydroxypregna-1,4-diene-3,20-dione (anhydrous). Prednisolone's molecular weight is 360.45. The molecular formula is $C_{21}H_{28}O_5$ and the structural formula is:



PRE-PRED™ Syrup, for oral administration, contains 15 mg of prednisolone in each 5 mL and alcohol 5% (v/v). Benzoic acid, 0.1% is added as a preservative. It also contains artificial cherry flavor, citric acid, edetate disodium, FD&C red #40, glycerin, propylene glycol, sodium saccharin, sucrose, and purified water. The pH of Prednisolone Syrup is 3.0 to 4.5.

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

Glucocorticoids such as prednisolone cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND USAGE: PRE-PRED™ Syrup 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
- Nonsuppurative thyroiditis
- Hypercalcemia associated with cancer

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
- Post-traumatic osteoarthritis
- Synovitis of osteoarthritis
- Epicondylitis

3. Collagen Diseases

During an exacerbation or as maintenance therapy in selected cases of:

- Systemic lupus erythematosus
- Acute rheumatic carditis

4. Dermatologic Diseases

- Pemphigus
- Bullous dermatitis herpetiforms
- Severe erythema multiform (Stevens-Johnson syndrome)
- Exfoliative dermatitis
- Mycosis fungoides
- Severe psoriasis
- Severe seborrheic dermatitis

5. Allergic States

Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment:

- Seasonal or perennial allergic rhinitis
- Bronchial asthma
- Contact dermatitis
- Atopic dermatitis
- Serum sickness
- Drug hypersensitivity reactions

6. Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:

- Allergic corneal marginal ulcers
- Herpes zoster opthalmicus
- Anterior segment inflammation
- Diffuse posterior uveitis and choroiditis
- Sympathetic ophthalmia
- Allergic conjunctivitis
- Keratitis
- Chorioretinitis
- Optic neuritis

Severe seborrheic dermatitis

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- Iritis and iridocyclitis

7. Respiratory Diseases
- Symptomatic sarcoidosis
- Loeffler's syndrome not manageable by other means
- Berylliosis
- Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy
- Aspiration pneumonitis

8. Hematologic Disorders
- Idiopathic thrombocytopenic purpura in adults
- Secondary thrombocytopenia in adults
- Acquired (autoimmune) hemolytic anemia
- Erythroblastopenia (RBC anemia)
- Congenital (erythroid) hypoplastic anemia

9. Neoplastic Diseases
For palliative management of:
- Leukemias and lymphomas in adults
- Acute leukemia of childhood

10. Edematous States
To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

11. Gastrointestinal Diseases
To tide the patient over a critical period of the disease in:
- Ulcerative colitis
- Regional enteritis

12. Miscellaneous
Tuberculous meningitis with subarachnoid block or impending block used concurrently with appropriate antituberculous chemotherapy. Trichinosis with neurologic or myocardial involvement.

In addition to the above indications **PRE-PRED™ Syrup** is indicated for systemic dermatomyositis (polymyositis).

CONTRAINDICATIONS: Systemic fungal infections.

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

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used.

Prolonged 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 fungi or viruses.

Use in pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancies, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

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Prolonged 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 fungi or viruses.

Use in pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancies, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

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.

While on corticosteroid therapy, patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

Children who are on drugs which suppress the immune system are more susceptible to infections than healthy children. Chickenpox 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 chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intravenous immunoglobulin (IVIG) may be indicated. (See the respective package inserts for complete VZIG and IVIG prescribing information). If chickenpox develops, treatment with antiviral agents may be considered.

NDC 59196-010-48

PRE-PRED™ SYRUP

(PREDNISOLONE SYRUP, USP)

15 mg per 5 mL

480 mL

APPROVED WE PHARMACEUTICALS, INC. 2 8 1998

DESCRIPTION: PRE-PRED™ contains 15 mg PREDNISOLONE in each 5 mL (teaspoonful) and alcohol 5%(v/v). Benzoic acid 0.1% added as a preservative.

Manufactured for:
WE PHARMACEUTICALS, INC.
Ramona, California 92065

Manufactured by:
KIEL LABORATORIES, INC.
Gainesville, Georgia 30504

NDC 59196-010-48

PRE-PRED™ SYRUP

(PREDNISOLONE SYRUP, USP)

15 mg per 5 mL

480 mL

VE PHARMACEUTICALS, INC.

USUAL DOSAGE: See accompanying circular.

"Rx ONLY"

Dispense in tight, light-resistant and child-resistant containers as defined in USP.

STORE AT CONTROLLED ROOM TEMPERATURE
15°-30°C (59°-86°F)
DO NOT REFRIGERATE

PHARMACIST: Dispense with a suitably Calibrated Measuring Device.

For your convenience, calibrated teaspoons are enclosed.

N 3 59196 01048 6

(PREDNISOLONE SYRUP, USP)

PRE-PRED™ SYRUP

NDC 59196-010-24

PRE-PRED™ SYRUP

(PREDNISOLONE SYRUP, USP)

15 mg per 5 mL

240 mL

WE PHARMACEUTICALS, INC.

DESCRIPTION: PRE-PRED™ contains 15 mg PREDNISOLONE in each 5 mL (teaspoonful) and alcohol 5%(v/v). Benzoic acid 0.1% added as a preservative.

Manufactured for:
WE PHARMACEUTICALS, INC.
Ramona, California 92065

Manufactured by:
KIEL LABORATORIES, INC.
Gainesville, Georgia 30504

NDC 59196-010-24

PRE-PRED™ SYRUP

(PREDNISOLONE SYRUP, USP)

15 mg per 5 mL

240 mL

WE PHARMACEUTICALS, INC.

28 1998

USUAL DOSAGE: See accompanying circular.

"Rx ONLY"

Dispense in tight, light-resistant and child-resistant containers as defined in USP.

STORE AT CONTROLLED ROOM TEMPERATURE 15°-30°C (59°-86°F) DO NOT REFRIGERATE

PHARMACIST: Dispense with a suitably Calibrated Measuring Device.

For your convenience, calibrated teaspoons are enclosed.

N 3 59196 01024 0

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 40192

CHEMISTRY REVIEW(S)

1. CHEMISTRY REVIEW NO. 4

2. ANDA # 40-192

3. NAME AND ADDRESS OF APPLICANT
WE Pharmaceuticals, Inc.
Attention: Craig H. Wheeler
P.O. Box 1142
Ramona, CA 92065

4. LEGAL BASIS FOR SUBMISSION
Listed Drug: Prezone Syrup (MURO Pharmaceuticals)

5. SUPPLEMENT(s): N/A

6. PROPRIETARY NAME: Pre-Pred Syrup

7. NONPROPRIETARY NAME
Prednisolone USP

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

9. AMENDMENTS AND OTHER DATES:
Original ANDA Submission Date June 7, 1996
`Refuse to File' Letter Date July 1, 1996
Original Amendment Date August 1, 1996
Major Amendment Date April 4, 1997
Minor Amendment Date November 11, 1997
Minor Amendment Date January 16, 1998
Telephone Amendment Date May 6, 1998
Telephone Amendment Date May 8, 1998

10. PHARMACOLOGICAL CATEGORY
Glucocorticoid

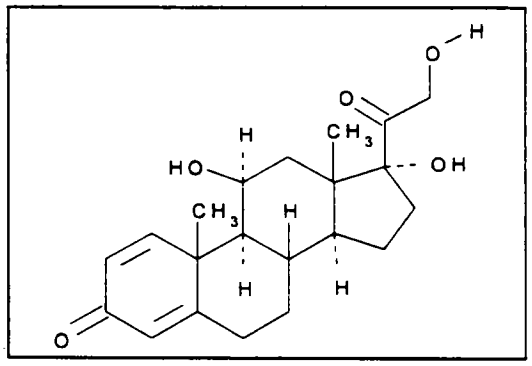
11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s):

13. DOSAGE FORM: Syrup

14. POTENCY: 15 mg/5 mL

15. CHEMICAL NAME AND STRUCTURE
Prednisolone USP $C_{21}H_{28}O_5$; M.W. = 360.45
CAS [50-24-8]



11ß,17,21-Trihydroxypregna-1,4-diene-3,20-dione (anhydrous).

16. RECORDS AND REPORTS N/A

17. COMMENTS
See individual review sections.

18. CONCLUSIONS AND RECOMMENDATIONS :
Approvable

19. REVIEWER:
Upinder S. Atwal

DATE COMPLETED:
April 10, 1998

DATE REVISED:
May 8, 1998

cc: ANDA 40-192
Division File
DUP File
Field Copy

Endorsements:

HFD-623/U.S. Atwal/4-11-98 5/14/98
HFD-623/V.Sayeed/4-13-98 ~
HFD-617/J.Wilson, PM/4-13-98
X:\NEW\FIRMSNZ\WE\LTRS&REV\40192.RV4
F/T by: bc/4-15-98

CHEMISTRY REVIEW - APPROVABLE

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 40192

BIOEQUIVALENCE REVIEW(S)

ANDA 40-192

WE Pharmaceuticals, Inc.
Attention: Craig H. Wheeler
P.O. BOX 1142
Ramona CA 92065

FEB - 4 1997

Dear Sir:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Prednisolone Syrup USP, 15 mg/5 mL.

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

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

Rabindra Patnaik, Ph.D.
Acting Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

JAN 28 1997

Prednisolone
Syrup, 15 mg/5 mL
(Pre-Pred® Syrup)
ANDA 40-192
Reviewer: L.A. Ouderkirk
WP No. 40192w.696

WE Pharmaceuticals, Inc.
Atlanta, Georgia
Submission Dated:
June 7, 1996

Review of a Wavier Request for a Soluble Dosage Form

The firm has filed an amendment dated 6/7/96 to its unapproved ANDA #40-192 requesting that the in-vivo bioequivalence requirements for its prednisolone syrup, 15 mg/5 mL be waived per 21 CFR 320.22 (b)(3). In support of this request, the firm has submitted the formula for its test product (**Table 1**). The formula for the reference product, Prelone® Syrup, 15 mg/5 mL, sponsored by Muro Pharmaceuticals is given in **Table 2** (formula was obtained from FDA files).

Comment:

1. The firm has met the criteria for waiver of the in-vivo bioequivalence study requirements for its prednisolone syrup, 15 mg/5 mL per 21 CFR 320.22 (b)(3), in that the test product:

   (i) Is an oral syrup.

   (ii) Contains an active drug ingredient in the same concentration and dosage form as a drug product that is the subject of an approved full new drug application.

   (iii) Contains no inactive ingredient or other change in formulation from the listed reference drug product that may significantly affect absorption of the active drug ingredient.

Recommendations:

1. The waiver of in-vivo bioequivalence study requirements for the firm's prednisolone syrup, 15 mg/5 mL (Pre-Pred® Syrup), is granted per 21 CFR 320.22 (b)(3). The test product is therefore deemed bioequivalent to a reference product, Prelone® syrup, 15 mg/5 mL, sponsored by Muro Pharmaceuticals.

2. From the bioequivalence viewpoint, the firm has met the bioequivalence requirements and the ANDA #40-192 is acceptable.

The firm should be advised of the Recommendations, above.

1-7-97

Larry A. Ouderkirk
Division of Bioequivalence
Review Branch 1

RD INITIALED YCHuang
FT INITIALED YCHuang

1/7/97

Concur: _____ Date: 1/28/97

Rabindra N. Patnaik, Ph.D.
Acting Director,
Division of Bioequivalence

cc: ANDA 40-192 (original, duplicate), HFD-652 (Huang, Ouderkirk), Drug File, Division File

lao X:\new\firmsnz\we\ltrs&rev\40192w.696

TABLE 1

COMPOSITION STATEMENT
PREDNISOLONE (PRE-PRED®) SYRUP, USP
15 MG/5 ML

WE PHARMACEUTICALS

COMPONENT	QUANTITY PER 5 ML
Prednisolone, USP	15.0 mg
Benzoic Acid, USP	
[redacted]	
Citric Acid, USP	
EDTA, USP	
Ethanol , USP	
FD&C Red #40	
Glycerin, USP	
Propylene Glycol, USP	
Sodium Saccharin, USP	
Sucrose, NF	
Purified Water	

TABLE 2

COMPOSITION STATEMENT
PRELONE® SYRUP, USP
15 MG/5 ML

MURO PHARMACEUTICALS

COMPONENT	QUANTITY PER 5 ML
Prednisolone, USP	15.0 mg
Benzoic Acid, USP	
Wild Cherry Flavor,	
Citric Acid, USP	
EDTA, Disodium	
Alcohol, USP	
FD&C Blue #1	
FD&C Red #40	
Glycerin, USP	
Propylene Glycol, USP	
Sodium Saccharin, USP	
Sucrose, NF	
Purified Water	

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 40192

ADMINISTRATIVE DOCUMENTS

ANDA **40-192** APPROVAL SUMMARY

DRUG PRODUCT: Prednisolone Syrup USP, 15 mg/5 mL

FIRM: WE Pharmaceuticals, Inc.

DOSAGE FORM: Syrup

STRENGTH: 15 mg/5 mL

cGMP STATEMENT/EIR UPDATE STATUS: EER Acceptable Date May 6, 1997

BIO STUDY: *APPROVE*, Letter Sent on January 30, 1997

VALIDATION: DS and DP are compendial

STABILITY: Six months accelerated, 40°C, and three months room temperature, 25°C/60% RH, data, in the market package sizes, 8 oz and 16 oz, stored on-side, provided. The container/closure systems used for the stability study are equivalent to the systems proposed for commercial use. All reported data are within specifications as listed. Thus, a 24 month expiration date is justified.

Tests and specifications for the drug product on stability include: Appearance/Description,

LABELING: *APPROVE*, Review Date March 24, 1998

STERILIZATION VALIDATION: (IF APPLICABLE): N/A

SIZE OF BIO BATCH: The bio batch, lot# GA180 (batch size is also the test batch. The DS supplier is ıs Adequate as of March 9, 1998).

SIZE OF STABILITY BATCHES: Stability batch is the same as the test batch, Lot# GA180 (batch size

PROPOSED PRODUCTION BATCHES: The proposed production batch size for Prednisolone Syrup USP is The manufacturing process for production batches remains the same as that for the test batch.

CHEMIST: **DATE:** 5/13/98

SUPERVISOR: **DATE:**

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 40192

CORRESPONDENCE

Noted

WE PHARMACEUTICALS, INC.

Allergy/Asthma Products

May 28, 1998

Via Fax 301-443-3847

Mr. Jerry Phillips, Director
Division of Labeling and Program Support
Office of Generic Drugs
Food and Drug Administration
7500 Standish Place
Rockville, MD 20857

RE: ANDA 40-192
15 mg/5 mL Prednisolone Syrup, USP

Dear Mr. Phillips:

Based on our telephone conversation today, I understand that **ANDA 40-192** is approvable subject to the product being renamed. WE Pharmaceuticals, Inc. commits to deleting all reference to the name "PRE-PRED" from the label, package insert and carton as a condition of approval. The product will be labeled as the generic name " Prednisolone Syrup, USP 15 mg per 5 mL."

Post approval, WE Pharmaceuticals, Inc. commits to submit to your office, as a further condition of approval, Final Labeling including the product label, package insert, and the carton prior to shipment of the product.

It is my understanding that these commitments will allow for the product approval letter to be issued today.

Sincerely,

Craig H. Wheeler
President and CEO

P.O. Box 1142, Ramona, California 92065 • (760) 788-9155 • (800) 262-9555 • FAX (760) 788-9445

KIEL LABORATORIES, INC.

April 4, 1997

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
FOOD AND DRUG ADMINISTRATION
7500 Standish Place
Rockville, Md 20857

NDA [illegible] AMENDMENT

N/AC

RE: MAJOR AMENDMENT TO ANDA 40-192
15 mg/5 mL PREDNISOLONE SYRUP

Dear Dr. Patel:

Kiel Laboratories, Inc. is under contract with WE Pharmaceuticals, Inc. to develop 15 mg/5 mL Prednisolone syrup. We were asked to respond to your letter of deficiency of January 14, 1997. Enclosed is our response.

The response is organized in the order of your comments/questions. First, we restate your comment/question and on the same page respond to it. Any documentation in support of the response is enclosed in the document.

It is our belief that all of your comments/questions have been adequately addressed. Should you need any further information, please feel free to contact us directly or through WE Pharmaceuticals, Inc. Our telephone number is 770-534-0079, and our FAX is 77-534-0229.

Sincerely yours,

Lewis H. Moore

Lewis H. Moore
Quality Assurance

Enclosure

cc: Mr. Craig H. Wheeler
President
WE Pharmaceuticals, Inc.

RECEIVED

[illegible] 1997

GENERIC DRUGS

2225 CENTENNIAL DRIVE • GAINESVILLE, GEORGIA 30504 • 770-534-0079 • FAX 770-534-0229

WE PHARMACEUTICALS, INC.

Allergy/Asthma Products

January 16, 1998

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20857

RE: ANDA 40-192 MINOR AMENDMENT DATED January 12, 1998
15 mg/5 mL Prednisolone Syrup, USP

Dear Dr. Patel:

Reference is made to your Minor Amendment facsimile dated January 12, 1998. WE Pharmaceuticals, Inc. (WE) submits today responses to labeling deficiencies communicated in the Minor Amendment notification. In addition, the responses to labeling deficiencies are addressed in the draft labeling that is included in this Amendment. A copy of your deficiency letter is also included.

The facility for manufacturing of this dosage form is Kiel Laboratories, Inc., located at 2225 Centennial Drive in Gainesville, Georgia.

Please direct any communications regarding this ANDA to me at the address or telephone number listed below. If you have any questions or require any additional information, please feel free to contact Jeffrey S. Kiel, Kiel Laboratories, Inc. at (770) 534-0079.

Sincerely,

Craig H. Wheeler
President

Enclosures

P.O. Box 1142, Ramona, California 92065 • (619) 788-9155 • (800) 262-9555 • FAX (619) 788-9445

Allergy/Asthma Products

November 11, 1997

NDA ORIG AMENDMENT

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, Md 20857

RE: MINOR AMENDMENT TO ANDA 40-192
15 mg/5 mL Prednisolone Syrup, USP

Dear Dr. Patel:

Reference is made to your Minor Amendment facsimile dated November 3, 1997. WE Pharmaceuticals, Inc. (WE) submits today responses to all chemistry deficiencies communicated in the minor amendment notification. In addition, the responses to labeling deficiencies are addressed in the draft labeling that is included in this amendment. A copy of your deficiency letter is also included.

The facility for manufacturing of this dosage form is Kiel Laboratories, Inc., located at 2225 Centennial Drive in Gainesville, Georgia.

Please direct any communications regarding this ANDA to me at the address or telephone number listed below. If you have any questions or require any additional information, please feel free to contact Jeffrey S. Kiel, President, Kiel Laboratories, Inc. at (770)534-0079.

Sincerely,

Craig H. Wheeler
President

RECEIVED
DEC 0 1 1997
GENERIC DRUGS

12-2-97

P.O. Box 1142, Ramona, California 92065 • (619) 788-9155 • (800) 262-9555 • FAX (619) 788-9445

WE PHARMACEUTICALS, INC.

Allergy/Asthma Products

RECEIVED

AUG 0 5 1996

GENERIC DRUGS

NDA ORIG AMENDMENT

August 1, 1996

Prednisolone Syrup USP (15 mg/5ml (PRE-PRED™SYRUP)

Office of Generic Drugs
Center for Drug Evaluation
Food and Drug Administration
Document Control Room
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

RE: Supplemental ANDA Submission 001 - ANDA #40-192
15mg/5ml PREDNISOLONE SYRUP

Dear Sir:

Enclosed please find the following documentation in response to the FDA refusal to file the letter of July 1, 1996 relating to ANDA 40-192 Prednisolone Syrup USP, 15mg/5ml. The information presented is organized and divided into Sections as they would appear in the ANDA.

SECTION II - Generic Drug Enforcement Act Certification
A revised Generic Drug Enforcement Act of 1992 Certification is supplied. This revision includes the certification that no affiliated person debarred under subsection (a) or (b)(section 306(a) or (b) was used in connection with this application.

SECTION IV.4 - Side By Side Labeling Comparison
Four copies of the proposed labeling are included. A side by side comparison of the proposed labeling and approved labeling is provided. All differences in the labeling are highlighted and explained as per 21 CFR 314.94(a)(8)(iv). In summary all differences are related to the different marketing company.

SECTION VIII.1.b - Prednisolone Certificate of Analysis from Drug Supplier
This section contains the Certificate of Analysis for the lot of prednisolone used in the manufacture of Batch GA180.

SECTION VIII.1.c - Prednisolone Specification from Drug Product Manufacturer
This section contains the Prednisolone raw material specification for FDA review.

SECTION VIII.2.a - Testing Specifications for Inactive Ingredients
This section contains the raw material specifications for the inactive ingredients.

P.O. Box 1142, Ramona, California 92065 • (619) 788-9155 • (800) 262-9555 • FAX (619) 788-9445

SECTION VIII.2.b - Inactive Ingredient Certificates of Analysis
This section contains the certificates of analysis for the purified water used in Batch GA180 and the previously submitted Batch GA165 as requested by the FDA. Also included in this section is the list of inactive ingredient suppliers and addresses as requested by the FDA. Also certificates of analysis for inactive ingredients used in Batch GA180 are supplied.

SECTION XII.1 - Executed Batch Record
In order to comply with the FDA request for a fully executed batch record, we have supplied information from batch GA180. These records include a fully executed batch record, including packaging records, label reconciliation and batch yield calculations. Due to the completeness of this batch record, Batch GA180 should be used as the example batch for the ANDA Submission. In order to submit complete data on this batch, additional data is included in this supplement. This data includes the following:

a. Certificate of Analysis for Batch GA180 (Section XV.2)
b. Certificate of Analysis and Specification for the Prednisolone raw material Used in Batch GA180 (Section VIII.1.b and VIII.1.c).
c. Specifications and Certificates of Analysis for each inactive ingredient used In Batch GA180 (Section VIII.2.a and VIII.2.b).
d. Three month stability data for Batch GA180 (Section XVII.4).

SECTION XV.2 - Certificate of Analysis for Batch GA180
A certificate of analysis for the finished product analysis of Batch GA180 is supplied for both 8 oz. and 16oz. bottles.

SECTION XVII.4 - Stability Data for Batch GA180
Three month stability data is supplied for Batch GA180, including room temperature, accelerated conditions (40°C), and cold conditions (15°C) in 8 oz. and 16 oz. Bottles.

Please contact me if you have any questions regarding this supplemental submission.

Sincerely yours,

Craig H. Wheeler
President

ANDA 40-192

WE Pharmaceuticals, Inc.
Attention: Craig H. Wheeler
P.O. Box 1142
Ramona, CA 92065

JUL 1 1996

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated June 7, 1996, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Prednisolone Syrup USP, 15 mg/mL.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

Your executed batch records are incomplete. You must supply packaging records for the test batch. These records should contain complete records for the packaging and labeling operations, including drug product and label reconciliation. Please note that the test batch must be completely packaged in the containers proposed for marketing. Please provide this information. We refer you to the Office of Generic Drugs, Policy and Procedure Guide #41-95 for Guidance on the Packaging of Test Batches.

Please provide a certificate of analysis for the inactive ingredient, purified water, used in your formulation.

Thus, it will not be filed as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

We note that while you have provided side-by-side comparisons of your proposed labeling with the approved labeling of the reference listed drug, you have failed to annotate and explain the differences. Please provide this comparison with the differences annotated and explained as per 21 CFR 314.94(a)(8)(iv).

Also, while we note that you have provided a list of convictions, please note that contractors responsible for the development of data and other information used to support the approval of an application are "affiliated persons". Please revise your list of convictions to include any affiliated persons.

Please provide the names and addresses for the sources of the inactive ingredients used to the prepare the test batch.

Within 30 days of the date of this letter you may amend your application to include the above information or request in writing an informal conference about our refusal to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusion, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(a)(3)If you do so, the application shall be filed over protest under 21 CFR 314.101(a)(2). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Ms. Anna Marie H. Weikel
Project Manager
(301) 594-0315

Sincerely yours,

7/1/96

Jerry Phillips
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 40-192
DUP/Jacket
Division File
HFD-82
Field Copy
HFD-600/Reading File
HFD-615/MBennett

Endorsement: HFD-615/PRickman, Act 7/1/96 date
HFD-615/AMWeikel, CSO date 6/27/96
HFD-623/VSayeed,Chem Brancn date
X:\new\firmsnz\we\ltrs&rev\40192.f
F/T bcw/6-27-96
ANDA Refuse to File!

Allergy/Asthma Products

June 7, 1996

Refuse to file
Dr. W. Docket
[illegible]
6/26/96

Prednisolone Syrup USP (15 mg/5ml)
(PRE-PRED™SYRUP)

Office of Generic Drugs
Center for Drug Evaluation
Food and Drug Administration
Document Control Room
7500 Standish Place, Room 150
Rockville, Maryland 20855-2773

RECEIVED

JUN 10 1996

GENERIC DRUGS

RE: Original ANDA Submission
15 mg/5ml PREDNISOLONE SYRUP

Dear Sir:

Please find enclosed an abbreviated New Drug Application 15 mg/5ml Prednisolone Syrup (PRE-PRED Syrup). PRE-PRED syrup is a generic equivalent of Prelone syrup (15 mg/5ml Prednisolone syrup) manufactured by MURO Pharmaceuticals.

Description of PRE-PRED Syrup (15 mg/5mg Prednisolone Syrup

The PRE-PRED Syrup (15 mg/5ml prednisolone syrup) consists of a single active ingredient, prednisolone, and ten inactive components used as non-aqueous solvents, to increase viscosity, antimicrobial preservation, pH buffer, flavor masking, and color. The ingredients in PRE-PRED Syrup are substantially equivalent to MURO Pharmaceutical's Prelone Syrup. UPS grade Prednisolone drug substance is obtained from the and is used in the manufacturing of PRE-PRED Syrup. The material specification, certificate of analysis and the DMF reference letter is presented in the Drug Substance Section. All other ingredients in PE-PRED Syrup are USP/NF compendial excipients except for the flavor which is food grade and the color is FD&C Red #40.

Indications Sought

The ANDA seeks the same labeling indications as Prelone syrup (MURO Pharmaceuticals). The package insert for PRE-PRED Syrup, which is included in the labeling section of this application, contains the requested labeling indications. A copy of the package insert for Prelone syrup (MURO Pharmaceuticals) is included as a reference in the labeling section of this application.

Draft Label copy for the three package sizes of 480ml, 240ml, and 20ml bottles are included in

P.O. Box 1142, Ramona, California 92065 • (619) 788-9155 • (800) 262-9555 • FAX (619) 788-9445

the Labeling section of this submission. The PRE-PRED Syrup label will have the Package Insert integrated into the label in the same way that Prelone (MURO Pharmaceuticals) is labeled. The 20 ml sample bottle will have the Package Insert supplied separately from the label.

Stability of PRE-PRED Syrup

Two analytical methods are used in the stability studies, and these methods have been validated. The method validation reports are included in this submission. The first method is stability indicating method for both the Prednisolone and Benzoic Acid content. Benzoic Acid is the antimicrobial preservative in the product. The stability indicating Prednisolone assay was validated against the USP Prednisolone Syrup test method and was shown to be a suitable alternate method for analyzing PRE-PRED Syrup.

A or alcohol content is also used for stability testing. The Alcohol method validation report is included in this submission.

Additional copies of each of the validation reports are included in separate binders of this submission.

Bioequivalence Waiver

WE Pharmaceuticals requests a Waiver of *in vivo* bioequivalence studies and the waiver request is included in the submission.

Please contact me if you have any questions regarding this submission.

Sincerely yours,

WE Pharmaceuticals, Inc.

Craig H. Wheeler
President