INDICATIONS AND USAGE:
DIPROFOS Suspension is indicated for the treatment of acute and chronic corticosteroid-responsive disorders. Corticosteroid hormone therapy is an adjunct to, and not a replacement for, conventional therapy.

Musculoskeletal and Soft Tissue Conditions:
Rheumatoid arthritis; osteoarthritis; bursitis; ankylosing spondylitis; epicondylitis; radiculitis; coccydynia; sciatica; lumbago; torticollis; ganglion cyst; exostosis; fasciitis. Allergic Conditions: Chronic bronchial asthma (including adjunctive therapy for status asthmaticus); hay fever; angioneurotic edema; allergic bronchitis; seasonal or perennial allergic rhinitis; drug reactions; serum sickness; insect bites.

Dermatologic Conditions:
Atopic dermatitis (nummular eczema); neurodermatitis (circumscribed lichen simplex); contact dermatitis; severe solar dermatitis; urticaria; hypertrophic lichen planus; nécrobiosis lipoidica diabeticorum; alopecia areata; discoïd lupus erythematosus; psoriasis; keloids; pemphigus; dermatitis herpetiformis; cystic acne.

Collagen Diseases:
Disseminated lupus erythematosus; scleroderma; dermatomyositis; periarteritis nodosa.

Neoplastic Diseases: For palliative management of leukemias and lymphomas in adults; acute leukemia of childhood.

Other Conditions: Adrenogenital syndrome; ulcerative colitis; regional ileitis; sprue; pediatric conditions (bursitis under heloma durum, hallux rigidus, digit quinto varus); affections requiring subconjunctival injection; corticosteroid-responsive blood dyscrasias; nephritis and nephrotic syndrome. Primary or secondary adrenocortical insufficiency may be treated with DIPROFOS Suspension but should be supplemented with mineralocorticoids, if applicable. DIPROFOS Suspension is recommended for (1) intramuscular injection in con-
DIPROFOS Suspension can be used in the treatment of various conditions responsive to systemic corticosteroids; (2) injection directly into the affected soft tissues where indicated; (3) intra-articular and periarticular injection in arthritides; (4) intrallesional injection in various dermatologic conditions; and (5) local injection in certain inflammatory and cystic disorders of the foot.

**DOSAGE AND ADMINISTRATION:**

**DOSE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE SPECIFIC DISEASE, ITS SEVERITY AND THE RESPONSE OF THE PATIENT.**

The initial dose should be maintained or adjusted until a satisfactory response is observed. If a satisfactory clinical response does not occur after a reasonable period of time, treatment with DIPROFOS Suspension should be discontinued and other appropriate therapy initiated.

**Systemic Administration:** For systemic therapy, treatment is initiated with 1 to 2 ml in most conditions and repeated as necessary. Administration is by deep intramuscular (IM) injection in the gluteal region. Dosage and frequency of administration will depend on the severity of the patient’s condition and the therapeutic response. Two ml might be required initially in a severe illness, such as lupus erythematosus or status asthmaticus which has been resolved by appropriate life-saving procedures.

A wide variety of dermatologic conditions respond effectively to an IM injection of 1 ml DIPROFOS Suspension, repeated according to the response of the condition.

In respiratory tract disorders, onset of relief from symptoms has occurred within a few hours after IM injection of DIPROFOS Suspension. Effective control of symptoms with 1 to 2 ml is obtained in bronchial asthma, hay fever, allergic bronchitis and allergic rhinitis.

In the treatment of acute or chronic bursitis, excellent results are obtained with 1 to 2 ml IM injection of DIPROFOS Suspension, repeated as necessary.

**Local Administration:** Concomitant use of a local anesthetic is rarely necessary. If coadministration of a local anesthetic is desired, DIPROFOS Suspension may be mixed (in the syringe, not the vial) with 1% or 2% procaine hydrochloride or lidocaine, using formulations which do not contain parabens. Similar local anesthetics may also be used. Anesthetics containing methylparaben, propylparaben, phenol, etc. should be avoided. The required dose of DIPROFOS Suspension is first withdrawn from the vial into the syringe. The local anesthetic is then drawn in, and the syringe is shaken briefly. In acute subdeltoid, subacromial, olecranon, and prepatellar bursitis, an intrabursal injection of 1 to 2 ml of DIPROFOS Suspension may relieve pain and restore full range of movement within a few hours. Chronic bursitis may be treated with reduced dosage once acute symptoms are controlled. In acute tenosynovitis, tendinitis, and peritendinitis, one injection of DIPROFOS Suspension should alleviate the condition. In chronic forms of these conditions, it may be necessary to repeat the injection as the patient’s condition requires. Following 0.5 to 2 ml intra-articular administration of DIPROFOS Suspension, relief from pain, soreness, and stiffness associated with rheumatoid arthritis and osteoarthritis may be experienced within two to four hours. Duration of relief, which varies widely in both diseases, is four or more weeks in the majority of cases. An intraarticular injection of DIPROFOS Suspension is well tolerated in the joint and periarticular tissues. Recommended doses for intra-articular injection are: large joints (knee, hip, shoulder), 1 to 2 ml; medium joints (elbow, wrist, ankle), 0.5 to 1 ml; small joints (foot, hand, chest), 0.25 to 0.5 ml.

Dermatologic conditions may respond to intrallesional administration of DIPROFOS Suspension. Response of some lesions not treated directly may be due to a slight systemic effect of the drug. In intrallesional treatment, an intradermal dosage of 0.2 ml/cm² of DIPROFOS Suspension evenly injected with a tuberculin syringe and a 26-gauge needle is recommended. The total amount of DIPROFOS Suspension injected at all sites each week should not exceed 1 ml.
DIPROFOS Suspension may be used effectively in disorders of the foot that are responsive to corticosteroid therapy. Bursitis under heloma durum may be controlled with two successive injections of 0.25 ml each. In some conditions, such as hallux rigidus, digit quinti varus and acute gouty arthritis, onset of relief may be rapid. A tuberculin syringe with a 25-gauge needle is suitable for most injections. Recommended doses at intervals approximately one week: bursitis under heloma durum or molle, 0.25 to 0.5 ml; bursitis under calcaneal spur, 0.5 ml; bursitis over hallux rigidus, 0.5 ml; bursitis over digit quinti varus, 0.5 ml; synovial cyst, 0.25 to 0.5 ml; Morton's neuralgia (metatarsalgia), 0.25 to 0.5 ml; tenosynovitis, 0.5 ml; periostitis of cuboid, 0.5 ml; acute gouty arthritis, 0.5 to 1 ml. After a favorable response is obtained, the proper maintenance dosage should be determined by decreasing the initial dose in small decrements at appropriate time intervals until the lowest dose which will maintain an adequate clinical response is determined. Exposure of the patient to stressful situations unrelated to the existing disease may necessitate an increased dose of DIPROFOS Suspension. If the drug is to be discontinued after long-term therapy, the dose should be decreased gradually.

DRUG AND LABORATORY TEST INTERACTIONS:

Drug Interactions: Concurrent use of phenobarbital, phenytoin, rifampin or ephedrine may enhance the metabolism of corticosteroids, reducing their therapeutic effects. Patients receiving both a corticosteroid and an estrogen should be observed for excessive corticosteroid effects. Concurrent use of corticosteroids with coumarin-type anticoagulants may increase or decrease the anticoagulant effects, possibly requiring adjustment in dosage. Combined effects of non-steroidal anti-inflammatory drugs or alcohol with glucocorticosteroids may result in an increased occurrence or increased severity of gastrointestinal ulceration. Corticosteroids may decrease blood salicylate concentrations. Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. Dosage adjustments of an antidiabetic drug may be necessary when corticosteroids are given to diabetics. Concomitant glucocorticosteroid therapy may inhibit the response to somatotropin.

Laboratory Test Interactions: Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

ADVERSE REACTIONS:

Adverse reactions to DIPROFOS Suspension, which have been the same as those reported for other corticosteroids, relate both to dose and to duration of therapy. Usually these reactions can be reversed or minimized by a reduction in dosage; this is generally preferable to withdrawal of drug treatment.

Fluid and electrolyte disturbances: sodium retention, potassium loss, hypokalemic alkalosis; fluid retention; congestive heart failure in susceptible patients; hypertension.

Musculoskeletal: muscle weakness, corticosteroid myopathy, loss of muscle mass; aggravation of myasthenic symptoms in myasthenia gravis; osteoporosis; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones; tendon rupture; joint instability (from repeated intra-articular injections).

Gastrointestinal: peptic ulcer with possible subsequent perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis.

Dermatologic: impaired wound healing; skin atro-
mandatory in the use of DIPROFOS Suspension. DIPROFOS Suspension contains two betamethasone esters, one of which, betamethasone sodium phosphate, disappears rapidly from the injection site. The potential for systemic effect produced by this soluble portion of DIPROFOS Suspension should therefore be taken into account by the physician when using this preparation. DIPROFOS Injection should be administered intramuscularly with caution to patients with idiopathic thrombocytopenic purpura. IM injections of corticosteroids should be given deep into large muscle masses to avoid local tissue atrophy. Soft tissue, intralesional and intra-articular administration of a corticosteroid may produce systemic as well as local effects. Examination of any joint fluid present is necessary to exclude a septic process. Local injection into a previously infected joint is to be avoided. A marked increase in pain and local swelling, further restriction of joint motion, fever and malaise are suggestive of septic arthritis. If the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted. Corticosteroids should not be injected into unstable joints, infected areas or intervertebral spaces. Repeated injections into joints of osteoarthritis may increase joint destruction. Avoid injecting corticosteroids directly into the substance of tendons because delayed appearance of tendon rupture has resulted. Following intra-articular corticosteroid therapy, care should be taken by the patient to avoid overuse of the joint in which symptomatic benefit has been obtained. Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measure should be taken prior to administration, especially when the patient has a history of allergy to any drug. With long-term corticosteroid therapy, transfer from parenteral to oral administration should be considered after weighing the potential benefits and risks. Dosage adjustments may be required with remission or exacerbation of the disease process, the patient’s
individual response to therapy and exposure of the patient to emotional or physical stress such as serious infection, surgery or injury. Monitoring may be necessary for up to one year following cessation of long-term or high-dose corticosteroid therapy. Corticosteroids may mask some signs of infection, and new infections may appear during use. When corticosteroids are used, decreased resistance and inability to localize infection may occur. Prolonged corticosteroid use may produce posterior subcapsular cataracts (especially in children), glaucoma with possible damage to the optic nerves, and may enhance secondary ocular infections due to fungi or viruses. Average and large doses of corticosteroids 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 considered. 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 receiving corticosteroids, especially high doses, because of possible hazards of neurological complications and lack of antibody response. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison disease. Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice. This is of particular importance in children. Corticosteroid therapy in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for management in conjunction with an appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary since reactivation of the disease may occur. During prolonged corticosteroid therapy, patients should receive chemoprophylaxis. If rifampin is used in a chemoprophylactic program, its enhancing effect on metabolic hepatic clearance of corticosteroids should be considered; adjustment in corticosteroid dosage may be required. The lowest possible dose of corticosteroid should be used to control the condition under treatment; when dosage reduction is possible, it should be gradual. Drug-induced secondary adrenocortical insufficiency may result from too rapid corticosteroid withdrawal and may be minimized by gradual dosage reduction. Such relative insufficiency may persist for months after discontinuation of therapy; therefore, if stress occurs during that period, corticotherapy should be reinstituted. If the patient is receiving corticosteroids already, dosage may have to be increased. Since mineralcorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently. Corticosteroid effect is enhanced in patients with hypothyroidism or in those with cirrhosis. Cautious use of corticosteroids is advised in patients with ocular herpes simplex because of possible corneal perforation. Psychic derangements may appear with corticosteroid therapy. Existing emotional instability or psychotic tendencies may be aggravated by corticosteroids. Corticosteroids should be used with caution in: nespecific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis. Since complications of glucocorticosteroid treatment are dependent on dose, size and duration of treatment, a risk/benefit decision must be made with each patient.

Since corticosteroid administration can disturb growth rates and inhibit endogenous corticosteroid production in infants and children, the growth and development of these patients receiving prolonged therapy should be followed carefully. Corticosteroids may alter the motility and number of spermatozoa in some patients.
USAGE DURING PREGNANCY AND LACTATION:
Since controlled human reproduction studies have not been done with corticosteroids, the use of DIPROFOS Suspension during pregnancy or in women of child-bearing age requires that the possible benefits of the drug be weighed against potential hazards to mother and fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism. Because of the potential for unwanted adverse effects from DIPROFOS Suspension in nursing infants, a decision should be made whether to discontinue nursing or to discontinue therapy, taking into account the importance of the drug to the mother.

OVERDOSAGE INFORMATION
Symptoms: Acute overdosage with glucocorticosteroids, including betamethasone, is not expected to lead to a life-threatening situation. Except at the most extreme dosages, a few days of excessive glucocorticosteroid dosing is unlikely to produce harmful results in the absence of specific contraindications, such as in patients with diabetes mellitus, glaucoma, or active peptic ulcer, or in patients on medications such as digitalis, coumarin-type anticoagulants or potassium-depleting diuretics.

Treatment: Complications resulting from the metabolic effects of the corticosteroid or from deleterious effects of the basic or concomitant illnesses or resulting from drug interactions should be handled as appropriate.
Maintain adequate fluid intake and monitor electrolytes in serum and urine, with particular attention to sodium and potassium balance. Treat electrolyte imbalance if necessary.

HOW SUPPLIED:
DIPROFOS Injection, 2 ml ampoule.

STORAGE:
Shake well before using. Stored not above 30° C. Protect from light and freezing.

*Trademark