Decreased carbohydrate tolerance
Manifestations of latent diabetes mellitus
Hyperglycemia
Increased requirements for insulin or oral hypoglycemic in diabetics
Hirsutism

Ophthalmic
Posterior subcapsular cataracts
Increased intraocular pressure
Glaucoma
Exophthalmos

Metabolic
Negative nitrogen balance due to protein catabolism

Cardiovascular
Myocardial repture following recent myocardial infraction (see warnings)

Other
Hypersentivity

Thromboembolism
Weight gain
Increased appetite
Nausea
Malaise
Hiccups

OVERDOSAGE

Reports of acute toxicity and / or death following overdosage of glucocorticoids are rare. In the event of overdosage, no specific sntidote is available; treatment is supportive and symptomatic. The oral LD 50 of dexamethasone in female mice was 6.5g/kg.

DOSAGE AND ASMINISTRATION

For oral administration

DOSAGE REQUIREMENT ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE AND THE RESPONSE OF THE PATIENT.

The initial dosage varies from 0.75 to 9 mg a day depending on the disease being treated. In less severe disease doses lower than 0.75 mg may suffice, while in severe diseases doses higher than 9 mg may be required. The initial dosage should be maintained or adjusted until the patient's response is satisfactory. If satisfactory , clinical response does not occur after a reasonable period of time, discontinue DEXAM™ tablets and transfer the patient to other therapy.

After a favorable initial response, the proper maintenance dosage should be determined by decreasing the initial dosage in small amounts to the lowest dosage that maintains an adequate clinical response.

Patients should be observed closely for signs that might dosage adjustment, including changes in clinical status resulting from remissions or exacerbations of the disease, individual drug responsiveness, and effect of stress (e.g surgery, infection, trauma). During stress it may be necessary to increase dosage temporarily.

If the drug is to be stopped after than a few days of treatment, it usually should be withdrawn gradually.

The following milligram facilitate changing to Dexamethasone from other glucocorticoids:

Dexamethasone Methylprednisolone and Triamcinotone Prednisolone and Prednisone Hydrocortisone Cortisone

0.75 mg = 4 mg = 5 mg = 20 mg =25 mg

In acute, sleft-limited allergic disorder or acute exacerbations of chronic allergic disorders, the following dosage schedule combining parenteral and oral therapy is suggested.

Dexamethasone sodium Phosphate Injection , 4 mg per ml:

First Day
1 or 2 ml, Intramuscularly

Dexamethasone tablets, 0.75 mg:

Second Day
4 tablets in two divided doses.

Third Day
4 tablets in two divided doses

Fourth Day
2 tablets in two divided doses.

Fifth Day
1 tablet

Sixth day
1 tablet

Seventh day
No treatment

Eight day

Follow-up visit

This schedule is designed to ensure therapy during acute episodes , while minimizing the risk of overdosage in chronic cases.

In cerebral edema, Dexamethsone Sodium Phosphate injection is generally administered initially in a dosage of cerebral edema subside. Response is usually noted within 12 to 24 hours and dosage may be reduced after two to four days and gradually discontinued over a period of five to seven days. For palliative management of patients with recurrent or inoperable brain tumors, maintenance therapy with either Dexamethasone Sodium Phosphate injection or Dexamethasone tablets in a dosage of two mg two or three times daily may be effective.

Dexamethasone suppression tests.

1. Tests for Cushing's syndrome

Give 1.0 mg of Dexamethasone orally at 11:00 p.m. Blood is drawn for plasma cortisol determination at 8.00 a.m. The following morning.

For greater accuracy, give 0.5 mg of decadron orally every 6 hours for 48 hours. Twenty- four hour urine collections are made for determination of 17-hydroxycorticosteriod excretion.

2. Test to distinguish cushing's syndrome due to pituitary ACTH excess from Cushing's syndrome due to other causes.

Give 2.0 mg of Dexamethasone orally every 6 hours of 48 hours. Twenty- four hour urine collections are made for determinations of 17-hydroxycorticosteriod excretion.

HOW SUPPLIED

They are available as follows:

DEXAM™	8 mg & 4 mg tablets, 5 strips of 8 tablets each
DEXAM™	Injection of 8 mg in 2ml vial.

Marketed by:
Getwell Oncology Pvt. Ltd.
(A unit of Getwell)
464, Udyog Vihar, Phase -V, Gurgaon -122 016, Haryana, India.

For Injection:
Manufactured by:
Getwell Pharmaceuticals
474, Udyog Vihar, Phase -V, Gurgaon -122 016, Haryana, India.

For Tablet:
Manufactured by:
Drugfarm Laboratories
Plot No. 907, M.I.E.
Bahadurgarh - 124 507, Haryana, India.

0700DDD

GETWELL

For the use of Registered Medical Practitioner or Hospital or a Laboratory only.

Dexamethasone Sodium Phosphate Injection IP

Dexamethasone Tablets IP

DEXAM™

Rx only

WARNING

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated. Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discountinuation of therapy : therefore, if any situation of stress occurring during that period, hormone therapy should be reinstituted. If the patient is receiving steroids already, dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and / or a mineralocorticoid should be administered concurrently. (See precautions). 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. Moreover, corticosteroids may affect the nitroblue-tetrazolium test for bacterial infection and produce false negative results.

In cerebral malaria, a double -blind trial has shown that the use of corticosteroids is associated with prolongation of coma and a higher incidence of pneumonia and gastrointestinal bleeding. Corticosteriods may activate latent amebiasis. Therefore, it is recommended that latent or active amebasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained diarrhea.

Prolonged used 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.

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

Corticosteriods appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects. Mothers taking pharmacologic doses of corticosteroids should be advised not to nurse.

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.

Administration of live virus vaccines, including smallpox, is contraindicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroid the expected serum antibody response may not be obtained. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., For Addison's disease.

Patients who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even total course in non-immune patients on corticosteroids. In such patients who have not had these diseases, particular care should be taken to avoid exposure. The risk of developing a disseminated infection varies among individuals and can be related to the dose, route and duration of corticosteroids administration as well as to the underlying disease. If exposed to chickenpox, prophylaxis with varicella zoster immunoglobulin (VZIG) may be indicated. If chickenpox develops , treatment with antiviral agents may be considered. If exposed to measles, prophyiaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for VZIG and IG for complete prescribing information.).

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

The use of DEXAM™ tablets/ injections 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.

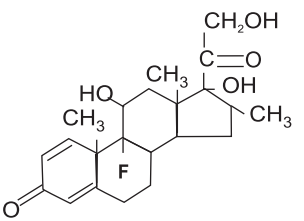
If conrticosteriods are indicated in patients with latent tuberculosis or tuberculin reactivity close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Literature reports suggest an apparent association between use of corticosteroids and left ventricular free wall rupture after a recent myocardial infarction, therefore, therapy with corticosteriods should be used with great caution in these patients.

DESCRIPTION

Glucocorticoids are adrenocortical steroids, whether naturally occurring or synthetic, are readily absorbed from the gastrointestinal tract.

Dexamethasone a synthetic adrenocortical steriod, is a white to practically white, odorless, crystalline powder. It is stable in air. It is practically insoluble in water. The molecular weight is 392.47. It is designated chemically as 9 fluoro-11 (beta), 17,21- trihydroxy-16(alpha) methylpregna-1, 4-diene-3, 20-dione. The empirical formula is $C_{22}H_{29}FO_5$ and the structural formula is :



COMPOSITION

Each uncoated tablet contains:

Dexamethasone IP	4mg & 8mg

Each ml contains:

Dexamethasone Sodium Phosphate IP	
Eqv. to Dexamethasone Phosphate	4 mg
Methylparaben IP	0.15% w/v
Propylparaben IP	0.02% w/v
(As Preservatives)	
Water for injection IP	q.s

ACTIONS

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

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

At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium retaining property of hydrocortisone and closely related derivatives of hydrocortisone.

INDICATIONS

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 excerbation) in :
Psoriatic arthritis
Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may required low dose maintenance therapy)
Ankylosing spondylitis
Acute and subacute bursitis
Acute nonspecific tenosynovitis
Acute gouty arthiritis
Post-traumatic osteoarthritis
Synovitis of osteoarthritis
Epicondylitis

3. Collagen Diseases

During an exacerbation or as maintenance therepy in selected cases of
Systemic lupus erythematosus
Acute rheumatic carditis

4. Dermatologic Diseases

Pemphigus
Bullous dermatitis herpetiformis
Severe erythema multiforme (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
Contract 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 conjunctivitis
Keratitis
Allergic corneal marginal ulcers
Herpes zoster ophthalmicus
Iritis and iridocyclitis
Chorioretinitis
Anterior segment inflammation
Diffuse posterior uveitis and choroiditis
Optic neuritis
Sympathetic ophthalmia

7. Respiratory Diseases

Symptomatic sarcoidosis
Loeffer'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 (automimmune) hemolytic anemia
Erythroblastopenia (RBC anemia)
Congential (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. Cerabral Edema associated with primary or metastatic brain tumor, craniotomy, or head injury. Use in cerebral edema is not a substitute for careful neurosurgical evaluation and definitive management such as neurosurgery or other specific therapy.

13. Miscellaneous

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

14. Diagnostic testing of adrenocortical hyperfunction.

CONTRAINDICATIONS

Systemic fungal infections Hypersensitivity to this drug.

PRECAUTIONS

Following prolonged therapy, withdrawal of corticosteroids may result in symptoms of the corticosteroid withdrawal syndrome including fever, myalgia, arthralgia and malaise.
This may occur in patients even without evidence of adrenal insufficiency.
There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.
Corticosteriods should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.
The lowest possible dose of corticosteroids should be used to control the condition under treatment, and when reduction in 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.
Co-administration of thalidomide with DEXAM™ tablets / injection should be employed cautiously, as toxic epidermal necrolysis has been reported with concomitant use.
Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia Steriods should be used with caution in nonspecific ulcerative colitis, it there is a probability of impending perforation, abscess, or other pyrogenic infection, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency , hypertension, osteoporosis and myasthenia gravis. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat ambolism has been reported as a possible complication of hypercortisonism.
When large doses are given, some authorities advise that corticosteroids be taken with meals and antacids taken between meals to help to prevent peptic ulcer.
Steriods may increase or decrease motility and number of spermatozoa in some patients.
Cytochrome P450 3A4 (CYP 3A4) enzyme inducers, such as phenytoin, barbiturates (e.g.Phenobarbital), carbamazepine, and rifampin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, thus requiring and increase in corticosteroid dosage.
Dexamethasone is metabolized by CYP 3A4, Concomitant administration of dexamethasone with inducers of CYP 3A4 (as listed above) has the potential to result in decreased plasma concentrations of dexamethasone in addition, concomitant administration of dexamethasone with known inhibitors of CYP 3A4 (e.g Ketoconazole, marcrolide antibiotics such as erythromycin) has the potential to result in increased plasma concentrations of dexamethasone. Effect of other drugs on the metabolism of dexamethasone may interfere with dexamethasone suppression tests, which should be interpreted with caution during administration of such drugs.
Dexamethasone is moderate inducer of CYP 3A4, Co-administration of dexamethasone with other drugs that are metabolized CYP 3A4 (e.g Indinavir, erythromycin) may increase their clearance, resulting in decreased plasma concentrations,
In post- marketing experience, there have been reports of both increases and decreases in phenytoin levels with dexamethasone co-administration, leading alterations in seizure control.
Although ketoconazole may increase dexamethasone plasma concentrations through inhibition of CYP 3A4, ketoconazole alone can inhibit adrenal corticosteroid synthesis and may cause adrenal insufficiency during corticosteroid withdrawal (see WARNINGS).
Ephedrine may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, thus requiring an increase in corticosteroid dosage.
False – negative results in the dexamethasone suppression test (DST) in patients being treated with indomethacin have been reported . Thus, result of the DST should be interpreted with caution in these patients.
The prothrombin time should be checked frequently in patients who are receiving corticosteriods and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants . Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to conmarins, although there have been some conflicting reports of potentiation and substantiated by studies.
When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalemia,
Information for patients
Susceptible 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.
Pediatric Use
Growth and development of pediatric on prolonged corticosteroid therapy should be carefully followed.

ADVERSE REACTIONS

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

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

Gastrointestinal
- Peptic ulcer with possible perforation and hemorrhage
- Perforation of the small and large bowel, particularly in patients with inflammatory bowel disease.
- Pancreatitis
- Abdominal distention
- Ulcerative esophagitis

Dermatologic
- Impaired wound healing
- Thin fragile skin
- Petechiae and ecchymoses
- Erythema
- Increased sweating
- May suppress reactions to skin tests, other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema

Neurologic
- Convulsions
- Increased intracranial pressure with papilledema (pseudotumor cerebral) usually after treatment
- Vertigo
- Headache
- Psychic disturbances

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.