DYNACORT Oral Suspension
(Deflazacort Oral Suspension 6 mg/5 ml)

INSERT:

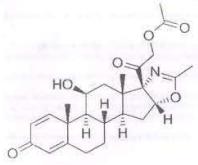
For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

DYNACORT 6 MG /18 MG/30MG TABLETS & 6 MG / 5 ML ORAL SUSPENSION

Deflazacort Tablets 6 mg /18 mg/30 mg/ & 6 mg / 5 ml Suspension

DYNACORT -6 MG
Each Uncoated Tablet Contains
Deflazacort 6 mg
DYNACORT -18 MG
Each Uncoated Tablet Contains
Deflazacort 18 mg
DYNACORT -30 MG
Each Uncoated Tablet Contains
Deflazacort 30 mg
DYNACORT ORAL SUSPENSION
Each 5 ml Suspension Contains:
Deflazacort 6 mg (After Reconstitution)
Flavoured Base .

DESCRIPTION
Deflazacort is a glucocorticoid. The molecular formula for deflazacort is C25H31NO6. The chemical name for deflazacort is (11β,16β)-21-(acetyloxy)11-hydroxy-2'-methyl-5'H-pregna-1,4-dieno[17,16-d]oxazole-3,20-dione, and the structural formula is: C25H31NO6



ATC Code : H02AB13

PHARMACOLOGICAL CLASSIFICATION

Deflazacort is a glucocorticoid used as an anti-inflammatory and immuno suppressant.

ROUTE OF ADMINISTRATION : Oral

PHARMACOLOGICAL ACTION:

Mechanism of Action

Deflazacort works by acting within cells to prevent the release of certain chemicals that are important in the immune system.
Deflazacort is a corticosteroid prodrug, whose active metabolite, 21-desDFZ, acts through the glucocorticoid receptor to exert anti-inflammatory and immunosuppressive effects. The precise mechanism by which deflazacort exerts its therapeutic effects in patients with Duchenne Muscular Dystrophy is unknown.

Pharmacokinetic Properties

Absorption
After oral administration in the fasted state, the median Tmax with deflazacort tablets or suspension is about 1 hour (range 0.25 to 2 hours).

Food Effect: Co-administration of deflazacort tablets with a high-fat meal reduced Cmax by about 30% and delayed Tmax by one hour, relative to administration under fasting conditions, but there was no effect on the overall systemic absorption as measured by AUC. The bioavailability of deflazacort tablets was similar to that of the oral suspension. The administration of deflazacort with food or crushed in applesauce did not affect the absorption and bioavailability of deflazacort.

Distribution
The protein binding of the active metabolite of deflazacort is about 40%.

Metabolism
Deflazacort is rapidly converted to the active metabolite 21-desDFZ by esterases after oral administration. 21-desDFZ is further metabolized by CYP3A4 to several other inactive metabolites.

Excretion
Urinary excretion is the predominant route of deflazacort elimination (about 68% of the dose), and the elimination is almost completed by 24 hours post dose. 21-desDFZ accounts for 18% of the eliminated drug in the urins.

INDICATIONS AND USAGE
A wide range of conditions may sometimes need treatment with glucocorticoids. The indications include:
- Anaphylaxis, asthma, severe hypersensitivity reactions
- Rheumatoid arthritis, juvenile chronic arthritis, polymyalgia rheumatica
- Systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease (other than systemic sclerosis), polyarteritis nodosa, sarcoidosis
- Pemphigus, bullous pemphigoid, pyoderma gangrenosum
- Minimal change nephrotic syndrome, acute interstitial nephritis
- Rheumatic carditis
- Ulcerative colitis, Crohn's disease
- Uveitis, optic neuritis
- Autoimmune haemolytic anaemia, idiopathic thrombocytopenic purpura
- Acute and lymphatic leukaemia, malignant lymphoma, multiple myeloma
- Immune suppression in transplantation

CONTRAINDICATIONS
Systemic infection unless specific anti-infective therapy is employed.
Hypersensitivity to deflazacort or any of the ingredients. Patients receiving live virus immunisation.

DOSAGE AND ADMINISTRATION :

Oral Administration.
May take with or without food.

Adults
Acute disorders: In the treatment of acute disorders, up to 120 mg/day may need to be given initially. Maintenance doses in most conditions are within the range 3-18 mg/day.

Rheumatoid arthritis: The maintenance dose is usually within the range 3-18 mg/day. The smallest effective dose should be used and increased if necessary.
Bronchial asthma: In the treatment of an acute attack, high doses of 48-72 mg/day may be needed depending on severity and gradually reduced once the attack has been controlled. For maintenance in chronic asthma, doses should be titrated to the lowest dose that controls symptoms.
Other conditions: The dose depends on clinical need titrated to the lowest effective dose for maintenance. Starting doses may be estimated on the basis of ratio of 5 mg prednisone or prednisolone to 6 mg Deflazacort.
Hepatic Impairment: In patients with hepatic impairment, blood levels of may be increased. Therefore the dose should be carefully monitored and adjusted to the minimum effective dose.
Renal Impairment: In renally impaired patients, no special precautions other than those usually adopted in patients receiving glucocorticoid therapy are necessary.
Elderly
In elderly patients, no special precautions other than those usually adopted in patients receiving glucocorticoid therapy are necessary.
Children
Doses usually lie in the range 0.25 - 1.5 mg/kg/day. Alternate day administration may be appropriate. However, glucocorticoids cause growth retardation in infancy, childhood & adolescence, therefore long-term administration of pharmacological doses should be avoided.
The following ranges provide general guidance:
Juvenile chronic arthritis: The usual maintenance dose is between 0.25 - 1.0 mg/kg/day.
Nephrotic syndrome: Initial dose of usually 1.5 mg/kg/day followed by down titration according to clinical need.
Bronchial asthma: On the basis of the potency ratio, the initial dose should be between 0.25 - 1.0 mg/kg on alternate days.
Tablets: If tablets are used, round up to the nearest possible dose; may use any combination of tablet strengths to achieve calculated dose.
Oral suspension: If the oral suspension is used, round up to the nearest tenth of a milliliter (mL).
Use boiled or cooled water to prepare suspension.
Shake suspension well before measuring dose.
Use reconstituted suspension within 7 days after reconstitution.
Discontinuation:
Dosage must be decrease gradually if the drug has been administered for more than a few days.
OR As directed by the Physician.

WARNINGS & PRECAUTIONS :
A patient information leaflet should be supplied with this product.
Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose galactose malabsorption should not take this medicine.
Undesirable effects may be minimised by using the lowest effective dose for the minimum period, and by administering the daily requirement as a single morning dose or whenever possible as a single morning dose on alternate days. Frequent patient review is required to appropriately titrate the dose against disease activity
Adrenal suppression
Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Withdrawal of corticosteroids after prolonged therapy must therefore always be gradual to avoid acute adrenal insufficiency which could be fatal, being tapered off over weeks or months according to the dose and duration of treatment. During prolonged therapy, any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage; if corticosteroids have been stopped following prolonged therapy, they may need to be temporarily reintroduced. Patients should carry 'Steroid treatment' cards which give clear guidance on the precautions to be taken to minimise risk and which provide details of prescriber, drug, dosage and the duration of treatment.

Antiinflammatory/ immunosuppressive effects and infection
Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity.
The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised.

Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chicken pox should be advised to avoid close personal contact with chickenpox or herpes zoster and, if exposed, they should seek urgent medical attention. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed by exposed nonimmune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment.
Corticosteroids should not be stopped and the dose may need to be increased.
Patients should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs. Prophylaxis with intramuscular normal immunoglobulin may be needed.
Live vaccines should not be given to individuals with impaired responsiveness. The antibody response to other vaccines may be diminished.
Systemic glucocorticoid treatment can cause chorioretinopathy which can lead to visual disorders including visual loss. Prolonged use of systemic glucocorticoid treatment even at low dose can cause chorioretinopathy
Prolonged use of glucocorticoids 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 active tuberculosis should be restricted to those cases of fulminating and disseminated tuberculosis in which deflazacort is used for management with appropriate antituberculosis regimen. If glucocorticoids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged glucocorticoid therapy, these patients should receive chemoprophylaxis.
Tendonitis and tendon rupture are known class effect of glucocorticoids. The risk of such reactions may be increased by coadministration of quinolones

Special precautions
The following clinical conditions require special caution and frequent patient monitoring is necessary :-
Cardiac disease or congestive heart failure (except in the presence of active rheumatic carditis), hypertension, thromboembolic disorders. Glucocorticoids can cause salt and water retention and increased excretion of potassium. Dietary salt restriction and potassium supplementation may be necessary.
Gastritis or oesophagitis, diverticulitis, ulcerative colitis if there is probability of impending perforation, abscess or pyogenic infections, fresh intestinal anastomosis, active or latent peptic ulcer.
Diabetes mellitus or a family history, osteoporosis, myasthenia gravis, renal insufficiency.
Emotional instability or psychotic tendency, epilepsy.
Previous corticosteroid-induced myopathy.
Liver failure.
Hypothyroidism and cirrhosis, which may increase glucocorticoid effect.
Ocular herpes simplex because of possible corneal perforation.
Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids . Symptoms typically emerge within a few days or weeks of starting the treatment. Risks may be higher with high doses/systemic exposure (see also pharmacokinetic interactions that can increase the risk of side effects) although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should also be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently.
Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.
Glucocorticoids are known to cause irregular menstruation and leukocytosis, care should be taken with deflazacort.
Paediatric population
Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence which may be irreversible.
Use in Elderly
The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions.
Since complications of glucocorticoid therapy are dependent on dose and duration of therapy, the lowest possible dose must be given and a risk/benefit decision must be made as to whether intermittent therapy should be used.
DRUG INTERACTIONS
The same precautions should be exercised as for other glucocorticoids. Deflazacort is metabolised in the liver. It is recommended to increase the maintenance dose of deflazacort if drugs which are liver enzyme inducers are coadministered, e.g. rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and aminoglutethimide. For drugs which inhibit liver enzymes, e.g. ketoconazole it may be possible to reduce the maintenance dose of deflazacort.
In patients taking estrogens, corticosteroid requirements may be reduced.

The desired effects of hypoglycaemic agents (including insulin), antihypertensives and diuretics are antagonised by corticosteroids and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics, beta 2 agonists, xanthines and carbenoxolone are enhanced.

The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding.
In patients treated with systemic corticosteroids, use of non depolarising muscle relaxants can result in prolonged relaxation and acute myopathy. Risk factors for this include prolonged and high dose corticosteroid treatment, and prolonged duration of muscle paralysis. This interaction is more likely following prolonged ventilation (such as in the ITU setting).

The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication.

As glucocorticoids can suppress the normal responses of the body to attack by microorganisms,
it is important to ensure that any anti infective therapy is effective and it is recommended to monitor patients closely. Concurrent use of glucocorticoids and oral contraceptives should be closely monitored as plasma levels of glucocorticoids may be increased. This effect may be due to a change in metabolism or binding to serum proteins. Antacids may reduce bioavailability, leave at least 2 hours between administration of deflazacort and antacids.

PREGNANCY AND LACTATION
Pregnancy
The ability of corticosteroids to cross the placenta varies between individual drugs, however, deflazacort does cross the placenta.
Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state.
Lactation
Corticosteroids are excreted in breast milk, although no data are available for deflazacort. Doses of up to 50 mg daily of deflazacort are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression but the benefits of breast feeding are likely to outweigh any theoretical risk.

ADVERSE REACTIONS
Deflazacort carries the risks common to all corticosteroids, including immune suppression, decreased bone density, and endocrine insufficiency. In clinical trials, the most common side effects (>10% above placebo) were Cushing's like appearance, weight gain, and increased appetite

OVERDOSAGE
It is unlikely that treatment is needed in cases of acute overdosage. The LD50 for the oral dose is greater than 4000 mg/kg in laboratory animals.

PRESENTATION:
Tablets : Alu-Alu Blister pack of 3 X 10 Tablets .
Suspension : 1 X 30 ml

STORAGE:
Store Tablet & Suspension in a cool dry place below 30°C.
Keep medicines out of reach of children.
Discard any unused oral suspension remaining after 7 days.

DYNACORT-6 MG

DYNACORT-18 MG

DYNACORT-30 MG

DYNACORT 6 MG / 5 ML SUSPENSION

Manufactured for / Fabriqué Pour:
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