reast-feeding
orticosteroids are excreted in small amounts in breast milk. Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid roduction in nursing infants.

NDESIRABLE EFFECTS:
wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood, and suicidal thoughts), psychotic reactions (including ania, delusions, hallucinations, and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including nfusion and amnesia have been reported. Reactions are common and may occur in both adults and children. In adults, the frequency of severe reactions has been estimated to be -6%. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown.

ithdrawal symptoms:
o rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency; hypotension and death. A steroid 'withdrawal syndrome' emingly unrelated to adrenocortical insufficiency may also occur following abrupt discontinuance of glucocorticoids. This syndrome includes symptoms such as: anorexia, ausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules, weight loss, and/or hypotension. These ffects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels. Psychological effects have been reported on withdrawal of rticosteroids.

verdose:
eports of acute toxicity and/or death following overdosage of glucocorticoids are rare. No specific antidote is available; treatment is supportive and symptomatic. Serum ectrolytes should be monitored.

igh systemic doses of corticosteroids caused by chronic use have been associated with adverse effects such as neuropsychiatric disorders (psychosis, depression, and allucinations), cardiac dysrhythmias and Cushing's syndrome.

HARMACOLOGICAL PROPERTIES:
harmacodynamic properties
harmacotherapeutic group: Corticosteroids for systemic use.

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

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

harmacokinetic properties
sorption: Prednisolone is rapidly and apparently almost completely absorbed after oral administration; it reaches peak plasma concentrations after 1-3 hours. There is however ide inter-subject variation suggesting impaired absorption in some individuals. Plasma half-life is about 3 hours in adults and somewhat less in children. Its initial absorption, but t its overall bioavailability, is affected by food. Prednisolone has a biological half-life lasting several hours, making it suitable for alternate-day administration regimens.

stribution: Prednisolone shows dose dependent pharmacokinetics, with an increase in dose leading to an increase in volume of distribution and plasma clearance. The degree of asma protein binding determines the distribution and clearance of free, pharmacologically active drug. Reduced doses are necessary in patients with hypoalbuminaemia.

otransformation: Prednisolone is metabolised primarily in the liver to a biologically inactive compound. Liver disease prolongs the half-life of Prednisolone and, if the patient has rpoalbuminaemia, also increases the proportion of unbound drug and may thereby increase adverse effects.

imination: Prednisolone is excreted in the urine as free and conjugated metabolites, together with small amounts of unchanged Prednisolone.

TEGORY: Prescription Only Medicine (POM).

TORAGE CONDITION: Store in a dry place below 30°C. Protect from light. Keep all medicines out of reach of children.

HELF LIFE: As per the product label.

RESENTATION: Pedsol® Tablets: packed in 1000's in HDPE container and in blisters of 10x10's in a unit box with literature.
edsol® Eye/Ear Drops: 5ml sterile solution in dropper vials.

TE OF LAST REVIEW: October 2017.

ICENCE HOLDER: LABORATORY & ALLIED LTD.

Laboratory & Allied Ltd.
Plot No. 209/10349, Mombasa Road,
P.O. Box 42875, Nairobi, Kenya

LTP002-00

PEDSOL®
Prednisolone preparations

COMPOSITION
Pedsol® Tablets: Each tablet contains Prednisolone BP 5mg. Contains Lactose Monohydrate.
Pedsol® Eye/Ear Drops: Contains Sodium Phosphate BP 0.518%w/v and Benzalkonium Chloride BP 0.02% as preservative.

PHARMACEUTICAL FORM
Pedsol® Tablets: White circular, biconvex tablet plain on both sides.
Pedsol® Eye/Ear Drops: A clear colourless liquid.

CLINICAL PARTICULARS
Therapeutic indications
Allergy and anaphylaxis: Bronchial asthma, drug hypersensitivity reactions, serum sickness, angioneurotic oedema, anaphylaxis.
Arteritis/collagenosis: giant cell arteritis/polymyalgia rheumatica, mixed connective tissue disease, polyarteritis nodosa, polymyositis.
Blood disorders: Haemolytic anaemia (auto-immune), leukaemia (acute and chronic lymphocytic), lymphoma, multiple myeloma.
Cardiovascular disorders: Post-myocardial infarction syndrome, rheumatic fever with severe carditis.
Endocrine disorders: Primary and secondary adrenal insufficiency, congenital adrenal hyperplasia.
Gastro-intestinal disorders: Crohn's disease, ulcerative colitis, persistent coeliac syndrome (coeliac disease unresponsive to gluten withdrawal), auto-immune chronic active hepatitis, multisystem disease affecting liver, biliary peritonitis.
Hypercalcaemia: Sarcoidosis, vitamin D excess.
Infections (with appropriate chemotherapy): helminthic infestations, Herxheimer reaction, infectious mononucleosis, miliary tuberculosis, mumps orchitis (adult), tuberculous meningitis, rickettsial disease.
Muscular disorders: Polymyositis, dermatomyositis.
Neurological disorders: Infantile spasms, Shy-Drager syndrome, sub-acute demyelinating polyneuropathy.
Ocular disease: Scleritis, posterior uveitis, retinal vasculitis, pseudo-tumours of the orbit, giant cell arteritis, malignant ophthalmic Grave's disease.
Renal disorders: Lupus nephritis, acute interstitial nephritis, minimal change glomerulonephritis.
Respiratory disease: Allergic pneumonitis, asthma, occupational asthma, pulmonary aspergillosis, pulmonary fibrosis, pulmonary alveolitis, aspiration of foreign body, aspiration of stomach contents, pulmonary sarcoid, drug induced lung disease, adult respiratory distress syndrome, spasmodic croup.
Rheumatic disorders: Rheumatoid arthritis, polymyalgia rheumatica, juvenile chronic arthritis, systemic lupus erythematosus, dermatomyositis, mixed connective tissue disease.
Skin disorders: Pemphigus vulgaris, bullous pemphigoid, systemic lupus erythematosus, pyoderma gangrenosum.
Miscellaneous: Sarcoidosis, hyperpyrexia, Behçets disease, immunosuppression in organ transplantation.
Pedsol Drops for Eye and Ear is indicated for short term treatment of steroid responsive inflammatory conditions of the eye after clinical exclusion of bacterial, viral and fungal infections and Non-infected inflammatory conditions of the ear.

Posology and method of administration
Tablets
Adults including the elderly: The lowest effective dose should be used for the minimum period in order to minimise side effects.
Initially: The initial dosage may vary from 5mg to 60mg daily in divided doses, as a single dose in the morning after breakfast, or as a double dose on alternate days. Dosage depends on the disorder being treated. The dose can often be reduced within a few days but may need to be continued for several weeks or months.
Maintenance: 2.5 to 15mg daily, but higher doses may be needed. Cushingoid side-effects more likely above 7.5mg daily.
Eyes and Ear Drops
Adults and Children (including the Elderly):
Eyes: 1 or 2 drops instilled into the eyes every one or two hours until control is achieved, then the frequency may be reduced.
Ears: 2 or 3 drops instilled into the ear every two or three hours until control is achieved, then the frequency can be reduced.
Posology for specific indications
Intermittent dosage regimen: A single dose of Prednisolone in the morning on alternate days or at longer intervals is acceptable therapy for some patients. When this regimen is

practical, the degree of pituitary-adrenal suppression can be minimised.

Specific dosage guidelines: The following recommendations for some corticosteroid-responsive disorders are for guidance only. Acute or severe disease may require initial high dose therapy with reduction to the lowest effective maintenance dose as soon as possible. Dosage reductions should not exceed 5-7.5mg daily during chronic treatment.

Allergic and skin disorders: Initial doses of 5-15mg daily are commonly adequate.

Collagenosis: Initial doses of 20-30mg daily are frequently effective. Those with more severe symptoms may require higher doses.

Rheumatoid arthritis: The usual initial dose is 10-15mg daily. The lowest daily maintenance dose compatible with tolerable symptomatic relief is recommended.

Blood disorders and lymphoma: An initial daily dose of 15-60mg is often necessary with reduction after an adequate clinical or haematological response. Higher doses may be necessary to induce remission in acute leukaemia.

Special populations

Elderly: Treatment of elderly patients, particularly if long-term, should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age.

Children: Although appropriate fractions of the actual dose may be used, dosage will usually be determined by clinical response as in adults. Prednisolone should be used only when specifically indicated, in a minimal dosage and for the shortest possible time.

Method of administration: Tablets for oral administration should be taken with or after food.

CONTRAINDICATIONS:

- Systemic infection unless specific anti-infective therapy is employed.
- Hypersensitivity to the active substance or to any of the excipients.
- Ocular herpes simplex because of possible perforation.
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

SPECIAL WARNINGS AND PRECAUTIONS FOR TABLETS:

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, 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 tampering/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 them or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.

Caution is necessary when oral corticosteroids, including Prednisolone, are prescribed in patients with the following conditions, and frequent patient monitoring is necessary.

- Tuberculosis: Those with a previous history of, or X-ray changes characteristic of, tuberculosis. The emergence of active tuberculosis can however, be prevented by the prophylactic use of anti-tuberculosis therapy.
- Inflammatory bowel disease: Symptoms recurred in a patient with Crohn's disease on changing from conventional to enteric-coated tablets of Prednisolone. This was not an isolated occurrence in the author's unit, and it was advocated that only non-enteric coated Prednisolone tablets should be used in Crohn's disease, and that the enteric coated form should be used with caution in any condition characterized by diarrhoea or a rapid transit time.
- Hypertension.
- Congestive heart failure.
- Liver failure.
- Hepatic disease: In patients with acute and active hepatitis, protein binding of the glucocorticoids will be reduced and peak concentrations of administered glucocorticoids increased. Elimination of Prednisolone will also be impaired. There is an enhanced effect of corticosteroids in patients with cirrhosis.
- Renal insufficiency.
- Diabetes mellitus or in those with a family history of diabetes.
- Osteoporosis: This is of special importance in post-menopausal females who are at particular risk.
- Corticosteroid requirements may be reduced in menopausal and post-menopausal women.
- Patients with a history of severe affective disorders and particularly those with a previous history of steroid-induced psychoses.
- Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids including prednisolone.
- Epilepsy, and/or seizure disorders
- Peptic ulceration.
- Previous steroid myopathy.
- Glucocorticoids should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy.
- Because cortisone has been reported rarely to increase blood coagulability and to precipitate intravascular thrombosis, thromboembolism, and thrombophlebitis, corticosteroids should be used with caution in patients with thromboembolic disorders.

Anti-inflammatory/ 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 when corticosteroids, including Prednisolone, are used. The immunosuppressive effects of glucocorticoids may result in the activation of latent infection or exacerbation of intercurrent infection.

Chickenpox: 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 chickenpox 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 non-immune 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.

Measles: Patients taking corticosteroids should be advised to take particular care to avoid exposure to measles and to seek immediate medical advice if exposure occurs.

Administration of live vaccines: Live vaccines should not be given to individuals on high doses of corticosteroids, due to impaired immune response. Live vaccines should be postponed until at least 3 months after stopping corticosteroid therapy.

Ocular Effects: Prolonged use of corticosteroids may produce posterior subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos, or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves. Establishment of secondary fungal and viral infections of the eye may also be enhanced in patients receiving glucocorticoids.

Use in the elderly: Treatment of elderly patients, particularly if long term, should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, hypokalaemia, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life threatening reactions.

Paediatric population: Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible, and therefore long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, treatment should be limited to the minimum suppression of the hypothalamo-pituitary adrenal axis and growth retardation. The growth and development of infants and children should be closely monitored.

SPECIAL WARNINGS AND PRECAUTIONS FOR EYE/EAR DROPS:

Topical corticosteroids should never be given for an undiagnosed red eye as inappropriate use is potentially blinding. Ophthalmological treatment with corticosteroid preparations should not be repeated or prolonged without regular review to exclude raised intraocular pressure, cataract formation or unsuspected infections.

The use of corticosteroids may reduce resistance to or mask the signs of infection. Appropriate anti-infective agents should be used if infection is present.

Systemic effects of nasal corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids and may vary in individual patients and between different corticosteroid preparations. Potential systemic effects may include Cushing's syndrome, Cushingoid features, adrenal suppression, cataract, glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders and anxiety.

Paediatric population

Prolonged use may lead to the risk of adrenal suppression in infants. Potential systemic effects may include growth retardation in children and adolescents and more rarely a range of psychological or behavioural effects including depression or aggression (particularly in children)

FERTILITY, PREGNANCY AND LACTATION:

Pregnancy

The ability of corticosteroids to cross the placenta varies between individual drugs; however, 88% of Prednisolone is inactivated as it crosses the placenta.

Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growthr 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. The use of corticosteroids, including Prednisolone, during pregnancy may also result in stillbirth.

Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important.

Cataracts have been observed in infants born to mothers treated with long-term prednisolone during pregnancy.

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.

Patients with pre-eclampsia or fluid retention require close monitoring