Prednisolone Dispersible Tablets
WYSOLONE® DT

1. GENERIC NAME

Prednisolone Dispersible Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Prednisolone Dispersible Tablets DT 5: Each uncoated dispersible tablet contains Prednisolone I.P. 5 mg.
Prednisolone Dispersible Tablets DT 10: Each uncoated dispersible tablet contains Prednisolone I.P. 10 mg.
Prednisolone Dispersible Tablets DT 20: Each uncoated dispersible tablet contains Prednisolone I.P. 20 mg.

List of Excipients

Lactose IP, Microcrystalline Cellulose IP, Indion 234 IH, Colloidal Silicon Dioxide IP, Magnesium Stearate IP.

All strengths/presentations mentioned in this document might not be available in the market.

3. DOSAGE FORM AND STRENGTH

Dispersible Tablets
5mg, 10mg and 20mg

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prednisolone Dispersible Tablets 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 mineral corticoids where

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applicable; in infancy mineral corticoids supplement is of particular importance); congenital adrenal hyperplasia; non-suppurative thyroiditis; hypercalcemia associated with cancer.

2. Rheumatic Disorders

As adjunctive therapy for short-term administration (to assist the patient during 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 non-specific 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; systemic dermatomyositis (polymyositis).

4. Dermatologic Diseases

Pemphigus; bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome); exfoliative dermatitis, mycosis fungoides, severe psoriasis, severe seborrheic dermatitis lichen planus, unresponsive to local treatment.

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 conjunctivitis, keratitis, allergic corneal margin 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; 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 purpura in adults; acquired (autoimmune) hemolytic anemia; erythroblastopenia (red blood cell 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 or that due to lupus erythematosus.

11. Gastrointestinal Diseases

To assist the patient during a critical period of the disease in: ulcerative colitis; regional enteritis.

12. Hepatic Diseases

Subacute hepatic necrosis: chronic active hepatitis; alcoholic hepatitis; non-alcoholic cirrhosis in women when ascites is not present.

13. Nervous System

Acute exacerbations of multiple sclerosis.

14. Miscellaneous

Tuberculosis meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculosis chemotherapy; trichinosis with neurologic or myocardial involvement; adjunctive therapy in severe typhoidal toxemia when the patient is responsive to conventional therapy; concomitantly with other immunosuppressive drugs to prevent rejection of transplanted organs.

4.2 Posology and Method of Administration

Dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient. The initial dosage of Wysolone DT 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 clinical response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, Wysolone DT should be discontinued and the patient transferred to other appropriate therapy.

After a favourable response is noted, the proper maintenance dosage should be determined before decreasing the initial drug dosage in small increments at appropriate time intervals until the lowest dosage, which will maintain an adequate clinical response, is reached. Frequent monitoring of drug dosage and effect is required. Situations that may necessitate dosage adjustments include remissions or exacerbations of the disease process, the patient's individual response to the drug, and exposure of the patient to emotional stress or

physical stress such as serious infection, surgery, or injury. Monitoring may be necessary for periods up to one year following cessation of long-term or high-dose therapy.

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

Withdrawal following long-term therapy with pharmacological doses of systemic glucocorticoids, including prednisolone, should be very gradual rather than abrupt until recovery of the hypothalamic-pituitary-adrenal (HPA) axis occurs (see section 4.4 – **Special Warnings and Precautions for Use,** Endocrine).

Severe Typhoidal Toxemia - Wysolone 40 mg to 60 mg daily for 2 or 3 days has been used in the treatment of severely toxic patients unresponsive to conventional therapy.

Multiple Sclerosis - In the treatment of acute exacerbations of multiple sclerosis, daily doses of 200 mg of Wysolone for a week followed by 80 mg every other day for one month have been shown to be effective.

Infants and Children - Although appropriate fractions of the actual dose may be used, dosage will usually be determined by clinical response as in adults. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimize suppression of the hypothalamo-pituitary adrenal axis and growth retardation, treatment should be administered where possible as a single dose on alternate days (see section 4.4 – **Special Warnings and Precautions for Use –** Use in Children).

Alternate Day Therapy - If long-term oral glucocorticoid use is required for disease therapy, an alternate-day regimen of an intermediate-acting glucocorticoid (such as Wysolone) should be considered. The alternate day dosage is administered as a single dose every other morning and is usually equivalent to twice the daily dose. The purpose of this mode of therapy is to provide the patient with the beneficial effects of glucocorticoid while minimizing certain undesirable effects, including hypothalmic-pituitary-adrenal axis suppression, the Cushingoid state, glucocorticoid withdrawal symptoms, and growth suppression in children. To use alternate-day therapy, the patient should have a normal or moderately responsive pituitary axis. In addition, the patient's condition should be stabilized before the transition to alternate day therapy is attempted.

When large doses of glucocorticoids are administered, concomitant use of antacids may help to prevent peptic ulcer formation. Gastric irritation may be reduced if glucocorticoids are taken with meals or with food or milk.

4.3 Contraindications

Known hypersensitivity to Wysolone, Systemic fungal infections.

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids.

4.4 Special Warnings and Precautions for Use

Immunosuppressant Effects/Increased Susceptibility to Infection:
Glucocorticoids, including prednisolone, increase susceptibility to and may mask some symptoms of infection. New infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids, including prednisolone are used. Infections with any pathogen, including viral, bacterial, fungal, protozoan or helminthic organisms, in any location in the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity, or neutrophil function. These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases.

The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

Monitor for the development of infection and consider withdrawal of corticosteroids or dosage reduction as needed.

Children who are on immunosuppressant drugs are more susceptible to infections than healthy children. Chicken pox and measles, for example, can have a more serious or even fatal course in children on immunosuppressant corticosteroids. Children, or adults who have not had these diseases, who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chicken pox and measles and, if exposed, to obtain medical advice. If exposure occurs, therapy with varicella zoster immunoglobulin (VZIG) or pooled intravenous immunoglobulin (IVIG), as appropriate, may be indicated. If chicken pox develops, treatment with antiviral agents may be considered.

Glucocorticoids may increase susceptibility to and may mask some symptoms of infection. New infections may appear during their use. There may be decreased resistance and inability to localize infection when glucocorticoids are used. The use of Wysolone tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the glucocorticoid is used for the management of the disease in conjunction with an appropriate antituberculous 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.

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy.

Immune System: Allergic reactions (e.g., angioedema) may occur.

Because rare instances of skin reactions and anaphylactic/anaphylactoid reactions have occurred in patients receiving corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.

Immunization procedures should not be undertaken in patients who are on glucocorticoids, especially on high dose, because of possible hazards of neurological complications and a lack of antibody response.

Endocrine: Patients maintained on corticosteroid therapy and subjected to unusual stress (e.g. infection, surgery, trauma) require increased corticosteroid dosage before, during, and after the stressful situation.

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration, and duration of glucocorticoid therapy. This effect may be minimized by use of alternate-day therapy (see section **4.2 Posology and Method of Administration**, Alternate-Day Therapy).

In addition, acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly. Drug-induced secondary adrenocortical insufficiency may therefore be minimized by gradual reduction of 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.

A steroid "withdrawal syndrome," seemingly unrelated to adrenocortical insufficiency, may also occur following abrupt discontinuance of glucocorticoids. This syndrome includes symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, joint pain, desquamation, myalgia, weight loss, and/or hypotension. These effects are thought to be due to the sudden change in glucocorticoid concentration rather than to low corticosteroid levels.

Because glucocorticoids can produce or aggravate *Cushing's syndrome*, glucocorticoids should be avoided in patients with Cushing's disease.

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

Metabolism and Nutrition: Corticosteroids, including prednisolone, can increase blood glucose, worsen pre-existing diabetes, and predispose those on long-term corticosteroid therapy to diabetes mellitus.

Psychiatric: Psychic derangements may appear when corticosteroids, including prednisolone, 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, including prednisolone.

Potentially severe psychiatric adverse reactions may occur with systemic steroids (see section **4.8 Undesirable effects**, Psychiatric disorders). Symptoms typically emerge within

a few days or weeks of starting treatment. Most reactions resolve after either dose reduction or withdrawal, although specific treatment may be necessary.

Psychological effects have been reported upon withdrawal of corticosteroids; the frequency is unknown. Patients/caregivers should be encouraged to seek medical attention if psychological symptoms develop in the patient, especially if depressed mood or suicidal ideation is suspected. Patients/caregivers should be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids.

Nervous System Effects: Corticosteroids should be used with caution in patients with seizure disorders.

Glucocorticoids should be used cautiously in patients with myasthenia gravis receiving anticholinesterase therapy (see section **4.5 Drug Interactions**).

There have been reports of epidural lipomatosis in patients taking corticosteroids, typically with long-term use at high doses.

Ocular: Prolonged use of glucocorticoids may produce posterior subcapsular cataracts, 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. Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible perforation.

Corticosteroid therapy has been associated with central serous chorioretinopathy, which may lead to retinal detachment.

Acetylsalicylic acid should be used cautiously in conjunction with glucocorticoids in hypoprothrombinemia.

Cardiac: Adverse effects of glucocorticoids on the cardiovascular system, such as dyslipidemia and hypertension, may predispose treated patients with existing cardiovascular risk factors to additional cardiovascular effects, if high doses and prolonged courses are used. Accordingly, corticosteroids should be employed judiciously in such patients, and attention should be paid to risk modification and additional cardiac monitoring if needed. Low dose and alternate day therapy may reduce the incidence of complications in corticosteroid therapy.

Systemic corticosteroids should be used with caution, and only if strictly necessary, in cases of congestive heart failure.

Vascular: 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.

Corticosteroids should be used with caution in patients with hypertension.

Gastrointestinal: High doses of corticosteroids may produce acute pancreatitis.

There is no universal agreement on whether corticosteroids per se are responsible for peptic ulcers encountered during therapy; however, glucocorticoid therapy may mask the symptoms of peptic ulcer so that perforation or hemorrhage may occur without significant pain. Glucocorticoid therapy may mask peritonitis or other signs or symptoms associated with gastrointestinal disorders such as perforation, obstruction or pancreatitis. In combination with NSAIDs, the risk of developing gastrointestinal ulcers is increased.

Corticosteroids should be used with caution in nonspecific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infection, diverticulitis, fresh intestinal anastomoses, or active or latent peptic ulcer.

Hepatobiliary: Hepatobiliary disorders have been reported which may be reversible after discontinuation of therapy. Therefore appropriate monitoring is required.

Musculoskeletal: An acute myopathy has been reported with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis) or in patients receiving concomitant therapy with anticholinergics, such as neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Cases of rhabdomyolysis have been reported. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Osteoporosis is a common but infrequently recognized adverse effect associated with a long-term use of large doses of glucocorticoid. Steroids should be used with caution in patients with osteoporosis.

Renal and Urinary: Corticosteroids should be used with caution in patients with renal insufficiency.

Caution is required in patients with systemic sclerosis because an increased incidence of scleroderma renal crisis has been observed with corticosteroids, including prednisolone and prednisone.

Investigations: 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.

Injury, Poisoning and Procedural Complications: Systemic corticosteroids are not indicated for, and therefore, should not be used to treat, traumatic brain injury, a multicenter study revealed an increased mortality at 2 weeks and 6 months after injury in patients administered methylprednisolone sodium succinate compared to placebo. A causal association with methylprednisolone sodium succinate treatment has not been established.

Other: Because complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Aspirin and nonsteroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids (see section **4.5 Drug Interactions**).

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

In post marketing experience tumor lysis syndrome (TLS) has been reported in patients with malignancies, including hematological malignancies and solid tumors, following the use of systemic corticosteroids alone or in combination with other chemotherapeutic agents. Patients at high risk of TLS, such as patients with tumors that have a high proliferative rate, high tumor burden and high sensitivity to cytotoxic agents, should be monitored closely and appropriate precautions should be taken.

Use in Children:

Corticosteroids cause growth retardation in infancy, childhood and adolescence and therefore, long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, the growth and development of infants and children should be closely monitored (see section **4.2 Posology and Method of Administration - Infants and Children**).

Infants and children on prolonged corticosteroid therapy are at special risk from raised intracranial pressure.

High doses of corticosteroids may produce pancreatitis in children.

4.5 Drug Interactions

Prednisolone is a cytochrome P450 enzyme (CYP) substrate and is mainly metabolized by the CYP3A4 enzyme. CYP3A4 catalyzes 6β-hydroxylation of steroids, the essential Phase I metabolic step for both endogenous and synthetic corticosteroids. Many other compounds are also substrates of CYP3A4, some of which (as well as other drugs) have been shown to alter glucocorticoid metabolism by induction (upregulation) or inhibition of the CYP3A4 enzyme.

Glucocorticoids may suppress reactions to skin tests.

CYP3A4 INDUCERS - Drugs that induce CYP3A4 (e.g., barbiturates, phenytoin, rifampin, ephedrine) may enhance metabolism of, and reduce glucocorticoid

concentrations. Patients stabilized on glucocorticoid therapy may require dosage adjustments if such drugs are added to or withdrawn from their drug regimen.

CYP3A4 INHIBITORS - Drugs that inhibit CYP3A4 (e.g. ketoconazole, troleandomycin) may decrease glucocorticoid clearance. Dosages of glucocorticoids given in combination with such drugs may need to be decreased to avoid potential adverse effects.

CYP3A4 SUBSTRATES - In the presence of another CYP3A4 substrate, the hepatic clearance of prednisolone may be affected, with corresponding dosage adjustments required. It is possible that adverse events associated with the use of either drug alone may be more likely to occur with co-administration.

NON-CYP3A4-MEDIATED EFFECTS – Other interactions and effects that occur with prednisolone are described in Table 1 below.

Table 1 provides a list and descriptions of the most common and/or clinically important drug interactions or effects with prednisolone.

Table 1. Important drug or substance interactions/effects with prednisolone

Drug Class or Type DRUG or SUBSTANCE	**Interaction/Effect**
Antibacterial -ISONIAZID	CYP3A4 INHIBITOR. In addition, there is a potential effect of prednisolone to increase the acetylation rate and clearance of isoniazid.
Antibiotic, Antitubercular -RIFAMPIN	CYP3A4 INDUCER
Oral anticoagulants -VITAMIN K ANTAGONISTS	The effect of prednisolone on vitamin K antagonist (e.g., warfarin, acenocoumarol, fluindione) is variable. There are reports of enhanced as well as diminished effects of these anticoagulants when given concurrently with corticosteroids. Therefore, coagulation indices should be monitored to maintain the desired anticoagulant effects.
Anticonvulsants -CARBAMAZEPINE	CYP3A4 INDUCER (and SUBSTRATE)
Anticonvulsants -PHENOBARBITAL -PHENYTOIN	CYP3A4 INDUCERS
Anticholinergics -NEUROMUSCULAR BLOCKERS	Corticosteroids may influence the effect of anticholinergics. 1) An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs (see section **4.4 Special Warnings and Precautions for Use**, Musculoskeletal). 2) Antagonism of the neuromuscular blocking effects of pancuronium and vecuronium has been reported in patients taking corticosteroids. This interaction may be expected with all competitive neuromuscular blockers.
Anticholinesterase agents	Interaction between glucocorticoids and anticholinesterase agents such as ambenonium, neostigmine, or pyridostigmine (and presumably organophosphate anticholinesterase pesticides) can produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase medication should be withdrawn at least 24 hours prior to initiation of glucocorticoid therapy.
Antidiabetic agents	Glucocorticoids may increase blood glucose levels. Patients with diabetes mellitus receiving concurrent insulin and/or oral

Drug Class or Type DRUG or SUBSTANCE	Interaction/Effect
	hypoglycemic agents may require dosage adjustments of such therapy.
Antiemetics -APREPITANT -FOSAPREPITANT	CYP3A4 INHIBITORS (and SUBSTRATES)
Antifungals -ITRACONAZOLE -KETOCONAZOLE	CYP3A4 INHIBITORS (and SUBSTRATES)
Antivirals -HIV-PROTEASE INHIBITORS	CYP3A4 INHIBITORS (and SUBSTRATES) 1) Protease inhibitors, such as indinavir and ritonavir, may increase plasma concentrations of corticosteroids. 2) Corticosteroids may induce the metabolism of HIV-protease inhibitors, resulting in reduced plasma concentrations.
Aromatase inhibitors - AMINOGLUTETHIMIDE	Aminoglutethimide-induced adrenal suppression may exacerbate endocrine changes caused by prolonged glucocorticoid treatment.
Calcium Channel Blocker -DILTIAZEM	CYP3A4 INHIBITOR (and SUBSTRATE)
Immunosuppressant -Cyclosporine	CYP3A4 INHIBITOR (and SUBSTRATE) Concomitant administration of prednisolone and cyclosporine may result in decreased plasma clearance of prednisolone, and plasma concentrations of cyclosporine may be increased during concomitant therapy with prednisolone. The need for appropriate dosage adjustment should be considered when these drugs are administered concomitantly.
Estrogens (including oral contraceptives containing estrogens)	CYP3A4 INHIBITOR (and SUBSTRATE) Estrogens may potentiate effects of hydrocortisone by increasing the concentration of transcortin and thus decreasing the amount of hydrocortisone available to be metabolized. Effects of other glucocorticoids that bind to transcortin could be similarly potentiated and dosage adjustments may be required if estrogens are added to or withdrawn from a stable dosage regimen.
-GRAPEFRUIT JUICE	CYP3A4 INHIBITOR
Immunosuppressant -CYCLOPHOSPHAMIDE -TACROLIMUS	CYP3A4 SUBSTRATES
Macrolide Antibacterial -CLARITHROMYCIN -ERYTHROMYCIN	CYP3A4 INHIBITORS (and SUBSTRATES)
Macrolide Antibacterial -TROLEANDOMYCIN	CYP3A4 INHIBITOR
Nonsteroidal anti-inflammatory agents	1) There may be increased incidence of gastrointestinal bleeding and ulceration when corticosteroids are given with NSAIDs. 2) Corticosteroids may increase the clearance of high-dose aspirin, which can lead to decreased salicylate serum levels. Discontinuation of corticosteroid treatment can lead to raised salicylate serum levels, which could lead to an increased risk of salicylate toxicity.
Potassium-depleting agents	Potassium-depleting diuretics (e.g., thiazides, furosemide, ethacrynic acid) and other drugs that deplete potassium, such as amphotericin B, xanthines, and beta2 agonists may enhance the potassium-wasting effect of glucocorticoids. Serum potassium should be closely monitored in patients receiving glucocorticoids and potassium-depleting agents.

4.6 Use in Special Populations

Fertility

Corticosteroids have been shown to impair fertility in animal studies (see section **6.1 Animal Toxicology or Pharmacology**).

Pregnancy

Some animal studies have shown that corticosteroids, when administered to the mother at high doses, may cause fetal malformations. However, corticosteroids do not appear to cause congenital anomalies when given to pregnant women.

Since adequate human reproduction studies have not been done with prednisolone, this medicinal product should be used during pregnancy only after a careful assessment of the benefit-risk ratio to the mother and fetus.

Some corticosteroids readily cross the placenta. One retrospective study found an increased incidence of low birth weights in infants born of mothers receiving corticosteroids. In humans, the risk of low birth weight appears to be dose related and may be minimized by administering lower corticosteroid doses.

The risk of using glucocorticoids in women who are not practicing any method of contraception should also be considered. Cataracts have been observed in infants born to mothers treated with long-term prednisolone during pregnancy.

Infants born to mothers who have received substantial doses of glucocorticoids during pregnancy should be carefully observed for signs of hypoadrenalism.

Lactation

Corticosteroids are excreted in breast milk. Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants. This medicinal product should be used during breast feeding only after a careful assessment of the benefit-risk ratio to the mother and infant.

Paediatric use

Long-term therapy with pharmacologic doses of glucocorticoids may cause growth suppression in children and should be avoided if possible. If prolonged therapy is required, growth and development of infants and children should be closely monitored. Alternate day therapy minimizes growth suppression and should be instituted if growth suppression occurs.

4.7 Effects on Ability to Drive and Use Machines

The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Undesirable effects, such as dizziness, vertigo, visual

disturbances and fatigue are possible after treatment with corticosteroids. If affected, patients should not drive or operate machinery.

4.8 Undesirable Effects

Glucocorticoids have many potential adverse effects which, in most instances, are extensions of their pharmacologic actions. The incidence of adverse reactions correlates with the dose, frequency and route of administration, duration of therapy, the age and conditions of the patient, and the underlying disease.

Adverse Drug Reactions Table

System Organ Class	Adverse Drug Reactions
Infections and infestations	Opportunistic infection; Infection
Blood and lymphatic system disorders	Leukocytosis
Immune system disorders	Drug hypersensitivity; Anaphylactic reaction; Anaphylactoid reaction
Endocrine disorders	Cushingoid; Hypothalamic pituitary adrenal axis suppression; Steroid withdrawal syndrome
Metabolism and nutrition disorders	Metabolic acidosis; Sodium retention; Fluid retention; Alkalosis hypokalaemic; Dyslipidaemia; Glucose tolerance impaired; Increased insulin requirement (or oral hypoglycemic agents in diabetics); Lipomatosis; Increased appetite (which may result in Weight increased)
Psychiatric disorders	Affective disorder (including Depressed mood, Euphoric mood, Affect lability, Drug dependence, Suicidal ideation); Psychotic disorder (including Mania, Delusion, Hallucination, and Schizophrenia); Mental disorder; Personality change; Confusional state; Anxiety; Mood swings; Abnormal behaviour; Insomnia; Irritability
Nervous system disorders	Epidural lipomatosis; Intracranial pressure increased with papilloedema (benign intracranial hypertension); Seizure; Amnesia; Cognitive disorder; Dizziness; Headache
Eye disorders	Central serous chorioretinopathy; Cataract; Glaucoma; Exophthalmos
Ear and labyrinth disorders	Vertigo
Cardiac disorders	Cardiac failure congestive (in susceptible patients)
Vascular disorders	Thrombosis Hypertension; Hypotension
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism; Hiccups
Gastrointestinal disorders	Peptic ulcer (with possible Peptic ulcer perforation and Peptic ulcer haemorrhage); Intestinal perforation; Gastric haemorrhage; Pancreatitis; Oesophagitis ulcerative; Oesophagitis; Abdominal distention; Abdominal pain; Diarrhoea; Dyspepsia; Nausea
Skin and subcutaneous	Angioedema; Hirsutism;

System Organ Class	Adverse Drug Reactions
tissue disorders	Petechiae; Ecchymosis; Skin atrophy; Erythema; Hyperhidrosis; Skin striae Rash erythematous; Rash; Pruritus; Urticaria; Acne, Panniculitis
Musculoskeletal and connective tissue disorders	Muscular weakness; Myalgia; Myopathy; Rhabdomyolysis Muscle atrophy; Osteoporosis; Osteonecrosis Pathological fracture; Neuropathic arthropathy; Arthralgia; Growth retardation
Reproductive system and breast disorders	Menstruation irregular
General disorders and administration site conditions	Impaired healing; Oedema peripheral; Fatigue; Malaise
Investigations	Intraocular pressure increased; Carbohydrate tolerance decreased; Blood potassium decreased; Urine calcium increased; Alanine aminotransferase increased; Aspartate aminotransferase increased; Blood alkaline phosphatase increased; Blood urea increased; Suppression of reactions to skin tests*
Injury, poisoning and procedural complications	Spinal compression fracture; Tendon rupture

* Not a MedDRA Preferred Term

4.9 Overdose

There is no clinical syndrome of acute overdosage with corticosteroids.

Humans ingesting massive doses of glucocorticoids should receive symptomatic supportive care. Vigorous therapy with broad spectrum antibiotics is indicated if infection occurs. The use of pharmacological measures to decrease the likelihood of gastrointestinal ulcer or hemorrhage should be considered.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Prednisolone, a synthetic glucocorticoid analog, is used primarily as anti-inflammatory, immunosuppressant agent. Because prednisolone has only minimal mineralocorticoid properties, it is inadequate alone for the management of adrenocortical insufficiency. If prednisolone is used in the treatment of this condition, concomitant therapy with a mineralocorticoid is also necessary.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli. At equipotent anti-inflammatory doses,

prednisolone has approximately half the mineralocorticoid activity of hydrocortisone and cortisone.

5.2 Pharmacodynamic Properties

Chemically, prednisolone is 17,21-trihydroxy-pregna-1,4-diene-3,20-dione. The empirical formula is $C_{21}H_{28}O_5$ and the molecular weight is 360. Prednisolone is a synthetic glucocorticoid.

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs 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.

Prednisolone is one of the highly potent glucocorticoid steroids having anti-inflammatory, hormonal, and metabolic effects similar to those of cortisone and hydrocortisone.

5.3 Pharmacokinetic Properties

Absorption

Prednisolone is rapidly and almost completely absorbed following oral administration. The initial absorption, but not the overall bioavailability, is affected by food. Peak plasma concentrations of Prednisolone are attained in 1 to 2 hours, and it has a plasma half-life of 2 to 4 hours. Maximum biologic activity, however, is achieved after the peak plasma concentration is reached: the biological half-life of Prednisolone is 12 to 36 hours. No relationship between plasma concentration and clinical response has been demonstrated.

Distribution

Prednisolone is extensively bound in plasma to corticosteroid binding globulin and albumin, although less so than hydrocortisone or cortisone. The drug exhibits dose dependent pharmacokinetics; an increase in dose leads to an increase in volume of distribution and plasma clearance. Hypoalbuminemic states may result in unusually high concentrations of free drug; with high doses of Prednisolone, binding decreases about 50% when serum albumin decreases from 4 g/100 mL to 2.5 g/100 mL.

Biotransformation

Prednisolone is metabolized primarily in the liver, but also in most body tissues, to biologically inactive compounds. Prednisolone can be reversibly converted to prednisone by 11β-hydroxysteroid dehydrogenase.

Elimination

The inactive metabolites are excreted in the urine as glucuronides, sulfates, and unconjugated products. Biliary and fecal excretion are of no quantitative importance in humans.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

Carcinogenic potential:

Prednisolone can increase the incidence of hepatocellular adenomas and carcinomas after oral administration in drinking water to male rats (for 2 years). These tumorigenic effects occurred at doses which were less than the typical clinical doses on a mg/m^2 basis.

Mutagenic potential:

Prednisolone has not been formally evaluated for genotoxicity. However, prednisolone farnesylate (PNF), which is structurally similar to prednisolone, was not mutagenic with or without metabolic activation in *Salmonella typhimurium* and *Escherichia coli* strains at 312 to 5,000 µg/plate. In a Chinese hamster fibroblast cell line, PNF produced a slight increase in the incidence of structural chromosomal aberrations with metabolic activation at the highest concentration tested 1,500 µg/mL.

Reproductive toxicity:

Corticosteroids have been shown to reduce fertility when administered to rats. Male rats were administered corticosterone at doses of 0, 10, and 25 mg/kg/day by subcutaneous injection once daily for 6 weeks and mated with untreated females. The high dose was reduced to 20 mg/kg/day after Day 15. Decreased copulatory plugs were observed, which may have been secondary to decreased accessory organ weight. The numbers of implantations and live fetuses were reduced.

Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. In animal (pregnant mice, rats, and rabbits) reproduction studies, glucocorticoids such as prednisolone have been shown to increase the incidence of cleft palate in the offspring, embryo-fetal lethality, and intra-uterine growth retardation.

Menstrual cycle irregularities may occur.

7. DESCRIPTION

Wysolone DT 5 - Clean round tablets with beveled edges engraved ‘5’ on one side and break line on the other side.
Wysolone DT 10 - Clean round tablets with beveled edges engraved ‘10’ on one side and break line on the other side.
Wysolone DT 20 - Clean round tablets with beveled edges engraved ‘20’ on one side and break line on the other side.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

None.

8.2 Shelf-life

24 months.

8.3 Packaging Information

15 tablets are blister packed using rear printed Aluminum foil and Amber coloured PVC foil.

8.4 Storage and Handling Instructions

Store at room temperature. Protect from light.

Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Patients should be informed of the following information before initiating therapy with Wysolone DT and periodically during the course of ongoing therapy.

• Patients should be warned not to discontinue the use of Wysolone DT abruptly or without medical supervision, to advise any medical attendants that they are taking it, and to seek medical advice at once should they develop fever or other signs of infection. Patients should be told to take Wysolone DT exactly as prescribed, follow the instructions on the prescription label, and not stop taking Wysolone DT without first checking with their healthcare providers, as there may be a need for gradual dose reduction.
• Patients should discuss with their physician if they have had recent or ongoing infections or if they have recently received a vaccine.
• Persons 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.
• There are a number of medicines that can interact with Wysolone DT. Patients should inform their healthcare provider of all the medicines they are taking, including over-the-counter and prescription medicines (such as phenytoin, diuretics, digitalis or digoxin, rifampin, amphotericin B, cyclosporine, insulin or diabetes medicines, ketoconazole, estrogens including birth control pills and hormone replacement therapy, blood thinners such as warfarin, aspirin or other NSAIDS, barbiturates, isoniazid), dietary supplements, and herbal products. If patients are taking any of these drugs, alternate therapy, dosage adjustment, and/or special test may be needed during the treatment.
• For missed doses, patients should be told to take the missed dose as soon as they remember. If it is almost time for the next dose, the missed dose should be skipped and the medicine taken at the next regularly schedule time. Patients should not take an extra dose to make up for the missed dose.

• Patients should be told to take Wysolone DTwith food. Patients should be advised not to break, divide, or chew Wysolone DT.
• Patients should be advised of common adverse reactions that could occur with Wysolone use to include fluid retention, alteration in glucose tolerance, elevation in blood pressure, behavioral and mood changes, increased appetite and weight gain.
If you notice the following, consult your doctor immediately:
• If you get swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty in swallowing or breathing.
You could also notice an itchy, lumpy rash (hives) or nettle rash (urticaria). This may mean you are having an allergic reaction.
You get severe stomach pain which may reach through to your back. This could be a sign of pancreatitis.
You pass black tarry stools or notice fresh or clotted blood in your stools (faeces).
You may also notice dark bits that look like coffee grounds in your vomit. These could be signs of a stomach ulcer.
Discuss with your doctor if:
• you have ever had severe depression
• osteoporosis (weakening of the bones) especially
in women who have passed menopause

10. DETAILS OF MANUFACTURER

Pfizer Limited, Plot No. L-137, Phase III A, Verna Industrial Estate, Verna, Salcete - Goa, India

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing Licence No*.: 545 dated 01 Dec 2024
(*The manufacturing license is renewed every 5 years as per Indian regulations).

12. DATE OF REVISION

May 2025