

**PRESCRIBING INFORMATION**

**Pr CORTEF\***  
**Hydrocortisone Tablets**  
10 mg, 20 mg

**CORTICOSTEROID**

Pfizer Canada Inc  
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## **PRESCRIBING INFORMATION**

### **NAME OF DRUG**

**CORTEF\***

**Hydrocortisone Tablets**

10 mg, 20 mg

### **PHARMACOLOGICAL CLASSIFICATION**

Corticosteroid

### **INDICATIONS AND CLINICAL USE**

**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.

**Rheumatic Disorders:** As adjunctive therapy for short-term administration (to tide the patient over 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.

**Collagen Diseases:** During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus, acute rheumatic carditis, systemic dermatomyositis (polymyositis).

**Dermatologic Diseases:** pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, mycosis fungoides, severe psoriasis and severe seborrheic dermatitis.

**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 and drug hypersensitivity reactions.

**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.

**Respiratory Diseases:** Symptomatic sarcoidosis, Löffler's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy, aspiration pneumonitis.

**Hematologic Disorders:** Idiopathic thrombocytopenic purpura in adults, secondary thrombocytopenia in adults, acquired (autoimmune) hemolytic anemia, erythroblastopenia (RBC anemia), congenital (erythroid) hypoplastic anemia.

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

**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.

**Gastrointestinal Diseases:** To tide the patient over a critical period of the disease in: ulcerative colitis, regional enteritis.

**CNS:** Acute exacerbations of multiple sclerosis.

**Miscellaneous:** Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy, trichinosis with neurologic or myocardial involvement.

## **CONTRAINDICATIONS**

CORTEF (hydrocortisone) is contraindicated in:

- Systemic fungal infections,
- Patients with known hypersensitivity to hydrocortisone or components of the tablet,
- Patients administered with live or live, attenuated vaccines while receiving immunosuppressive doses of corticosteroids,
- herpes simplex of the eye, except when used for short-term or emergency therapy as in acute sensitivity reactions,
- patients with vaccinia and varicella, except when used for short-term or emergency therapy as in acute sensitivity reactions

## **WARNINGS and PRECAUTIONS**

### **General**

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

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. 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.

Advise patients to inform subsequent physicians of the prior use of corticosteroids.

The existence of diabetes, osteoporosis, renal insufficiency, chronic psychosis, hypertension, myasthenia gravis or predisposition to thrombophlebitis requires that CORTEF (hydrocortisone) be administered with caution.

Aspirin and nonsteroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids.

### **Carcinogenesis and Mutagenesis**

Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy. Discontinuation of corticosteroids may result in clinical remission.

Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids, including hydrocortisone. Corticosteroids should only be administered to patients

with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

No adequate studies have been conducted in animals to determine whether corticosteroids have a potential for carcinogenesis or mutagenesis.

### **Cardiovascular/Renal**

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. As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, corticosteroids should be used with caution in patients with congestive heart failure, hypertension, or renal insufficiency.

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.

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

Thrombosis including venous thromboembolism has been reported to occur with corticosteroids. As a result corticosteroids should be used with caution in patients who have or may be predisposed to thromboembolic disorders.

### **Endocrine and Metabolism**

Patients should be monitored for Hypothalamic-pituitary adrenal (HPA) axis suppression, Cushing's syndrome and hyperglycemia with chronic use. Corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticoid insufficiency after withdrawal of treatment. Drug induced secondary adrenocortical insufficiency may 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 reinstated. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids in patients with hypothyroidism. Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly. 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. Drug-induced adrenocortical insufficiency may be minimized by gradual reduction of dosage.

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

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

### **Gastrointestinal**

Steroids should be used with caution in active or latent peptic ulcers, diverticulitis, fresh intestinal anastomoses, and nonspecific ulcerative colitis when steroids are used as direct or adjunctive therapy, since they may increase the risk of a perforation. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent.

### **Hematologic**

ASA and nonsteroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinemia. See Drug Interactions.

### **Hepatic/Biliary/Pancreatic**

Hydrocortisone may have an increased effect in patients with liver disease since the metabolism and elimination of hydrocortisone is significantly decreased in these patients. There is an enhanced effect of corticosteroids in patients with cirrhosis.

High doses of corticosteroids may produce acute pancreatitis.

### **Immune**

Persons who are on corticosteroids are more susceptible to infections than are healthy individuals. 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. Infections with any pathogen including viral, bacterial, fungal, protozoan or helminthic infections, 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.

### ***Special pathogens***

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Amoeba, Candida, Cryptococcus, Mycobacterium, Nocardia, Pneumocystis, Toxoplasma. It is recommended that amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained diarrhea.

Host defenses are impaired in patients receiving large doses of glucocorticoids and this effect increases susceptibility to fungus infections as well as bacterial and viral infections.

### ***Fungal Infections***

Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure (see CONTRAINDICATIONS; DRUG INTERACTIONS).

### ***Viral Infections***

Chickenpox and measles, for example, can have a more serious or even fatal course in nonimmune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled i.m. immunoglobulin (IG) may be indicated. If chickenpox develops, treatment with antiviral agents may be considered. Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation. In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia.

Corticosteroids should not be used in cerebral malaria. There is currently no evidence of benefit from steroids in this condition.

### ***Vaccination***

**Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids** (see CONTRAINDICATIONS). Killed or inactivated vaccines may be administered however the response to such vaccines may be diminished. Indicated immunization procedures may be undertaken in patients receiving non-immunosuppressive doses of corticosteroids.

While on corticosteroid therapy patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially in high doses, because of possible hazards of neurological complications and lack of antibody response.

### ***Tuberculosis***

The use of hydrocortisone 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 corticosteroids 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.

### **Musculoskeletal**

An acute myopathy has been observed 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 neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriplegia. Elevations of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

Osteoporosis is an adverse effect associated with long-term use of corticosteroids at any age. Corticosteroids decrease bone formation and increase bone resorption both through their effect on calcium regulation (e.g., decreasing absorption and increasing excretion) and inhibition of osteoblast function. This, together with a decrease in protein matrix of the bone secondary to an increase in protein catabolism, and reduced sex hormone production, may lead to inhibition of bone growth in pediatric patients and the development of osteoporosis at any age. Special consideration should be given to patients at increased risk of osteoporosis (i.e., postmenopausal women) before initiating corticosteroid therapy.

Corticosteroids should be used with caution in patients with myasthenia gravis.

### **Neurological disorders**

Corticosteroids should be used with caution in patients with seizure disorders.

Convulsions have been reported with concurrent use of methylprednisolone and cyclosporine. Since concurrent administration of these agents results in a mutual inhibition of metabolism, it is possible that convulsions and other adverse events associated with the individual use of either drug may be more apt to occur.

Systemic corticosteroids, including CORTEF, are not indicated for, and therefore should not be

used for the treatment of traumatic brain injury, as demonstrated by the results of a multicenter study. The study results revealed an increased mortality in the 2 weeks and 6 months after injury in patients administered methylprednisolone sodium succinate compared to placebo.

There have been reports of epidural lipomatosis in patients taking corticosteroids (including cases in children).

### **Ophthalmologic**

Use 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 bacteria, fungi, or viruses. As intraocular pressure may become elevated in some individuals, if steroid therapy is continued for more than 6 weeks, intraocular pressure should be monitored. The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes. Corticosteroids should be used cautiously in patients with ocular herpes simplex because of corneal perforation. Corticosteroids should not be used in active ocular herpes simplex.

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

### **Psychiatric**

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.

Potentially severe psychiatric adverse reactions may occur with systemic steroids (see ADVERSE REACTIONS). Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions recover 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.

### **Sensitivity**

Allergic reactions (eg, 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 (see ADVERSE REACTIONS).

### **Sexual Function/Reproduction**

Steroids may increase or decrease motility and number of spermatozoa in some patients. Corticosteroids have been shown to reduce fertility when administered to rats.

### **Special Populations**

#### **Pregnant Women**

Corticosteroids readily cross the placenta. Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to human dose. Animal studies in which corticosteroids have been given to pregnant mice, rats, and rabbits, have yielded an increase incidence of cleft palate in the off-spring. There are no adequate and well-controlled studies in pregnant women. Since there is inadequate evidence of safety in human pregnancy, this drug should be used in pregnancy or by women of child bearing potential only if clearly needed and the potential benefit justifies the potential risk to the mother and embryo or fetus.

Infants born of mothers who have received substantial doses of corticosteroids during pregnancy must be carefully observed and evaluated for signs of adrenal insufficiency. There are no known effects of corticosteroids on labour and delivery.

Cataracts have been observed in infants born to mothers undergoing long-term treatment with corticosteroids during pregnancy.

#### **Nursing Women**

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Because of the potential for serious adverse reactions in nursing infants from corticosteroids, a decision should be made whether to continue the drug, taking into account the importance of the drug to the mother.

#### **Pediatric Use**

Pediatric patients may experience a decrease in their growth velocity observed at low systemic doses and in the absence of laboratory evidence of HPA axis suppression (i.e., cosyntropin stimulation and basal cortisol plasma levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. In order to minimize the potential growth effects of corticosteroids, pediatric patients should be titrated to the lowest effective dose over the shortest period of time.

Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis.

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

intracranial pressure.

High doses of corticosteroids may produce pancreatitis in children.

### **Geriatric Use**

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

### **Monitoring and Laboratory testing:**

Corticosteroids may suppress reactions to skin tests.

Dosage adjustments may be required based on the following conditions: during remission or exacerbation of the disease process; the patient's individual response to therapy; or upon exposure of the patient to emotional or physical stress such as serious infection, surgery or injury.

Monitoring for signs and symptoms of drug-induced secondary adrenocortical insufficiency may be necessary for up to one year following cessation of long-term or high-dose corticosteroid therapy.

### **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.

## **ADVERSE REACTIONS**

**Note:** The following are typical for all systemic corticosteroids. Their inclusion in this list does not necessarily indicate that the specific event has been observed with this particular formulation.

<b>System Organ Class</b>	<b>Frequency Not Known (Cannot be estimated from available data)</b>
<b><i>Infections and infestations</i></b>	Infection masked; Opportunistic infection (with any pathogen, in any location in the body, from mild to fatal); Infection (becoming active including reactivation of tuberculosis); Infection susceptibility increased
<b><i>Neoplasms benign, malignant and</i></b>	Kaposi's sarcoma (has been reported to occur in patients

<b>Table 1 Adverse Reactions</b>	
<b>System Organ Class</b>	<b>Frequency Not Known (Cannot be estimated from available data)</b>
<i>unspecified (including cysts and polyps)</i>	receiving corticosteroid therapy)
<i>Blood and lymphatic system disorders</i>	Leukocytosis
<i>Immune system disorders</i>	Allergic or hypersensitivity reactions (including anaphylaxis and anaphylactoid reactions [e.g. bronchospasm, laryngeal oedema, urticaria]); Angioedema; May suppress reactions to skins
<i>Endocrine disorders</i>	Cushingoid; Pituitary-adrenal axis suppression particularly at times of stress as in trauma, surgery or illness; Hirsutism; Hypertrichosis; Abnormal fat deposits; Weight increased; Moon face; Glycosuria
<i>Metabolism and nutrition disorders</i>	Sodium retention; Fluid retention; Alkalosis hypokalemic; Glucose tolerance impaired
<i>Psychiatric disorders</i>	Psychic derangements/psychotic manifestations (Euphoric mood, Insomnia, Mood swings, Personality change, Depression, Exacerbation of preexisting Affect lability or Psychotic behaviour)
<i>Nervous system disorders</i>	Intracranial pressure increased with papilloedema (benign intracranial hypertension) usually following discontinuation of treatment; Convulsions; Headache; Neuritis; Neuropathy peripheral; Paraesthesia; Vertigo; Arachnoiditis; Meningitis; Paraparesis/paraplegia;

<b>Table 1 Adverse Reactions</b>	
<b>System Organ Class</b>	<b>Frequency Not Known (Cannot be estimated from available data)</b>
	Epidural lipomatosis
<i>Eye disorders</i>	Cataract subcapsular (associated with prolonged, high dose systemic therapy); Exophthalmos; Glaucoma; Central serous chorioretinopathy
<i>Cardiac disorders</i>	Cardiac failure congestive (in susceptible patients); Bradycardia; Cardiac arrest; Arrhythmia; Cardiomegaly; Circulatory collapse; Fat embolism; Hypertrophic cardiomyopathy in premature infants; Myocardial rupture following recent myocardial infarction (see WARNINGS); Pulmonary oedema; Syncope; Tachycardia; Embolism; Thrombophlebitis; Vasculitis
<i>Vascular disorders</i>	Hypertension Thrombosis
<i>Respiratory, thoracic and mediastinal disorders</i>	Pulmonary embolism
<i>Gastrointestinal disorders</i>	Peptic ulcer (with possible perforation and hemorrhage); Gastric hemorrhage; Pancreatitis; Oesophagitis ulcerative; Intestinal perforation (of the small and large intestine, particularly in patients with inflammatory bowel disease); Abdominal distension; Increased appetite; Nausea; Elevation in serum liver enzyme levels (usually reversible upon discontinuation)

<b>Table 1 Adverse Reactions</b>	
<b>System Organ Class</b>	<b>Frequency Not Known (Cannot be estimated from available data)</b>
<b><i>Skin &amp; subcutaneous tissue disorders</i></b>	Petechiae; Ecchymosis; Cutaneous and subcutaneous atrophy; Skin atrophy; Acne; Dermatitis allergic; Burning sensation or tingling (especially in the perineal area, after intravenous injection); Dry skin / Skin exfoliation; Erythema; Skin hyperpigmentation; Skin hypopigmentation; Hyperhidrosis; Rash; Abscess sterile; Skin striae; Alopecia; Facial erythema
<b><i>Musculoskeletal, connective tissue and bone disorders</i></b>	Myopathy; Muscular weakness; Osteonecrosis of femoral and humeral heads; Osteoporosis; Pathological fracture; Growth retardation; Neuropathic arthropathy; Muscle atrophy; Malaise
<b><i>Reproductive system and breast disorders</i></b>	Menstruation irregular; Spermatozoa progressive motility abnormal / sperm concentration abnormal
<b><i>General disorders and administration site conditions</i></b>	Impaired healing (usually at high doses); Hiccups
<b><i>Investigations</i></b>	Intraocular pressure increased; Carbohydrate tolerance decreased; Increased insulin requirement (or oral hypoglycemic agents in diabetics); Blood potassium decreased which are correctable and largely preventable by restricting sodium intake to 500

<b>Table 1 Adverse Reactions</b>	
<b>System Organ Class</b>	<b>Frequency Not Known (Cannot be estimated from available data)</b>
	mg per day and supplementing potassium intake; Nitrogen balance negative (due to protein catabolism); Urine calcium increased; Alanine aminotransferase increased; Aspartate aminotransferase increased; Blood alkaline phosphatase increased; Hepatomegaly
<b><i>Injury, poisoning and procedural complications</i></b>	Spinal compression fracture; Tendon rupture (particularly of the Achilles tendon)

## **DRUG INTERACTIONS**

### **Drug-Drug Interactions**

**Aminoglutethimide:** Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.

**Antibiotics:** Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.

**Anticoagulants:** The effect of corticosteroids on oral anticoagulants is variable. There are reports of enhanced as well as diminished effects of anticoagulant when given concurrently with corticosteroids. Therefore, coagulation indices should be monitored to maintain the desired anticoagulant effect.

**Anticholinesterases:** Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.

**Antitubercular drugs:** Serum concentrations of isoniazid may be decreased.

**Cardiac glycosides:** Concurrent use of corticosteroids with cardiac glycosides may enhance the possibility of arrhythmias or digitalis toxicity associated with hypokalemia. In all patients taking any of these drug therapy combinations, serum electrolyte determinations, particularly potassium levels, should be monitored closely.

**Cholestyramine:** Cholestyramine may increase the clearance of corticosteroids.

**Cyclosporine:** Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

**Hormones:** Patients receiving both a corticosteroid and an estrogen should be observed for excessive corticosteroid effects.

Concomitant glucocorticosteroid therapy may inhibit the response to somatropin.

**Hepatic Enzyme Inducers** (e.g., barbiturates, phenobarbital, phenytoin, carbamazepine, rifampin): Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.

**Hepatic Enzyme Inhibitors** (e.g., ketoconazole, macrolide antibiotics such as erythromycin and troleandomycin): Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids. Therefore the dose of corticosteroids should be titrated to avoid steroid toxicity.

**Hypoglycemics:** Dosage adjustments of an antidiabetic drug may be necessary when corticosteroids are given to diabetics. Corticosteroids may increase blood glucose; diabetic control should be monitored, especially when corticosteroids are initiated, discontinued, or changed in dose.

**Ketoconazole:** Ketoconazole has been reported to significantly decrease the metabolism of certain corticosteroids by up to 60%, leading to an increased risk of corticosteroid side effects.

**Nonsteroidal anti-inflammatory agents (NSAIDs):** Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.

**Potassium depleting agents (e.g.: diuretics, amphotericin B):** When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., amphotericin-B, diuretics), patients should be observed closely for development of hypokalemia. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.

**Skin Tests:** Corticosteroids may suppress reactions to skin tests.

**Vaccines:** Patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines due to inhibition of antibody response. Corticosteroids

may also potentiate the replication of some organisms contained in live attenuated vaccines. Routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued if possible (see WARNINGS AND PRECAUTIONS).

### **Drug-Food Interactions**

Grapefruit juice is a CYP3A4 inhibitor. See DRUG INTERACTIONS: HEPATIC ENZYME INHIBITORS above.

## **DOSAGE AND ADMINISTRATION**

The initial dosage may vary from 20 to 240 mg of hydrocortisone 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 response is noted. If after a reasonable period of time there is a lack of satisfactory clinical response, hydrocortisone should be discontinued and the patient transferred to another appropriate therapy.

**It should be emphasized that dosage requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient.**

After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of hydrocortisone for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually.

## **OVERDOSAGE**

Treatment of acute overdosage is by supportive and symptomatic therapy. For chronic overdosage in the face of severe disease requiring continuous steroid therapy, the dosage of corticosteroid may be reduced only temporarily, or alternate day treatment may be introduced.

In case of drug overdose, contact your doctor, or a Poison Control Centre or go to emergency room of a hospital near you immediately, even if there are no symptoms
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## **ACTIONS AND CLINICAL PHARMACOLOGY**

Hydrocortisone (cortisol) is a corticosteroid secreted by the adrenal cortex. In physiologic doses, it is administered to replace deficient endogenous hormones. In larger (pharmacologic) doses, hydrocortisone decreases inflammation and suppresses the immune response. It stimulates erythroid cells of the bone marrow, prolongs survival time of erythrocytes and platelets, and produces neutrophilia and eosinopenia. Hydrocortisone promotes protein catabolism, gluconeogenesis, and redistribution of fat from peripheral to central areas of the body. It reduces intestinal absorption and increases renal excretion of calcium.

In pharmacologic doses, systemically administered glucocorticoids suppress release of corticotropin from the pituitary. The degree and duration of hypothalamic-pituitary-adrenal (HPA) axis suppression produced is highly variable among patients and depends on the dose, frequency and time of administration, and duration of therapy. If suppressive doses are administered for prolonged periods, the adrenal cortex atrophies and patients develop cushingoid features and respond to stress like patients with primary adrenocortical insufficiency. The duration of anti-inflammatory activity approximately equals the duration of HPA-axis suppression. In one study, the duration of HPA-axis suppression after a single oral dose of hydrocortisone 250 mg was 1.25 to 1.5 days.

Hydrocortisone is extensively bound to the plasma proteins, corticosteroid binding globulin (transcortin) and albumin. With physiologic concentrations, it is bound primarily to transcortin and only 5 to 10% of cortisol in plasma is unbound.

Hydrocortisone is metabolized in most tissues, but primarily in the liver to biologically inactive compounds. The half-life of hydrocortisone may be prolonged in patients with hypothyroidism. Inactive metabolites are excreted by the kidneys, primarily as glucuronides and sulfates, but also as unconjugated products. Negligible amounts are excreted in bile.

## **STORAGE CONDITIONS**

Store between 15 and 30°C (59° to 86° F)

## **AVAILABILITY OF DOSAGE FORMS**

10 mg: Each white, round, scored, compressed tablet, engraved “CORTEF 10”, contains: hydrocortisone 10 mg. Nonmedicinal ingredients: calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, sucrose. Sodium: <1 mmol. Gluten- and tartrazine-free. Bottles of 100.

20 mg: Each white, round, compressed tablet, engraved “**CORTEF 20**”, contains: hydrocortisone 20 mg. Nonmedicinal ingredients: calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, sucrose. Sodium: <1 mmol. Gluten- and tartrazine-free. Bottles of 100.

**PART III: CONSUMER INFORMATION**

**PrCORTEF®  
(Hydrocortisone Tablets)**

This leaflet is Part III of a three-part “Product Monograph” published when Cortef® was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about Cortef®. Contact your doctor or pharmacist if you have any questions about this drug.

**ABOUT THIS MEDICATION**

**What the medication is used for:**

Cortef (hydrocortisone) is used in the treatment of various conditions such as allergy or inflammation; it is used to replace corticosteroid hormone when the body does not produce enough due to problems with the adrenal glands (e.g. adrenal insufficiency).

**What it does:**

Cortef is a corticosteroid hormone (glucocorticoid). It decreases the body’s immune response to certain diseases and reduces symptoms such as swelling and redness

**When it should not be used:**

Do not use CORTEF® if you have:

- had an allergic reaction to hydrocortisone or any other steroid medicine or any of the ingredients in Cortef tablets; or
- any fungal infection or any untreated infection
- herpes simplex of the eye
- chickenpox or smallpox
- received a type of vaccine called a live or live / attenuated vaccine

**What the medicinal ingredient is:**

**Hydrocortisone**

**What the nonmedicinal ingredients are:**

CORTEF® tablets contain calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, sucrose and sodium.

**What dosage forms it comes in:**

CORTEF® 10 mg: each tablet is available as a white, round scored tablet, engraved with “CORTEF 10”. Supplied in bottles of 100 tablets

CORTEF® 20 mg: each tablet is available as a white

round, unscored tablet, engraved with “CORTEF 20”. Supplied in bottles of 100 tablets.

**WARNINGS AND PRECAUTIONS**

Before taking CORTEF®, talk to your doctor or pharmacist if:

- you have or have had an infection (such as herpes simplex, chicken pox, tuberculosis, threadworm); **If you or your child is exposed to measles or chickenpox during treatment with CORTEF®, contact your doctor immediately.**
- you have bleeding problem; blood clotting problem
- you have brittle bone (osteoporosis)
- you have high blood pressure
- you have heart problems such as heart failure
- you have kidney disease
- you have or have had seizures (convulsions) or other neurological problems
- you have thyroid problem
- you have muscle pain or weakness (such as myasthenia gravis)
- you have skin cancer (Kaposi’s sarcoma), or a tumor of the adrenal glands (Pheochromocytoma)
- you have certain eye disease such as glaucoma, cataracts, herpes infection or any problems with the retina
- you have liver disease such as cirrhosis
- you have certain mental or mood conditions (such as depression)
- you have or have had stomach or gut problems (ulcer, ulcerative colitis)
- you have low potassium or calcium
- you have a weak immune response
- you have Cushing’s disease (caused by an excess of cortisol hormone)
- you are pregnant or trying to become pregnant
- you are breast-feeding or planning to breast-feed

**Before you have any operation,** tell your doctor, dentist or anesthetist that you are taking CORTEF.

**Children:** Corticosteroids can affect growth in children

## INTERACTIONS WITH THIS MEDICATION

Before taking CORTEF<sup>®</sup>, please talk to your doctor or pharmacist about all your other medications including those you bought without prescription, herbal or natural product and especially if are taking the following:

- drugs to treat glaucoma and epilepsy such as acetazolamide
- drugs to ‘thin’ the blood (anticoagulant such as warfarin, coumadin)
- drugs to treat myasthenia gravis ( a muscle condition) such as distigmine and neostigmine
- antibiotics (erythromycin, clarithromycin and troleandomycin, Rifampicin and rifabutin)
- aspirin and non steroidal anti-inflammatory drugs (such as ibuprofen)
- drugs to treat inflammatory conditions (such as methylprednisolone)
- drugs to treat epilepsy (such as barbiturates and phenytoin)
- drugs for antifungal infections (such as ketoconazole)
- cyclosporine
- drugs for heart problems or high blood pressure as digoxin and diltiazem
- drugs to treat high cholesterol (cholestyramine)
- water pills (diuretics)
- drugs to treat HIV infections such as indinavir or ritonavir
- hormones, such as estrogen and somatropin
- drugs to treat diabetes
- drugs to treat tuberculosis
- vaccines – tell your doctor if you have recently had or are about to have any vaccination.

## PROPER USE OF THIS MEDICATION

### Usual adult dose:

Take CORTEF<sup>®</sup> tablets exactly as directed by your doctor. When your condition has improved, your doctor will reduce your dose gradually. CORTEF<sup>®</sup> should not be stopped abruptly. Do not stop taking CORTEF<sup>®</sup> without talking to your doctor.

If you are being treated for diabetes, high blood pressure or water retention (oedema) tell your doctor

as he/she may need to adjust the dose of the medicines used to treat these conditions.

Do not eat grapefruit or drink grapefruit juice while taking CORTEF<sup>®</sup>.

### Overdose:

In case of drug overdose, contact your doctor, or a Poison Control Centre or go to emergency room of a hospital near you immediately, even if there are no symptoms

### Missed Dose:

If you miss a dose, take it as soon as possible. However, if it is almost time for your next dose, skip the missed dose and continue your regular dosing schedule. Do not take a double dose to make up for a missed one.

## SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The following is a list of side effects that may occur with CORTEF<sup>®</sup>. This is not a complete list. Therefore, **check with your doctor immediately if you notice or are bothered by any unusual symptoms.**

CORTEF<sup>®</sup> may hide symptoms of infections, may cause latent infections to become active, and may induce infections by normally inoffensive organisms due to lowered body resistance.

Potential side effects of CORTEF<sup>®</sup> include:

### Allergic Reactions:

- anaphylaxis (a severe, life-threatening allergic reaction)
- cardiac arrest
- bronchospasm (narrowing of the airway)

### Cardiovascular:

- heart failure
- heart attack
- arrhythmia (irregular heartbeat)
- high and low blood pressure
- blood clots
- thrombophlebitis (vein inflammation)
- thrombosis (blood clot within a blood vessel)

### Dermatologic:

- thin fragile skin
- impaired wound healing

## IMPORTANT: PLEASE READ

- swelling
- ecchymosis (spots caused by ruptured blood vessels)
- petechiae (reddish spot containing blood that appears in skin)
- stretch marks
- dry, scaly skin
- rash
- redness
- itching
- acne
- increased sweating
- lightening or darkening of an area of skin
- abscess
- suppressed reactions to skin tests
- thinning hair

### Endocrine and Metabolism:

- development of Cushingoid state (abnormal bodily condition caused by excess corticosteroids)
- moon face (enlargement of chin and forehead)
- weight gain
- abnormal fat deposits
- suppression of pituitary-adrenal axis (a condition that could lead to disabling the body's responses to physiological stress such as severe infections or trauma)
- suppression of growth in children
- abnormal hair growth
- new symptoms of diabetes

### Gastrointestinal:

- stomach ulcer
- stomach bleeding
- inflammation of the pancreas and esophagus
- perforation of the bowel
- nausea
- vomiting or altered sense of taste (with rapid administration of large doses)
- abdominal pain
- bloating
- diarrhea
- indigestion
- bowel/bladder dysfunction
- increased appetite

### Hepatic:

- enlarged liver

### Musculoskeletal:

- loss of muscle mass
- muscle weakness
- muscle pain

- malaise (feeling of general discomfort or uneasiness)
- osteoporosis
- pathological fractures
- vertebral compression fractures
- tendon rupture, (particularly of the Achilles tendon)
- Charcot joint disease (neuropathic arthropathy)
- joint pain

### Neurologic:

- seizures
- headache
- dizziness
- amnesia
- vertigo
- pain and tenderness
- impaired sensation, strength, and reflexes
- sensation of tingling, tickling, prickling, or burning of a person's skin

### Ophthalmologic:

- cataracts
- increased intraocular pressure
- glaucoma

### Psychiatric:

- anxiety
- confusion
- depression
- hallucination
- emotional instability
- euphoria (intense feelings of well-being, elation, happiness, excitement and joy)
- insomnia
- mood swings
- personality changes
- suicidal ideation

### Sexual Function/Reproduction:

- menstrual irregularities
- increased or decreased motility and number of sperm

### Hematology:

- Above normal white blood cell count
- Abnormal blood tests

### Other:

- fatigue, hiccups

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
	Only if severe	In all cases	
Congestive heart failure			√
Fluid retention, swelling		√	
High blood pressure (symptoms of which are headaches or feeling unwell)		√	
Muscle weakness			√
Stomach ulcers (burst or bleeding ulcers; symptoms of which are stomach pain, blood in stools and/or vomiting blood)			√
Wounds that are slow to heal	√		
Convulsions			√
Psychological disorders (feeling depressed including thinking about suicide, feeling anxious, insomnia)		√	
Irregular menstrual periods	√		

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and call your
	Only if severe	In all cases	
Diabetes (symptoms of which can be frequent urination and thirst)		√	
Cramps and spasms		√	
Visual problems, failing eyesight		√	
Reactivation of tuberculosis (symptoms of which could be coughing blood or pain in the chest)			√
Infections (symptoms might include a raised temperature and feeling unwell)			√
Bone/joint pain			√
Bone thinning			√
Allergic reactions in the form of angioedema (a severe skin reaction with swelling, itching and large welts).			√

*This is not a complete list of side effects. For any unexpected effects while taking Cortef, contact your doctor or pharmacist.*

#### HOW TO STORE IT

Store at room temperature (15°C to 30°C).

Keep out of the reach and sight of children.

This leaflet was prepared by Pfizer Canada Inc.

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**REPORTING SUSPECTED SIDE EFFECTS**

**You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:**

- **Report online at**  
**www.healthcanada.gc.ca/medeffect**
- **Call toll-free at 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**  
**Health Canada**  
**Postal Locator 0701E**  
**Ottawa, Ontario**  
**K1A 0K9**

**Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect).**

***NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.***

**MORE INFORMATION**

This document plus the full product monograph, prepared for health professionals, can be found at: <http://www.pfizer.ca> or by contacting the sponsor, Pfizer Canada Inc., at: 1-800-463-6001.