Product Monograph

Including Patient Medication Information

[Pr]CORTEF

Hydrocortisone Tablets

Tablet, 10 mg, 20 mg

For oral use

The Anatomical Therapeutic Chemical (ATC) Code: D07XA01

Corticosteroid

USP

Pfizer Canada ULC
17,300 Trans-Canada Highway
Kirkland, Quebec H9J 2M5

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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, Immune	04/2025
7 WARNINGS AND PRECAUTIONS, Gastrointestinal	04/2025
7 WARNINGS AND PRECAUTIONS, Ophthalmologic	04/2025
7 WARNINGS AND PRECAUTIONS, 7.1.3 Pediatrics	04/2025
7 WARNINGS AND PRECAUTIONS, Musculoskeletal	06/2025

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Certain sections or subsections that are not applicable at the time of the preparation of the most recent authorized product monograph are not listed.

Part 1: Healthcare Professional Information

1 Indications

CORTEF (hydrocortisone) is indicated for:

- **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 nonspecific tenosynovitis, acute gouty arthritis, posttraumatic 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.

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

1.1 Pediatrics

Pediatrics (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of CORTEF in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. See **7 WARNINGS AND PRECAUTIONS**, **7.1.3 Pediatrics**.

1.2 Geriatrics

Geriatrics (>65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness. See **7 WARNINGS AND PRECAUTIONS**, **7.1.4 Geriatrics**.

2 Contraindications

- CORTEF (hydrocortisone) is contraindicated in systemic fungal infections. See **7 WARNINGS AND PRECAUTIONS** and **9.4 Drug-Drug Interactions**.
- CORTEF (hydrocortisone) is contraindicated in patients who are hypersensitive to hydrocortisone or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see **6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING** and **7 WARNINGS AND PRECAUTIONS**.
- CORTEF (hydrocortisone) is contraindicated in patients administered with live or live, attenuated vaccines while receiving immunosuppressive doses of corticosteroids. See **7 WARNINGS AND PRECAUTIONS** and **9.4 Drug-Drug Interactions**.
- CORTEF (hydrocortisone) is contraindicated in herpes simplex of the eye, except when used for short-term or emergency therapy as in acute sensitivity reactions.
- CORTEF (hydrocortisone) is contraindicated in patients with vaccinia and varicella, except when used for short-term or emergency therapy as in acute sensitivity reactions. See **7 WARNINGS AND PRECAUTIONS** and **9.4 Drug-Drug Interactions**.

4 Dosage and Administration

4.1 Dosing Considerations

- 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 tablets 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. See **7 WARNINGS AND PRECAUTIONS**.

4.2 Recommended Dose and Dosage Adjustment

The initial dosage of hydrocortisone tablets may vary from 20 to 240 mg of hydrocortisone per day depending on the specific disease entity being treated. It should be emphasized that dosage requirements are variable and must be individualized on the basis of the disease under treatment, its severity, and the response of the patient over the entire duration of treatment. A risk/benefit decision must be made in each individual case on an ongoing basis. In situations of less severity lower doses for the minimum period 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 tablets should be discontinued and the patient transferred to another appropriate therapy.

4.5 Missed Dose

Missed dose should be taken as soon as possible. However, if it is almost time for the next dose, your regular dosing schedule should be maintained. Doubling a dose to make up for a missed one is not recommended.

5 Overdose

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.

Hydrocortisone is dialyzable.

For the most recent information in the management of a suspected drug overdose, contact your regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669).

6 Dosage Forms, Strengths, Composition and Packaging

Table – Dosage Forms, Strengths, and Composition

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
oral	Tablet, 10 mg and 20 mg of hydrocortisone	calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, sucrose. Sodium: <1 mmol. Gluten and tartrazine free.

10 mg: Each white, round, scored, compressed tablet, engraved "**CORTEF 10**",

20 mg: Each white, round, compressed tablet, engraved "**CORTEF 20**"

7 Warnings and Precautions

General

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.

Patients should be advised to inform subsequent health professionals 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. See **9.4 Drug-Drug Interactions**.

Carcinogenesis and Genotoxicity

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

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

Cardiovascular

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 hypertension and only if strictly necessary, in cases of congestive heart failure.

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 therapy may reduce the incidence of complications in corticosteroid therapy.

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.

Driving and Operating Machinery

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.

Endocrine and Metabolism

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

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.

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. Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) axis 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 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.

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, including hydrocortisone, 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.

Glucocorticoid therapy may mask peritonitis or other signs or symptoms associated with gastrointestinal disorders such as perforation, obstruction or pancreatitis.

In combination with nonsteroidal anti-inflammatory drugs (NSAIDs), such as Aspirin (acetylsalicylic acid), the risk of developing gastrointestinal ulcers is increased.

Hematologic

Acetylsalicylic acid and nonsteroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids in patients with hypoprothrombinemia. See **9.4 Drug-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. Hepatobiliary disorders have been reported which may be reversible after discontinuation of therapy. Therefore appropriate monitoring is required.
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 increase susceptibility to infection, may mask some signs of infection, exacerbate existing infections, increase the risk of reactivation or exacerbation of latent infections 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.

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

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 **2 CONTRAINDICATIONS** and **9.4 Drug-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.

The role of corticosteroids in septic shock has been controversial, with early studies reporting both beneficial and detrimental effects. More recently, supplemental corticosteroids have been suggested to be beneficial in patients with established septic shock who exhibit adrenal insufficiency. However, their routine use in septic shock is not recommended. A systematic review of short-course, high dose corticosteroids did not support their use. However, meta-analyses, and a review suggest that longer courses (511 days) of low dose corticosteroids might reduce mortality, especially in patients with vasopressor dependent septic shock.

Vaccination
Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids (see **2 CONTRAINDICATIONS** and **9.4 Drug-Drug Interactions**). 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.

Monitoring and Laboratory Tests

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.

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 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 an adverse effect generally associated with long-term use and large doses 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.

Corticosteroids should be used with caution in patients with osteoporosis and in 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.

Neurologic

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), typically with long-term use at high doses.

Ophthalmologic

Prolonged use of corticosteroids may produce posterior subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos, or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves, 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 except when used for short-term or emergency therapy as in acute sensitivity reactions. 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 **8 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.

Renal

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

Other

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.

Reproductive Health

See **7.1.1 Pregnancy**

- **Fertility**

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

Sensitivity/Resistance

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 **8 ADVERSE REACTIONS**.

This medicine contains lactose produced from cow's milk. Caution should be exercised in patients with a known or suspected hypersensitivity to cow's milk or its components or other dairy products because it may contain trace amounts of milk ingredients.

7.1 Special Populations

7.1.1 Pregnancy

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 (see **16 NON-CLINICAL TOXICOLOGY**). 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. Some retrospective studies have 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.

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

7.1.2 Breastfeeding

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. This medicinal product should be used during breast feeding only after a careful assessment of the benefit risk ratio to the mother and infant.

7.1.3 Pediatrics

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.

The growth and development of pediatric patients on prolonged corticosteroid therapy 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. Growth may be suppressed in children receiving long-term, daily-divided dose glucocorticoid therapy. The use of such a regimen should be restricted to the most serious indications.

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

High doses of corticosteroids may produce pancreatitis in children.

Hypertrophic cardiomyopathy was reported as one of the adverse effects of prophylactic or therapeutic administration of hydrocortisone to prematurely born infants and few months old babies (< 12 months), therefore appropriate diagnostic evaluation and monitoring of cardiac function and structure must be performed (preferably two-dimensional echocardiography).

7.1.4 Geriatrics

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.

8 Adverse Reactions

8.1 Adverse Reaction Overview

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.

Table 1 Adverse Drug Reactions

System Organ Class	Frequency Not Known (Cannot be estimated from available data)
Infections and infestations	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
Neoplasms benign, malignant and unspecified (including cysts and polyps)	Kaposi's sarcoma (has been reported to occur in patients receiving corticosteroid therapy)
Blood and lymphatic system disorders	Leukocytosis
Immune system disorders	Allergic or hypersensitivity reactions (including anaphylaxis and anaphylactoid reactions [e.g. bronchospasm, laryngeal oedema])
Endocrine disorders	Cushingoid; Hypothalamic 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; Steroid withdrawal syndrome
Metabolism and nutrition disorders	Metabolic acidosis; Sodium retention; Fluid retention; Alkalosis hypokalemic; Dyslipidemia; Glucose tolerance impaired;

Table 1 Adverse Drug Reactions

System Organ Class	Frequency Not Known (Cannot be estimated from available data)
	Increased insulin requirement (or oral hypoglycemic agents in diabetics); Lipomatosis; Increased appetite (which may result in Weight increased)
Psychiatric disorders	Psychic derangements/psychotic manifestations (Euphoric mood, Insomnia, Mood swings, Personality change, Depression, Exacerbation of preexisting Affect lability or Psychotic behaviour); Affective disorder (including Depression, 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 behavior; Insomnia; Irritability
Nervous system disorders	Intracranial pressure increased; with papilloedema (benign intracranial hypertension;) usually following discontinuation of treatment; Seizure; Amnesia; Cognitive disorder; Dizziness; Headache; Neuritis; Neuropathy peripheral; Paraesthesia; Arachnoiditis; Meningitis; Paraparesis/paraplegia; Epidural lipomatosis
Eye disorders	Cataract subcapsular (associated with prolonged, high dose systemic therapy); Cataract; Exophthalmos; Glaucoma; Chorioretinopathy
Ear and labyrinth disorders	Vertigo
Cardiac disorders	Cardiac failure congestive (in susceptible patients); Bradycardia; Cardiac arrest; Arrhythmia; Cardiomegaly; Circulatory collapse; Fat embolism; Hypertrophic cardiomyopathy in premature infants;

Table 1 Adverse Drug Reactions

System Organ Class	Frequency Not Known (Cannot be estimated from available data)
	Myocardial rupture following recent myocardial infarction (see WARNINGS AND PRECAUTIONS); Pulmonary oedema; Syncope; Tachycardia; Embolism; Thrombophlebitis; Vasculitis
Vascular disorders	Hypotension; Hypertension; Thrombosis
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism; Hiccups
Gastrointestinal disorders	Peptic ulcer (with possible Peptic ulcer perforation and Peptic ulcer hemorrhage); Gastric hemorrhage; Pancreatitis; Oesophagitis ulcerative; Intestinal perforation (of the small and large intestine, particularly in patients with inflammatory bowel disease); Abdominal distension; Abdominal pain; Diarrhoea; Dyspepsia; Nausea; Elevation in serum liver enzyme levels (usually reversible upon discontinuation)
Skin & subcutaneous tissue disorders	Angioedema; Petechiae; Ecchymosis; Urticaria; Pruritus; 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; Panniculitis Hyperhidrosis;

Table 1 Adverse Drug Reactions

System Organ Class	Frequency Not Known (Cannot be estimated from available data)
	Rash; Abscess sterile; Skin striae; Alopecia; Facial erythema
Musculoskeletal, connective tissue and bone disorders	Arthralgia; Myopathy; Rhabdomyolysis; Myalgia; Muscular weakness; Osteonecrosis of femoral and humeral heads; Osteoporosis; Pathological fracture; Growth retardation; Neuropathic arthropathy; Muscle atrophy;
Reproductive system and breast disorders	Menstruation irregular; Spermatozoa progressive motility abnormal / sperm concentration abnormal
General disorders and administration site conditions	Impaired healing (usually at high doses); Oedema peripheral; Fatigue; Malaise
Investigations	Intraocular pressure increased; Carbohydrate tolerance decreased; Blood potassium decreased which are correctable and largely preventable by restricting sodium intake to 500 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; Blood urea increased; Hepatomegaly; Suppression of reactions to skin tests*
Injury, poisoning and procedural complications	Spinal compression fracture; Tendon rupture (particularly of the Achilles tendon)

* Not a MedDRA PT

9 Drug Interactions

9.2 Drug Interactions Overview

Hydrocortisone is metabolized by 11β hydroxysteroid dehydrogenase type 2 (11β HSD2) and the cytochrome P450 (CYP) 3A4 enzyme. The CYP3A4 enzyme 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 have been shown to alter glucocorticoid metabolism by induction (upregulation) or inhibition of the CYP3A4 enzyme.

9.4 Drug-Drug Interactions

CYP3A4 INHIBITORS - May decrease hepatic clearance and increase the plasma concentrations of hydrocortisone. In the presence of a CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, clarithromycin, and grapefruit juice), the dose of hydrocortisone may need to be decreased to avoid steroid toxicity.

CYP3A4 INDUCERS - May enhance the metabolism of corticosteroids. May increase hepatic clearance and decrease the plasma concentrations of hydrocortisone. In the presence of a CYP3A4 inducer (e.g., barbiturates, rifampin, carbamazepine, phenobarbital, and phenytoin), the dose of hydrocortisone may need to be increased to achieve the desired response.

CYP3A4 SUBSTRATES - In the presence of another CYP3A4 substrate, the hepatic clearance of hydrocortisone 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 coadministration.

NON-CYP3A4-MEDIATED EFFECTS - Other interactions and effects that occur with hydrocortisone are described in Table 2 below.

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 2. Established or Potential Drug-Drug Interactions

Drug Class or Type **- DRUG or SUBSTANCE**	**Interaction/Effect**
Antibacterial - ISONIAZID	CYP3A4 INHIBITOR Serum concentrations of isoniazid may be decreased.
Antibiotic, Antitubercular - RIFAMPIN	CYP3A4 INDUCER
Antibiotic, Macrolides - CLARITHROMYCIN - ERYTHROMYCIN	CYP3A4 INHIBITOR (and SUBSTRATES) Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.
Anticoagulants (oral)	The effect of corticosteroids on vitamin K antagonist (e.g., warfarin, acenocoumarol, fluindione) is variable. There are reports of enhanced as well

Drug Class or Type - DRUG or SUBSTANCE	Interaction/Effect
-VITAMIN K ANTAGONISTS	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. An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs. See **7 WARNINGS AND PRECAUTIONS**, **Musculoskeletal**. 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.
Anticholinesterases	Steroids may reduce the effects of anticholinesterases in myasthenia gravis. 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.
Antidiabetics	Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.
Antiemetic - APREPITANT - FOSAPREPITANT	CYP3A4 INHIBITORS (and SUBSTRATES)
Antifungals - ITRACONAZOLE - KETOCONAZOLE	CYP3A4 INHIBITORS (and SUBSTRATES) 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.
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. Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.

Drug Class or Type **- DRUG or SUBSTANCE**	**Interaction/Effect**
Calcium Channel Blocker - DILTIAZEM	CYP3A4 INHIBITOR (and SUBSTRATE)
Cardiac Glycosides - DIGOXIN	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.
Estrogens (including oral contraceptives containing estrogens)	CYP3A4 INHIBITOR (and SUBSTRATE) Patients receiving both a corticosteroid and an estrogen should be observed for excessive corticosteroid effects. Estrogens may potentiate effects of hydrocortisone by increasing the concentration of transcortin and thus decreasing the amount of hydrocortisone available to be metabolized. Dosage adjustments of hydrocortisone may be required if estrogens are added to or withdrawn from a stable dosage regimen.
Hormones -SOMATROPIN	Concomitant glucocorticosteroid therapy may inhibit the response to somatropin.
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.
Immunosuppressant - CYCLOSPORINE	CYP3A4 INHIBITOR (and SUBSTRATE) Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.
Immunosuppressant - CYCLOPHOSPHAMIDE - TACROLIMUS	CYP3A4 SUBSTRATES
Macrolide Antibacterial - TROLEANDOMYCIN	CYP3A4 INHIBITOR Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.
NSAIDs - high-dose ASPIRIN (acetylsalicylic acid)	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. 3) Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Drug Class or Type - DRUG or SUBSTANCE	Interaction/Effect
Potassium Depleting Agents	When corticosteroids are administered concomitantly with potassium depleting agents (i.e. amphotericin-B, diuretics), patients should be observed closely for development of hypokalemia. There is also an increased risk of hypokalemia with concurrent use of corticosteroids with amphotericin B, xanthines, or beta2 agonists. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure.
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 **7 WARNINGS AND PRECAUTIONS**, **Immune**.

9.5 Drug-Food Interactions

Grapefruit or its juice are known to inhibit CYP3A and may increase hydrocortisone plasma concentration. Patients should avoid this fruit during CORTEF treatment. See **9.4 Drug-Drug Interactions**.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Corticosteroids may suppress reactions to skin tests.

10 Clinical Pharmacology

10.1 Mechanism of Action

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt retaining properties, are used as replacement therapy in adrenocortical deficiency states.

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.

10.2 Pharmacodynamics

Hydrocortisone (cortisol) is a corticosteroid (glucocorticoid) secreted by the adrenal cortex. In physiologic doses, it is administered to replace deficient endogenous hormones. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. 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.

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 anti-inflammatory effects in disorders of many organ systems.

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

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.

10.3 Pharmacokinetics

The pharmacokinetics of hydrocortisone tablets in healthy male subjects demonstrated nonlinear kinetics following a single oral dose of 10, 30, and 50 mg of hydrocortisone.

Absorption:
After oral administration of a 20 mg hydrocortisone tablet, hydrocortisone levels followed the classical one-compartment model. The absolute bioavailability averaged 96 ± 20%, indicating complete oral absorption.

Distribution:
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. The plasma protein binding of hydrocortisone in humans is approximately 92%. The serum half-life of hydrocortisone tablets is 1.5 hours.

Metabolism:
Hydrocortisone is metabolized in most tissues, but primarily in the liver to biologically inactive compounds. Hydrocortisone is metabolized by 11β-HSD2 to cortisone, and further to dihydrocortisone and tetrahydrocortisone. Other metabolites include dihydrocortisol, 5α-dihydrocortisol, tetrahydrocortisol, and 5α-tetrahydrocortisol. Cortisone can be converted to cortisol through 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1).

Hydrocortisone is also metabolized by CYP3A4 to 6β-hydroxycortisol (6β-OHF), and 6β-OHF varied from 2.8% to 31.7% of the total metabolites produced, demonstrating large inter-individual variability.

Elimination:
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. Free-cortisol reduces to tetrahydrocortisol in the liver and inactivates by conjugation with glucuronic acid.

11 Storage, Stability and Disposal

Store between 15 and 30°C

12 Special Handling Instructions

This information is not available for this drug product.

Part 2: Scientific Information

13 Pharmaceutical Information

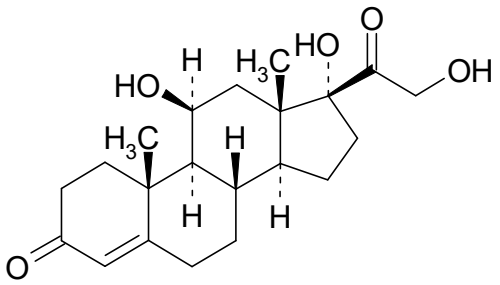
Drug Substance

Non-proprietary name of the drug substance: Hydrocortisone

Chemical name: pregn-4-ene-3,20-dione,11,17,21-trihydroxy-, (11β)

Molecular formula and molecular mass: $C_{21}H_{30}O_5$ (362.46)

Structural formula:



Physicochemical properties: White to practically white, odourless, crystalline powder

14 Clinical Trials

The clinical trial data on which the original indication was authorized is not available.

15 Microbiology

No microbiological information is required for this drug product.

16 Non-Clinical Toxicology

Carcinogenesis: Hydrocortisone did not increase tumour incidences in male and female rats during a 2-year carcinogenicity study.

Genotoxicity: Corticosteroids, a class of steroid hormones that includes hydrocortisone, are consistently negative in the bacterial mutagenicity assay. Hydrocortisone and dexamethasone induced chromosome aberrations in human lymphocytes in vitro and in mice in vivo. Fludrocortisone (9α-fluorohydrocortisone, structurally similar to hydrocortisone) was negative in the human lymphocyte chromosome aberration assay.

Reproductive and Developmental 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 reproduction studies, glucocorticoids have been shown to increase the incidence of malformations (cleft palate, skeletal malformations), embryo-fetal lethality (e.g., increase in resorptions), and intra-uterine growth retardation. With hydrocortisone, cleft palate was observed when administered to pregnant mice and hamsters during organogenesis.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]CORTEF[*]
Hydrocortisone Tablets

This patient medication information is written for the person who will be taking **CORTEF**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This patient medication information is a summary. It will not tell you everything about this medication. If you have more questions about this medication or want more information about **CORTEF**, talk to a healthcare professional.

What CORTEF is used for:

CORTEF is used in adults:

- to treat various conditions caused by allergy or inflammation.
- to replace corticosteroid hormone when the body does not produce enough. This is due to problems with the adrenal glands.

How CORTEF works:

CORTEF is a corticosteroid hormone. It decreases the body's immune response to certain diseases and reduces symptoms such as swelling and redness.

The ingredients in CORTEF are:

Medicinal ingredients: hydrocortisone
Non-medicinal ingredients: calcium stearate, cornstarch, lactose, mineral oil, sorbic acid, sodium and sucrose

CORTEF comes in the following dosage forms:

Tablets: 10 mg, 20 mg

Do not use CORTEF if:

- you are allergic to hydrocortisone, any other steroid medicine, or any of the non-medicinal ingredients in CORTEF (see **What are the ingredients in CORTEF?**)
- you have a fungal infection or any other untreated infection
- you have herpes simplex of the eye
- you have chickenpox or smallpox
- you have recently received a type of vaccine called a live or live / attenuated vaccine. Do not receive this type of vaccine during treatment with CORTEF.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take CORTEF. Talk about any health conditions or problems you may have, including if you:

- are lactose intolerant or have one of the following rare hereditary diseases:

- Galactose intolerance
- Lapp lactase deficiency
- Glucose-galactose malabsorption

Because lactose is a non-medicinal ingredient in CORTEF.

- 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 healthcare professional immediately. Serious or fatal side effects can occur if you or your child have not already had these infections.**
- have recently had or are about to have any vaccination
- have bleeding problems or blood clotting problems
- have diabetes
- have brittle bones (osteoporosis)
- have high blood pressure
- have heart problems, such as heart failure, heart disease or have had a heart attack
- have edema (water retention)
- have kidney problems
- have or have had seizures (convulsions) or other neurological problems
- have thyroid problems
- have myasthenia gravis, a condition that causes progressive muscle pain and weakness
- have skin cancer (Kaposi's sarcoma), or a tumor of the adrenal glands (pheochromocytoma)
- have certain eye problems, such as glaucoma, cataracts, herpes infection or any problems with the retina
- have liver disease, such as cirrhosis
- have mental health problems, such as depression
- have or have had stomach or gut problems, such as ulcers, ulcerative colitis
- have low levels of potassium or calcium in your blood
- have a weak immune response. Talk to your healthcare professional if you suspect an infection has occurred, as corticosteroids can make infections more likely and may mask their signs
- have Cushing's disease (caused by an excess of cortisol hormone)

Other warnings you should know about:

Serious Side Effects: CORTEF can cause serious side effects, including:

- **skin cancer (Kaposi's sarcoma):** Kaposi's sarcoma has been reported with the use of corticosteroids ,such as CORTEF. Stopping treatment with CORTEF may result in signs of the cancer going away.
- **pheochromocytoma:** tumor of the adrenal glands. This tumor has been reported with corticosteroid therapy, such as CORTEF. Pheochromocytoma may cause death.
- epidural lipomatosis: fat deposition on or outside the lining of the spine. Taking corticosteroids in high doses for a long period of time can cause epidural lipomatosis.
- **Tumor lysis syndrome (TLS):** the sudden, rapid death of cancer cells due to treatment. TLS can cause life-threatening kidney failure and heart problems.
- **Suppression of hypothalamic pituitary-adrenal axis and Infections:** CORTEF can make it hard for your body to respond to stress and illness. It can make you more likely to get infections, it can make infections that might be hidden in your body active again, and it can make existing infections worse. You should avoid coming into contact with people who have measles or

chicken pox while taking CORTEF. If you are exposed, talk to your healthcare professional right away.

Surgery: Before you have any operation, including dental surgery, tell your healthcare professional that you are taking CORTEF.

Pregnancy and breastfeeding:

- If you are pregnant, or planning to become pregnant while being treated with CORTEF, there are specific risks you must discuss with your healthcare professional.
- This medicine can cross the placenta and harm your baby.
- Tell your healthcare professional right away if you become pregnant while taking CORTEF.
- If you are breastfeeding or planning to breastfeed, talk to your healthcare professional about the best way to feed your baby during treatment. CORTEF can pass into your breast milk and harm your baby.

Male fertility: Taking CORTEF may affect male fertility.

Stopping treatment: If you suddenly stop taking CORTEF, you may experience:

- **Adrenal insufficiency,** a condition where your body does not make enough of the cortisol hormone. This includes symptoms such as fainting, weakness, restlessness, nausea, vomiting, headache, dizziness, muscle weakness or joint pain and may cause death.
- **Withdrawal syndrome**. This includes symptoms such as decreased appetite, nausea, vomiting, lack of energy, headache, fever, joint pain, peeling of skin, muscle pain, weight loss, low blood pressure or fainting.
- Tell your healthcare professional right away if you experience any of these symptoms after changing or stopping your treatment. Some of these symptoms can last for months after you stop taking CORTEF.

Immunosuppression:

- CORTEF may:
    - hide symptoms of infection
    - reactivate dormant infections
    - worsen existing infections
    - cause infections due to lowered body resistance

Osteoporosis: When using medicines like CORTEF for long-term treatment, you may be at risk of:

- Breaking a bone (bone fractures)
- Weak bones (osteoporosis; increased risk of broken bones)

Take extra care to avoid any injury, especially falls.

Blood Tests: CORTEF can cause abnormal blood test results. Your healthcare professional will decide when to perform blood tests and will interpret the results. If you are going to have a skin test for allergies, talk to your healthcare professional as CORTEF may interfere with the results.

Driving and Using Machines: CORTEF can cause dizziness, vertigo, vision changes and fatigue. Give yourself time after taking CORTEF to see how you feel before driving a vehicle or using machinery.

Children (less than 18 years of age):

- Corticosteroid can affect growth in children. Your healthcare professional will prescribe the lowest dose to minimize this risk.
- Your healthcare professional will regularly monitor growth and development in growing children.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with CORTEF:

- medicines to treat glaucoma
- medicines to treat epilepsy, such as barbiturates, carbamazepine, phenobarbital, phenytoin
- medicines to "thin" the blood and prevent blood clots, such as warfarin, acenocoumarol, fluindione)
- medicines to treat myasthenia gravis (a muscle condition) such as distigmine, neostigmine
- antibiotics, used to treat bacterial infections, such as erythromycin, clarithromycin, rifampicin, rifabutin, troleandomycin
- acetylsalicyclic acid, and non-steroidal anti-inflammatory drugs (NSAIDs), used to treat pain and inflammation, such as ibuprofen
- medicines to treat inflammatory conditions such as methylprednisolone
- medicines to treat epilepsy such as barbiturates, carbamazepine, phenobarbital, phenytoin
- medicines to treat fungal infections such as itraconazole, ketoconazole, amphotericin-B
- medicines used to suppress the immune system, such as cyclosporine, cyclophosphamide, tacrolimus
- medicines to treat heart problems or high blood pressure, such as calcium channel blockers, digoxin, diltiazem, and "water pills" or diuretics
- medicines to treat high cholesterol such as cholestyramine
- medicines to treat HIV infections such as indinavir or ritonavir
- hormones, such as estrogen and somatropin
- medicines to treat diabetes
- medicines to treat tuberculosis such as isoniazid and rifampin
- medicines to prevent nausea and vomiting such as aprepitant and fosaprepitant
- medicines used to relax you during surgery, such as pancuronium, vecuronium
- medicines called anticholinesterases that can be used to treat Alzheimer's Disease and other conditions
- medicines called aromatase inhibitors used to treat breast cancer
- vaccines
- grapefruit and grapefruit juice

How to take CORTEF:

- Take CORTEF exactly how your healthcare professional has told you.

- Do not stop taking CORTEF or change your dose without talking to your healthcare professional. Your healthcare professional will tell you how to reduce your dose gradually when you no longer need to take CORTEF.

Usual dose:
Your healthcare professional will decide on the dose that is right for you based on the condition you are being treated for.

Overdose:

If you think you, or a person you are caring for, have taken too much CORTEF, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or 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 with your regular dosing schedule. Do not take a double dose to make up for a missed one.

Possible side effects from using CORTEF:
These are not all the possible side effects you may have when taking CORTEF. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:
- nausea, vomiting
- diarrhea
- indigestion
- altered sense of taste
- abdominal pain
- bloating
- increased appetite
- weight gain
- hiccups
- headache
- dizziness, spinning sensation (vertigo)
- fatigue
- muscle cramps, spasms and pain
- dark urine or reduced urine output
- rash
- redness, itching
- painful red or tender bumps on your skin
- acne
- lightening or darkening of an area of skin
- thinning hair
- sensation of tingling, tickling, prickling, or burning in the hands or feet

Serious side effects and what to do about them

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Unknown			
Suppression of hypothalamic pituitary-adrenal axis: dizziness, nausea, vomiting, abdominal pain, weakness, fatigue, generally feeling unwell, headache		√	
Allergic reaction: rash, hives, itching, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing, skin rash with swelling, itching and large welts, chest pain or tightness			√
Blood clots: **In the leg or arm:** pain, redness and swelling, skin is warm to the touch **In the lung:** chest pain, usually worse with breathing, shortness of breath, cough that may contain blood, dizziness, loss of consciousness			√
Rhabdomyolysis (breakdown of damaged muscle): Muscle weakness, muscle tenderness, muscle pain, dark urine, reduced urine output			√
Muscle Weakness			√
Osteoporosis (thin, fragile bones): bone/joint pain, broken bones, back pain that gets worse when standing or walking			√
Congestive heart failure (heart does not pump blood as well as it should): shortness of breath with activity or when lying down, fatigue, weakness, dizziness, swelling in the legs, ankles and feet, rapid or irregular heartbeat, cough or wheezing			√
Cushing's Syndrome (high blood cortisol): round "moon face", rapid weight gain especially around the		√	

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
body, excess sweating, thinning of the skin, easy bruising, dry skin, stretch marks, muscle weakness, fat deposits between the shoulder blades (buffalo hump), wounds that are slow to heal			
Diabetes: frequent urination, hunger and thirst		√	
Edema: fluid retention, swelling of the hands, legs or feet		√	
Eye problems: **Cataracts:** blurry vision, eye pain **Glaucoma:** increased pressure in your eyes, eye pain, halos around lights or coloured images, red eyes **Central serous chorioretinopathy (CSCR):** blurry vision or other changes in vision		√	
Heart attack: chest pain, pressure or discomfort, pain in the arm, shoulder, jaw, neck or back, shortness of breath, lightheadedness			√
High blood pressure: headaches, feeling unwell, shortness of breath		√	
Hormonal changes: irregular menstrual periods, abnormal hair growth	√		
Infections: fever, chills, feeling unwell, sore throat, body aches, fatigue			√
Mental health problems: feeling depressed including thinking about suicide, feeling anxious, insomnia, confusion, hallucinations (seeing or hearing things that are not really there), euphoria (intense feelings of well-being, elation, happiness, excitement and joy), mood swings, personality changes, memory problems		√	
Reactivation of tuberculosis: coughing blood, pain in the chest, loss of appetite, unexplained			√

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
weight loss, fever, chills, night sweats			
Seizures: convulsions or fits, with or without loss of consciousness			√
Stomach ulcers (burst or bleeding ulcers)**:** stomach pain, blood in stools and/or vomiting blood			√
Liver problems: yellowing of the skin or whites of eyes (jaundice), dark urine, pale stool, nausea, vomiting, upper abdominal pain		√	
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heart beat, nausea, vomiting, tenderness when touching the abdomen		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

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

Keep out of the reach and sight of children.

If you want more information about CORTEF:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this

Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html); the manufacturer's website http://www.pfizer.ca, or by calling 1-800-463-3001.

This leaflet was prepared by Pfizer Canada ULC.

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