PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr]MEDROL*

methylprednisolone

4mg & 16mg tablets, for oral use

USP

Glucocorticoid

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

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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, General, Endocrine and Metabolism	01/2023
8 ADVERSE REACTIONS	01/2023

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1. INDICATIONS

Medrol (methylprednisolone) is indicated for:

1. 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.

2. 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.

3. Collagen Diseases

During an exacerbation or as maintenance therapy in selected cases of: systemic lupus erythematosus; systemic dermatomyositis (polymyositis); acute rheumatic carditis; polymyalgia rheumatica; giant cell arteritis.

4. Dermatologic Diseases

Pemphigus; bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-Johnson syndrome); exfoliative dermatitis; mycosis fungoides; severe psoriasis; severe seborrheic dermatitis.

5. Allergic States

Control of severe of incapacitating allergic conditions intractable to adequate trials of conventional treatment: seasonal or perennial allergic rhinitis; serum sickness; bronchial asthma; drug hypersensitivity reactions; contact dermatitis; atopic dermatitis.

6. Ophthalmic Diseases

Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: allergic corneal marginal ulcers; herpes zoster ophthalmicus; anterior segment inflammation; diffuse posterior uveitis and choroiditis; sympathetic ophthalmia; allergic conjunctivitis; keratitis; chorioretinitis; optic neuritis; iritis and iridocyclitis.

7. Gastrointestinal Diseases

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

8. Respiratory Diseases

Symptomatic sarcoidosis; Loeffler's syndrome not manageable by other means; berylliosis; fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate anti-tuberculosis chemotherapy; aspiration pneumonitis.

9. Hematologic Disorders

Idiopathic thrombocytopenic purpura in adults; secondary thrombocytopenia in adults; acquired (autoimmune) hemolytic anemia; erythroblastopenia (RBC anemia); congenital (erythroid) hypoplastic anemia.

10. Neoplastic Diseases

For palliative management of: leukemias and lymphomas in adults; acute leukemia of childhood.

11. 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.

12. Nervous System

Acute exacerbations of multiple sclerosis; management of edema associated with brain tumour.

13. Miscellaneous

Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate anti-tuberculosis chemotherapy. Trichinosis with neurologic or myocardial involvement.

14. Organ Transplantation

1.1 Pediatrics

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

1.2 Geriatrics

Geriatrics: Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see 4.1 Dosing Considerations).

2. CONTRAINDICATIONS

MEDROL is contraindicated:

- in patients with known hypersensitivity to any components of the product (see 6 DOSAGE FORMS, STRENGTH, COMPOSITION AND PACKAGING**);**
- in patients with systemic fungal infections;

- in patients administered with live or live, attenuated vaccines while receiving immunosuppressive doses of corticosteroids;
- in herpes simplex of the eye, except when used for short-term or emergency therapy as in acute sensitivity reactions;
- in patients with vaccinia and varicella, except when used for short-term or emergency therapy as in acute sensitivity reactions.

4. DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

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 physicians of the prior use of MEDROL.

The existence of diabetes, osteoporosis, renal insufficiency, chronic psychosis, cardiovascular disease, myasthenia gravis or predisposition to thrombophlebitis requires that MEDROL be administered with caution.

Geriatrics: 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.

4.2 Recommended Dose and Dosage Adjustment

The initial dosage of MEDROL tablets may vary from 4 to 48 mg as methylprednisolone per day depending on the specific disease entity being treated. The lowest possible dose of corticosteroid should be used to control the condition under treatment.

If after a reasonable period of time there is lack of satisfactory clinical response, MEDROL tablets should be discontinued and the patient transferred to other appropriate therapy. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

After a favourable 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.

Dosage adjustments may be required based on the following:

- during remission
- exacerbation of the disease process
- the patient's individual response to therapy
- upon exposure of the patient to emotional or physical stress such as serious infection, surgery or injury. MEDROL dosage may need to be increased during and after the stressful situation.

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.

Alternate Day Therapy: Alternate day therapy is a corticosteroid dosing regimen in which twice the usual daily dose of corticosteroid is administered every other morning.

The purpose of this mode of therapy is to provide a patient requiring long-term, pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects, including pituitary-adrenal suppression, the cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.

4.5 Missed Dose

If a patient misses a dose, advise them to take the dose as soon as possible. If it is almost time for the patient's next dose, advise the patient to skip the missed dose and go back to their normal schedule. Patients should not take 2 doses at the same time.

5. 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**.** Methylprednisolone is dialyzable.

For management of a suspected drug overdose, contact your regional poison control centre.

6. DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Oral	Tablet 4mg, 16mg	calcium stearate, cornstarch, lactose, mineral oil, sucrose, and sorbic acid. Gluten-free.

Each elliptical, cross-scored tablet contains: methylprednisolone 4 mg (white, engraved "MEDROL 4") or 16 mg (white, engraved "MEDROL 16").

Available in bottles of 100 tablets.

7. WARNINGS AND PRECAUTIONS

General

Patients should be advised to inform subsequent physicians of the prior use of MEDROL.

Carcinogenesis and Mutagenesis

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

Animal studies found corticosteroids to have possible tumorigenic and mutagenic potential (see 16 NON-CLINICAL TOXICOLOGY, Carcinogenicity and Genotoxicity).

Cardiovascular

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 the 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.

As sodium retention with resultant edema and potassium loss may occur in patients receiving corticosteroids, these agents should be used with caution in patients with congestive heart failure (use only if strictly necessary), hypertension, or renal insufficiency (see also 7 WARNINGS AND PRECAUTIONS, Endocrine and Metabolism).

Endocrine and Metabolism

Corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for glucocorticosteroid 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 reinstituted.

In addition, 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. 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 mineralocorticoid should be administered concurrently.

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

Average and large doses of cortisone or hydrocortisone 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. See also 7 WARNINGS AND PRECAUTIONS, Cardiovascular.

There is an enhanced effect of corticosteroids on 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.

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

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

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

Gastrointestinal

Glucocorticoid therapy may mask the symptoms of peptic ulcer so that perforation or hemorrhage may occur without significant pain. Glucocorticoid therapy may mask peritonitis or other signs or symptoms associated with gastrointestinal disorders such as perforation, obstruction or pancreatitis. In combination with NSAIDs (such as Aspirin), the risk of developing gastrointestinal ulcers is increased.

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

Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. See also 9 DRUG INTERACTIONS.

Hepatic/Biliary/Pancreatic

There is an enhanced effect of corticosteroids on patients with cirrhosis.

High doses of corticosteroids may produce acute pancreatitis.

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

Immune

Corticosteroids may suppress the immune system and increase susceptibility to infection, 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 organisms, in any location in the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity or neutrophil function. These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complication increases.

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; 9 DRUG INTERACTIONS).

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 latent amebiasis or active 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.

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.

Tuberculosis

The use of corticosteroids 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 antituberculosis regimen. If corticosteroids are indicated in patients with latent tuberculosis reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Vaccinations

Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids (see 2 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.

Viral Infections

Chicken pox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In pediatric and adult patients who have not had these diseases, particular care should be taken to avoid exposure. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chicken pox develops, treatment with antiviral agents should be considered.

Recent studies do not support MEDROL use during septic shock, and suggest that increased mortality may occur in some subgroups at higher risk (e.g., elevated serum creatinine greater than 2.0 mg/dL or secondary infections).

Monitoring and Laboratory Tests

Corticosteroids may suppress reactions to skin tests.

Since methylprednisolone suppresses endogenous adrenocortical activity, it is highly important that the patient receiving MEDROL be under careful observation, not only during the course of treatment but for some time after treatment is terminated. 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 reported with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g., myasthenia gravis), or in patients receiving concomitant therapy with anticholinergics, such as neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

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 increased risk of osteoporosis (e.g., postmenopausal women) before initiating corticosteroid therapy. Osteoporosis is a common but infrequently recognized adverse effect associated with a long-term use of glucocorticoids.

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

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

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

Ophthalmologic

Use of corticosteroids may produce posterior sub-capsular 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 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 systemic 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 possible 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, and therefore these patients should be treated with caution.

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

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

Corticosteroids should be used with caution in patients with renal insufficiency.

Reproductive Health: Female and Male Potential

Steroids may increase or decrease motility and number of spermatozoa in some patients.

Sensitivity/Resistance

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

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 Pregnant Women

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, rabbits have yielded an increase incidence of cleft palate in the offspring (see 16 NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology).

One retrospective study found an increased incidence of low birth weights in infants born of mothers receiving corticosteroids. Cataracts have been observed in infants born to mothers undergoing long-term treatment with corticosteroids during pregnancy.

Since adequate human reproductive studies have not been done with methylprednisolone, this drug should be used during pregnancy at the lowest possible dose, only if clearly needed, where the potential benefit to the mother justifies the potential risk to the embryo or fetus.

Infants born to 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.

7.1.2 Breast-feeding

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 careful benefit-risk assessment should be conducted and a decision should be made whether to discontinue nursing, or discontinue the drug, taking into account the importance of the drug to the mother.

7.1.3 Pediatrics

Pediatrics: Growth may be suppressed in children receiving long-term daily, divided dose glucocorticoid therapy and use of such regimen should be restricted to the most urgent indication. Alternate day glucocorticoid therapy may minimize this side effect (see 4.2 Recommended Dose and Dosage

Adjustment, Alternate Day Therapy). Pediatric patients may experience a decrease in their growth velocity at low systemic doses and in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression. 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.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed. 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.

7.1.4 Geriatrics

Geriatric populations are associated with different efficacy responses and safety. Treatment of elderly patients with corticoids should be cautious starting with a low dose because the existence of concomitant conditions in elderly patients such as decreased hepatic, renal and cardiac function and the presence of diabetes or osteoporosis.

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.

Allergic reactions: Allergic or hypersensitivity reactions, anaphylactoid reaction, anaphylaxis, angioedema.

Blood and lymphatic system disorders: Leukocytosis

Cardiovascular: Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, flushing, hypertension, hypotension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, thrombosis, vasculitis.

Dermatologic: Acne, allergic dermatitis, cutaneous and subcutaneous atrophy, dry scaly skin, ecchymoses and petechiae, edema, erythema, hyperpigmentation, hypopigmentation, impaired wound healing, increased sweating, rash, pruritus, sterile abscess, striae, suppressed reactions to skin tests, thin fragile skin, thinning scalp hair, and urticaria. Kaposi's sarcoma has been reported to occur in patients receiving corticosteroid therapy.

Endocrine: Decreased carbohydrate and glucose tolerance, development of cushingoid state, moon face, weight gain, abnormal fat deposits, glycosuria, hirsutism, hypertrichosis, increased requirements for insulin or oral hypoglycemic agents in diabetes, manifestations of latent diabetes mellitus, menstrual irregularities, secondary adrenocortical and hypothalamic pituitary adrenal axis suppression (particularly in times of stress, as in trauma, surgery, or illness), suppression of growth in pediatric patients, metabolic acidosis.

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.

Fluid and electrolyte disturbances: Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, urine calcium increased hypokalemic alkalosis.

Gastrointestinal: Abdominal distention, abdominal pain, diarrhea, dyspepsia, bowel/bladder dysfunction (after intrathecal administration), increased appetite, nausea, pancreatitis, peptic ulcer with possible subsequent perforation and hemorrhage, perforation of the small and large intestine (particularly in patients with inflammatory bowel disease), gastric hemorrhage, esophagitis, ulcerative esophagitis, peritonitis (peritonitis may be the primary presenting sign or symptom of a gastrointestinal disorder such as perforation, obstruction or pancreatitis).

Hepatic: Increases in alanine transaminase (ALT, SGPT), aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation. Hepatomegaly has also been observed.

Immune system*:* Masking of infections, decreased resistance to infection, latent infections becoming active, opportunistic infections, hypersensitivity reactions including anaphylaxis, may suppress reactions to skin tests**.**

Investigations**:** Blood urea increased, suppression of reactions to skin tests.

Metabolic*:* Negative nitrogen balance due to protein catabolism, dyslipidemia.

Musculoskeletal: Arthralgia, aseptic necrosis of femoral and humeral heads, calcinosis (following intra-articular or intralesional use), Charcot-like arthropathy, myalgia, loss of muscle mass, muscle weakness, malaise, osteoporosis, pathologic fracture of long bones, steroid myopathy, tendon rupture, particularly of the Achilles tendon, vertebral compression fractures.

Neurologic/Psychiatric: Convulsions, headache, dizziness, vertigo, amnesia, cognitive disorder, increased intracranial pressure with papilledema (pseudotumor cerebri) usually following discontinuation of treatment, neuritis, neuropathy, paresthesia, epidural lipomatosis, insomnia, mood swings, depression, emotional instability, euphoria, abnormal behavior, personality changes, psychological dependence, psychic disorders, affect lability, suicidal ideation, anxiety, confusional state, psychotic behavior, mania, delusion, hallucination, schizophrenia (aggravation of).

Ophthalmic: cataracts, increased intraocular pressure, glaucoma, exophthalmos, central serous chorioretinopathy.

Reproductive System: Increased or decreased motility and number of spermatozoa, menstruation irregular.

Other: Fatigue, hiccups, pulmonary embolism, oedema peripheral

9. DRUG INTERACTIONS

9.2 Drug Interactions Overview

Methylprednisolone is a cytochrome P450 enzyme (CYP) substrate and is mainly metabolized by the CYP3A4 enzyme. CYP3A4 is the dominant enzyme of the most abundant CYP subfamily in the liver of adult humans. It catalyzes 6β-hydroxylation of steroids, the essential Phase I metabolic step for both endogenous and synthetic corticosteroids.

CYP3A4 SUBSTRATES - Many compounds are also substrates of CYP3A4, some of which (as well as other drugs) have been shown to alter glucocorticoid metabolism by induction (up regulation) or inhibition of the CYP3A4 enzyme. In the presence of another CYP3A4 substrate, the hepatic clearance of methylprednisolone 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.

CYP3A4 INHIBITORS - Drugs that inhibit CYP3A4 activity, such as ketoconazole, erythromycin, clarithromycin, diltiazem, and cyclosporine (see Table 1 below), generally decrease hepatic clearance and increase the plasma concentration of CYP3A4 substrate medications, such as methylprednisolone. In the presence of a CYP3A4 inhibitor, a lower dose of methylprednisolone may be required to avoid toxicity.

CYP3A4 INDUCERS - Drugs that induce CYP3A4 activity, such as Phenobarbital, rifampin, carbamazepine, and phenytoin (see Table 1 below), generally increase hepatic clearance, resulting in decreased plasma concentration of medications that are substrates for CYP3A4. Coadministration may require an increase in methylprednisolone dosage to achieve the desired result.

Withdrawal of these inhibitors or inducers reverses these clinical changes and may require careful dosage re-adjustment.

9.3 Drug-Behavioral Interactions

Dizziness, vertigo, visual disturbances and fatigue are possible side effects associated with corticosteroid use. If affected, patients should not drive or operate machinery.

9.4 Drug-Drug Interactions

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

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

Table 1. Important drug interactions/effects with methylprednisolone

Drug Class or Type - DRUG	Interaction/Effect
Antibacterial -ISONIAZID	CYP3A4 INHIBITOR. In addition, there is a potential effect of methylprednisolone to increase the acetylation rate and clearance of isoniazid.
Antibiotic - RIFAMPIN	CYP3A4 INDUCER Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Anticoagulants (oral)	The effect of methylprednisolone on oral anticoagulants is variable. There are reports of enhanced as well as diminished effects of anticoagulants when given concurrently with corticosteroids. Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effects.
Anticonvulsants - CARBAMAZEPINE	CYP3A4 INDUCER (and SUBSTRATE) Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Anticonvulsants - PHENOBARBITAL - PHENYTOIN	CYP3A4 INDUCERS Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
Anticholinergics - NEUROMUSCULAR BLOCKERS	Corticosteroids may influence the effect of anticholinergics. 1) An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs. (see 7 WARNINGS AND PRECAUTIONS, Musculoskeletal and connective tissue disorders) 2) Antagonism of the neuromuscular blocking effects of pancuronium and vecuronium has been reported in patients taking corticosteroids. This interaction may be expected with all competitive neuromuscular blockers.
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) Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids. Therefore the dose of methylprednisolone should be titrated to avoid steroid toxicity.
Antitubercular Drugs • ISONIAZID	CYP3A4 INDUCER Serum concentrations of isoniazid may be decreased. Drugs which induce cytochrome P450 3A4 enzyme activity may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased.
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.
Calcium Channel Blocker - DILTIAZEM	CYP3A4 INHIBITOR (and SUBSTRATE)
Contraceptives (oral) - ETHINYLESTRADIOL/ NORETHINDRONE	CYP3A4 INHIBITOR (and SUBSTRATE) Estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect.
Digitalis glycosides	Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.
Immunosuppressant - CYCLOSPORINE	CYP3A4 INHIBITOR (and SUBSTRATE) 1) Mutual inhibition of metabolism occurs with concurrent use of cyclosporine and methylprednisolone, which may increase the plasma concentrations of either or both drugs. Therefore, it is possible that adverse events associated with the use of either drug alone may be more likely to occur upon coadministration. 2) Convulsions have been reported with concurrent use of methylprednisolone and cyclosporine. 3) Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently.
Immunosuppressant - CYCLOPHOSPHAMIDE - TACROLIMUS	CYP3A4 SUBSTRATES
Macrolide Antibacterial - CLARITHROMYCIN - ERYTHROMYCIN	CYP3A4 INHIBITORS (and SUBSTRATES) Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance. Drugs which inhibit cytochrome P450 3A4 have the potential to result in increased plasma concentrations of corticosteroids. Therefore the dose of methylprednisolone should be titrated to avoid steroid toxicity.

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.
NSAIDs (nonsteroidal anti-inflammatory drugs) - high-dose ASA (acetylsalicylic acid)	1) There may be increased incidence of gastrointestinal bleeding and ulceration when corticosteroids are given with NSAIDs. 2) Methylprednisolone may increase the clearance of high-dose ASA. This decrease in salicylate serum levels could lead to an increased risk of salicylate toxicity when methylprednisolone is withdrawn. ASA should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothromboinemia.
Potassium-depleting agents	When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., 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, xanthenes, 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.
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.
Cholestyramine	Cholestyramine may increase the clearance of oral corticosteroids. `
Vaccines	Patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or attenuated 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, Infections, *Vaccinations*).

9.5 Drug-Food Interactions

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

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

Corticosteroids bind to intracellular glucocorticoid receptors. The corticoid receptor complex mediates changes in gene expression that lead to multiple downstream effects over hours to days. Corticosteroid action results in inhibiting pro-inflammatory signals and promoting anti-inflammatory signals. Glucocorticoids inhibit neutrophil apoptosis and demargination; they inhibit phospholipase A2, which decreases the formation of arachidonic acid derivatives; they inhibit other inflammatory transcription factors and they promote anti-inflammatory genes like interleukin-10.

Lower doses of corticosteroids provide an anti-inflammatory effect, while higher doses are immunosuppressive. High doses of glucocorticoids for an extended period bind to mineralocorticoid receptors, raising sodium levels and decreasing potassium levels.

10.2 Pharmacodynamics

Methylprednisolone is a potent anti-inflammatory steroid. It has greater anti-inflammatory potency than prednisolone and less tendency than prednisolone to induce sodium and water retention. The relative potency of methylprednisolone to hydrocortisone is at least four to one.

10.3 Pharmacokinetics

Methylprednisolone pharmacokinetics is linear, independent of route of administration.

Absorption: Methylprednisolone is rapidly absorbed and the maximum plasma methylprednisolone concentration is achieved around 1.5 to 2.3 hours across doses following oral administration in normal healthy adults. The absolute bioavailability of methylprednisolone in normal healthy subjects is generally high (82% to 89%) following oral administration.

Distribution: Methylprednisolone is widely distributed into the tissues, crosses the blood-brain barrier, and is secreted in breast milk. Its apparent volume of distribution is approximately 1.4L/kg. The plasma protein binding of methylprednisolone in humans is approximately 77%.

Metabolism: In humans, methylprednisolone is metabolized in the liver to inactive metabolites; the major ones are 20α-hydroxymethylprednisolone and 20β-hydroxymethylprednisolone. Metabolism in the liver occurs primarily via the CYP3A4 enzyme (see 9 DRUG INTERACTIONS).

Methylprednisolone, like many CYP3A4 substrates, may also be a substrate for the ATP-binding cassette (ABC) transport protein p-glycoprotein, influencing tissue distribution and interactions with other medicines.

Elimination: The mean elimination half-life for total methylprednisolone is in the range of 1.8 to 5.2 hours. Total clearance is approximately 5 to 6 mL/min/kg.

11. STORAGE, STABILITY AND DISPOSAL

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

Keep in a safe place out of the reach and sight of children.

12. SPECIAL HANDLING INSTRUCTIONS

There are no special handling instructions for this drug product.

PART II: SCIENTIFIC INFORMATION

13. PHARMACEUTICAL INFORMATION

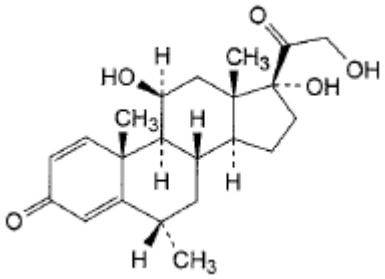
Drug Substance

Proper name: methylprednisolone

Chemical name: pregna-1,4-diene-3,20-dione, 11, 17, 21-trihydroxy-6-methyl-,(6α, 11β)

Molecular formula and molecular mass: $C_{22}H_{30}O_5$ and 374.5

Structural formula:



Physicochemical properties: white crystal powder

14. CLINICAL TRIALS

This information is not available for this drug product.

15. MICROBIOLOGY

No microbiological information is required for this drug product.

16. NON-CLINICAL TOXICOLOGY

Conventional studies of safety, pharmacology and repeated- dose toxicity using intravenous, intraperitoneal, subcutaneous, intramuscular, and oral routes of administration, were done in mice, rats, rabbits and dogs using methylprednisolone sodium succinate. The toxicities seen in the repeated-dose studies are those expected to occur with continued exposure to exogenous adrenocortical steroids.

Carcinogenicity:
Methylprednisolone has not been evaluated in rodent carcinogenicity studies.
Variable results have been obtained with other glucocorticoids tested for carcinogenicity in mice and rats. However, published data indicate that several related glucocorticoids including budesonide, prednisolone, and triamcinolone acetonide can increase the incidence of hepatocellular adenomas and carcinomas after oral administration in drinking water to male rats. These tumorigenic effects occurred at doses which were less than the typical clinical doses on a mg/m^2 basis.

Genotoxicity:
Methylprednisolone has not been evaluated for genotoxicity.

However, methylprednisolone sulfonate, which is structurally similar to methylprednisolone sodium succinate, was not mutagenic with or without metabolic activation in Salmonella typhimurium, or in a mammalian cell gene mutation assay using Chinese hamster ovary cells. Methylprednisolone suleptanate did not induce unscheduled DNA synthesis in primary rat hepatocytes. Moreover, a review of published data indicates that prednisolone farnesylate (PNF), which is structurally similar to methylprednisolone, was not mutagenic with or without metabolic activation in Salmonella typhimurium and Escherichia coli strains. In a Chinese hamster fibroblast cell line, PNF produced a slight increase in the incidence of structural chromosomal aberrations with metabolic activation at the highest concentration tested.

Reproductive and Developmental Toxicology:
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 in untreated females mated with males treated at the administered doses of 10 and 25 mg/kg/day.

Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. In animal reproduction studies, glucocorticoids such as methylprednisolone 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.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]MEDROL*

Methylprednisolone tablets USP

Read this carefully before you start taking **MEDROL** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **MEDROL**.

What is MEDROL used for?

MEDROL is used in the treatment of various conditions such as allergy or inflammation; it can also be used to replace the corticosteroid hormone when your body does not produce enough due to problems with your adrenal glands (a condition called adrenal insufficiency)

How does MEDROL work?

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

What are the ingredients in MEDROL?

Medicinal ingredients: Methylprednisolone

Non-medicinal ingredients: Calcium stearate, cornstarch, lactose, mineral oil and sucrose. In addition, the 4 mg tablet contains sorbic acid.

MEDROL comes in the following dosage forms:

Each elliptical, cross-scored tablet contains: methylprednisolone 4 mg (white, engraved "MEDROL 4") or 16 mg (white, engraved "MEDROL 16").

Do not use MEDROL if:

- you have allergies to methylprednisolone or any other steroid medicine or any of the ingredients in MEDROL tablets; or
- you have any fungal infection or any untreated infection.
- you have viral diseases including vaccinia (cowpox), varicella (chicken pox), and herpes simplex of the eye.
- you have recently received a type of vaccine called a live or live / attenuated vaccine. Do not receive this vaccine during treatment with MEDROL.

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

- have a known or suspected allergy to cow's milk or its components or other dairy products.
- have an infection (such as herpes simplex, chicken pox, tuberculosis, threadworm); **If you or your child is exposed to measles or chickenpox during treatment with MEDROL, 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 vaccine
- have recently had heart problems such as a heart attack (myocardial infarction), heart failure or heart disease
- have bleeding or blood clotting problems (thromboembolic disorders)
- have brittle bone (osteoporosis);
- have high blood pressure
- have water retention (oedema);
- have kidney disease;
- have diabetes or high blood sugar;
- have seizures (fits) or other nervous system problems;
- have thyroid problems;
- have muscle pain or weakness (such as myasthenia gravis);
- have skin cancer (Kaposi's sarcoma), or a tumor of the adrenal glands (pheochromocytoma);
- have certain eye disease such as glaucoma, cataracts; herpes infection or any problems with the retina;
- have liver disease such as cirrhosis;
- have certain mental or mood conditions (such as depression)
- have stomach or gut problems (such as ulcers or ulcerative colitis);
- have low potassium or calcium;
- have weak immune response; Tell 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 (a condition caused by having an excess of cortisol hormone);
- have had any prior use of MEDROL;
- have a condition known as systemic sclerosis. This is a condition in which your body makes too much of a protein called collagen.

Other warnings you should know about:

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

- skin cancer (Kaposi's sarcoma): Kaposi's sarcoma has been reported with corticosteroid therapy, such as MEDROL. Stopping treatment of MEDROL may result in signs of this cancer going away.
- tumor of the adrenal glands (pheochromocytoma). This tumor has been reported with corticosteroid therapy, such as MEDROL. Pheochromocytoma may cause death.
- fat deposition on or outside the lining of the spine (epidural lipomatosis). Taking corticosteroids in high doses for a long period of time can cause epidural lipomatosis.

Surgery
Before you have any operation, tell your healthcare professional (for example your doctor, dentist or anesthetist) that you are taking MEDROL.

Pregnancy and breastfeeding:

- If you are pregnant, or still able to get pregnant and/or breast-feed, there are specific risks you must discuss with your healthcare professional. Taking MEDROL may:
    - slow the growth and cause low birth weight of the baby.

    - cause cataracts in babies. This risk is associated with mothers who take corticosteroids for a long period of time during pregnancy.
- If you are breastfeeding or planning to breastfeed, tell your healthcare professional.
- You should tell your healthcare professional if you are breast feeding as small amounts of corticosteroid medicines may get into breast milk.

Male fertility:
Taking MEDROL may affect male fertility.

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

- Serious adrenal insufficiency. This is when the body does not make enough of the cortisol hormone. This may cause death.
- "Withdrawal syndrome". This includes symptoms such as anorexia, nausea, vomiting, lack of energy, headache, fever, joint pain, peeling of skin, muscle pain, weight loss, and/or low blood pressure.

Skin:
- Tell your healthcare professional you are taking MEDROL since it can affect the results of skin tests.

Children (less than 18 years of age):
- Children may have their growth slowed with use of MEDROL.
- Your healthcare professional will give the child the lowest dose to reduce the risk of slowing growth.
- Your healthcare professional will carry out tests on the child if they are taking MEDROL for a long period of time. Taking methylprednisolone will increase the risk of developing a growing pressure in the skull (high intracranial pressure).
- Your healthcare professional may need to monitor the heart if methylprednisolone is given to a prematurely born baby.

Driving and Using Machines

MEDROL may cause dizziness, vertigo, vision problems and fatigue. If you experience these side effects you should not drive or operate machinery

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 MEDROL:

- **Medicines used to:**
    - treat glaucoma and epilepsy such as acetazolamide
    - prevent or treat nausea and vomiting such as aprepitant or fosaprepitant
    - treat cancer such as aminoglutethimide or cyclophosphamide
    - "thin" the blood or prevent blood clotting (anticoagulants such as acenomoumarol, phenindione and warfarin
    - treat myasthenia gravis (a muscle condition) such as distigmine and neostigmine

- treat bacterial and fungal infections (antibiotics and antifungals) such as ketoconazole, itraconazole, amphotericin B, erythromycin, clarithromycin, troleandomycin, rifampin, rifampicin and rifabutin)
- treat inflammation such as aspirin and non-steroidal anti-inflammatory medicines (also called NSAIDs) like ibuprofen
- treat epilepsy such as barbiturates, carbamezipine, phenobarbital, phenytoin and primidone
- treat heartburn and acid indigestion such as cimetidine
- treat heart problems or high blood pressure as digoxin and diltiazem
- reduce extra fluid in the body (water pills or diuretics)
- for hormone replacement therapy or hormonal oral contraceptive (such as ethinyl estradiol and norethindrone)
- treat high cholesterol (such as cholestyramine)
- treat HIV infections such as indinavir or ritonavir
- in surgery to block signals between nerves and muscles (neuromuscular blocking agents) such as pancuronium or vercuronium
- help prevent organ rejection such as cyclosporine and tacrolimus
- vaccines. Tell your healthcare professional if you have recently had, or are about to have any vaccination
- treat diabetes
- treat tuberculosis (such as isoniazid)

How to take MEDROL:

Usual dose:

Between 4 mg to 48 mg daily, based on your condition and how severe it is.

Your healthcare professional may tell you to take your daily dose as a single dose or in divided doses.

Swallow the tablets with water. Do not eat grapefruit or drink grapefruit juice while taking MEDROL.

When your condition has improved, your dose will be lowered gradually.

MEDROL should not be stopped suddenly. Do not stop taking MEDROL without talking to your healthcare professional.

Overdose:

If you think you, or a person you are caring for, have taken too much MEDROL, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

Take the missed dose as soon as you remember. However, if it is almost time for the next dose, skip the missed dose and take your next scheduled dose. Do not take two doses to make up for a missed one.

What are possible side effects from using MEDROL?

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

Infections:
MEDROL may:

- hide symptoms of infections
- reactivate dormant infections
- induce infections due to lowered body resistance

Allergic Reactions:

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

Heart problems:

- heart failure
- heart attack
- arrhythmia (irregular heartbeat)
- high and low blood pressure
- blood clots
- thrombophlebitis (vein inflammation)
- thrombosis (blood clot within a blood vessel)
- cardiac arrest
- pediatric hypertrophic cardiomyopathy (thickening of heart muscle)
- facial blushing

Skin problems:

- thin fragile skin
- impaired wound healing
- 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 problems:

- 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 hypothalamic 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
- lowered carbohydrate (sugar) tolerance
- buildup of acid in the body (metabolic acidosis)
- sodium and fluid retention

Gastrointestinal problems:

- 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
- bowl/bladder dysfunction
- increased appetite
- peritonitis

Liver problems:

- enlarged liver

Musculoskeletal problems:

- 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
- aseptic necrosis (tissue death)

Nervous system problems:

- 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
- inflammation of nerves (neuritis)
- nerve damage
- abnormal amount of fat deposit around the spine (epidural lipomatosis)

Eye problems:

- cataracts
- increased eye pressure
- glaucoma
- protrusion of the eyeball
- retinal detachment

Psychiatric problems:

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

Sexual Function/Reproduction problems:

- irregular periods
- increased or decreased motility and number of sperm

Blood problems:

- Above normal white blood cell count
- Above normal cholesterol or triglicerides
- Abnormal blood tests (ex. liver enzymes and urea)

Other:

- fatigue, hiccups, swelling
- Tumor lysis syndrome (TLS): This is the sudden, rapid death of cancer cells due to treatment. TLS can cause life-threatening kidney failure and heart problems.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Stomach ulcers (burst or bleeding ulcers): symptoms of which are stomach pain, black or bloodstained stools and/or vomiting blood			√
Flare up of a previous Tuberculosis: symptoms of which could be coughing blood or pain in the chest			√
Infection: symptoms might include a raised temperature and feeling unwell.		√	
High blood pressure: headaches or generally feeling unwell		√	
Swelling		√	
Cramps and spasms		√	
Vision changes		√	
Mental problems: feeling high (mania), mood swings, depression, suicidal thinking, agitation, anxiety, trouble sleeping, confusion, losing your memory		√	
Feeling, seeing or hearing things which do not exist.		√	
Increased thirst and urination		√	
Fast/pounding or irregular heartbeat		√	
Acne	√		
Poor wound healing	√		
Thinning of skin	√		
Increased hair growth	√		
Congestive heart failure: Dizziness, fatigue, weakness, shortness of breath			√
Muscle weakness			√
Bone and joint pain			√
Prone to bone fracture or breaking			√

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 (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

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

Storage:

Store between 15°C and 30°C in the original package. Do not take MEDROL after the expiry date shown on the package. Keep out of reach and sight of children.

If you want more information about MEDROL:

- 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 1-800-463-6001.

This leaflet was prepared by Pfizer Canada ULC.

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