PRODUCT MONOGRAPH

Including Patient Medication Information

[Pr]DEPO-MEDROL® WITH LIDOCAINE

methylprednisolone acetate with lidocaine hydrochloride injectable suspension
(with benzyl alcohol and myristyl-gamma-picolinium chloride (MGPC))
For intrasynovial, intra-articular, intrabursal, periarticular use
40 mg/mL of methylprednisolone acetate and 10 mg/mL of lidocaine hydrochloride

USP

Glucocorticoid with local anaesthetic

Pfizer Canada ULC
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RECENT MAJOR LABEL CHANGES

7 WARNINGS AND PRECAUTIONS, Immune	01/2025
7, WARNINGS AND PRECAUTIONS, Musculoskeletal	05/2025

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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

DEPO-MEDROL with Lidocaine (methylprednisolone acetate and lidocaine hydrochloride) is indicated for:

- adjunctive therapy for short-term local administration (to tide the patient over an acute episode or exacerbation) in: synovitis of osteoarthritis, rheumatoid arthritis, acute and subacute bursitis, acute gouty arthritis, epicondylitis, acute nonspecific tenosynovitis, post-traumatic osteoarthritis.

- DEPO-MEDROL with Lidocaine may also be useful in cystic tumors of an aponeurosis or tendon (ganglia).

1.1 Pediatrics

Pediatrics (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of DEPO-MEDROL with Lidocaine in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use (see 2 CONTRAINDICATIONS; 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 4.1 Dosing Considerations).

2 CONTRAINDICATIONS

DEPO-MEDROL with Lidocaine is contraindicated:

- in patients with known hypersensitivity to any components of DEPO-MEDROL, Lidocaine or other local anesthetics of the amide type.

- in patients with systemic fungal infections.

- in idiopathic thrombocytopenic purpura when administered intramuscularly

- 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.

- for epidural, intravascular (e.g., intravenous) and intrathecal administration.

- for use by the intramuscular route of administration.

- for intra-articular injection in unstable joints.

- for use in premature infants because the formulation contains benzyl alcohol. (see 7.1.3, Pediatrics).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Multidose use of DEPO-MEDROL with Lidocaine (methylprednisolone acetate and lidocaine hydrochloride) from a single vial requires special care to avoid contamination. Although initially sterile, any multidose use of vials may lead to contamination unless strict aseptic technique is observed. Particular care, such as use of disposable sterile syringes and needles is necessary. When multidose vials are used, special care to prevent contamination of the contents is essential. A povidone-iodine solution or similar product is recommended to cleanse the vial top prior to aspiration of contents.

- Because of possible physical incompatibilities, DEPO-MEDROL with Lidocaine should not be diluted or mixed with other solutions. Parenteral suspensions should be inspected visually for foreign particulate matter and discolouration prior to administration whenever drug product and container permit.

- In order to minimize the incidence of dermal and subdermal atrophy, care must be exercised not to exceed recommended doses in injections. Multiple small injections into the area of the lesion should be made whenever possible. The technique of intra-articular injection should include precautions against injection or leakage into the dermis.

- Caution must be used in renal insufficiency, hypertension, osteoporosis, and myasthenia gravis, when steroids are used as direct or adjunctive therapy.

- 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. DEPO-MEDROL with Lidocaine dosage may need to be increased during and after the stressful situation.

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, increased risk for osteoporosis and fluid retention (with possible resultant hypertension) and of concomitant disease or other drug therapy.

4.2 Recommended Dose and Dosage Adjustment

Although administration of DEPO-MEDROL with Lidocaine may ameliorate symptoms, it is not a cure and the hormone has no effect on the cause of the inflammation. Hormone therapy should be used as an adjunct to conventional therapy.

1. **Rheumatoid arthritis and Osteoarthritis**

The methylprednisolone dose for intra-articular administration depends upon the size of the joint and varies with the severity of the condition in the individual patient. In chronic cases, injections may be repeated at intervals ranging from one to five or more weeks depending upon the degree of relief obtained from the initial injection. The methylprednisolone doses in the following table are given as a general guide:

Table 1. General guide for methylprednisolone dosage

Size of Joint	Examples	Range of Methylprednisolone Dosage
Large	Knees Ankles Shoulders	20 to 80 mg
Medium	Elbows Wrists	10 to 40 mg
Small	Metacarpophalangeal Interphalangeal Sternoclavicular Acromioclavicular	4 to 10 mg

Procedure: It is recommended that the anatomy of the joint involved be reviewed before attempting intra-articular injection. In order to obtain the full anti-inflammatory effect, it is important that the injection be made into the synovial space. Employing the same sterile technique as for a lumbar puncture, a sterile 20 to 24 gauge needle (on a dry syringe) is quickly inserted into the synovial cavity. The aspiration of only a few drops of joint fluid proves the joint space has been entered by the needle.

The injection site for each joint is determined by that location where the synovial cavity is most superficial and most free of large vessels and nerves. With the needle in place, the aspirating syringe is removed and replaced by a second syringe containing the desired amount of DEPO-MEDROL with Lidocaine. The plunger is then pulled outward slightly to aspirate synovial fluid and to make sure the needle is still in the synovial space. After injection, the joint is moved

gently a few times to aid mixing of synovial fluid and the suspension. The site is covered with a small sterile dressing.

Suitable sites for intra-articular injection are the knee, ankle, wrist, elbow, shoulder, phalangeal, and hip joints. Since difficulty is occasionally encountered in entering the hip joint, precautions should be taken to avoid any large blood vessels in the area. Joints not suitable for injection are those that are anatomically inaccessible such as the spinal joints and those like the sacroiliac joints that are devoid of synovial space. Treatment failures are most frequently the result of failure to enter the joint space, however, treatment failure may also occur despite a proper injection into the synovial space as confirmed by aspiration of fluid. If treatment failures occur even when injections into the synovial spaces have been confirmed by aspiration of fluid, repeated injections are usually futile and not recommended.

Following intra-articular steroid therapy, care should be taken to avoid overuse of joints in which symptomatic benefit has been obtained. Negligence in this matter may permit an increase in joint deterioration that will more than offset the beneficial effects of the steroid.

Unstable joints should not be injected (see 2 CONTRAINDICATIONS). Repeated intra-articular injection may in some cases result in instability of the joint. X-ray follow-up is suggested in selected cases to detect deterioration.

2. **Bursitis**

The area around the injection site is prepared in a sterile way and local anesthesia is administered as necessary.
A 20 to 24 gauge needle attached to a dry syringe is inserted into the bursa and the fluid aspirated. The needle is left in place and the aspirating syringe changed for a small syringe containing the desired dose. After injection, the needle is withdrawn and a small dressing applied.

3. **Miscellaneous: Ganglion, Tendinitis, Epicondylitis**

In the treatment of conditions such as tendinitis or tenosynovitis, care should be taken, to inject the suspension into the tendon sheath rather than into the substance of the tendon. The tendon may be readily palpated when placed on a stretch. When treating conditions such as epicondylitis, the area of greatest tenderness should be outlined carefully and the suspension infiltrated into the area.

For ganglia of the tendon sheaths, the suspension is injected directly into the cyst.

Sterile precautions should be observed, with each injection.

The dose in the treatment of the various conditions of the tendinous or bursal structures listed above varies with the condition being treated and ranges from 4 to 30 mg. In recurrent or chronic conditions, repeated injections may be necessary.

5 OVERDOSAGE

Methylprednisolone

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.

Lidocaine

Symptoms of acute systemic toxicity

Central nervous system toxicity presents with symptoms of increasing severity. Patients may present initially with circumoral paraesthesia, numbness of the tongue, light-headedness, hyperacusis and tinnitus. Visual disturbance and muscular tremors or muscle twitching are more serious and precede the onset of generalized convulsions. These signs must not be mistaken for neurotic behaviour. Unconsciousness and grand mal convulsions may follow, which may last from a few seconds to several minutes. Hypoxia and hypercapnia occur rapidly following convulsions due to increased muscular activity, together with the interference with normal respiration and loss of the airway. In severe cases, apnea may occur. Acidosis increases the toxic effects of local anesthetics.

Effects on the cardiovascular system may be seen as well. Hypotension, bradycardia, arrhythmia and cardiac arrest may occur as a result of high systemic concentrations, with potentially fatal outcome.

Recovery occurs as a consequence of redistribution of the local anesthetic drug from the central nervous system and metabolism and may be rapid unless large amounts of the drug have been injected.

Treatment of acute toxicity

If signs of acute systemic toxicity appear, injection of the anesthetic should be stopped immediately.

Treatment will be required if convulsions and CNS depression occurs. The objectives of treatment are to maintain oxygenation, stop the convulsions and support the circulation. A patent airway should be established and oxygen should be administered, together with assisted ventilation (mask and bag) if necessary. The circulation should be maintained with infusions of plasma or intravenous fluids. Where further supportive treatment of circulatory depression is required, use of a vasopressor agent may be considered although this involves a risk of CNS excitation. Convulsions may be controlled by the intravenous administration of Diazepam or Thiopentone Sodium, bearing in mind that anti-convulsant drugs may also depress respiration and the circulation. Prolonged convulsions may jeopardize the patient's ventilation and oxygenation and early endotracheal intubation should be considered. If cardiac arrest should occur, standard cardiopulmonary resuscitation procedures should be instituted. Continual optimal oxygenation and ventilation and circulatory support as well as treatment of acidosis are of vital importance.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

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
Intrasynovial Injection (including periarticular and intrabursal) Intra-articular injection	40 mg/mL methylprednisolone acetate + 10 mg/mL lidocaine hydrochloride sterile aqueous suspension	Benzyl alcohol, myristyl-gamma-picolinium chloride, polyethylene glycol 3350, sodium chloride and water for injection.

DEPO-MEDROL with Lidocaine is available in 1, 2 and 5 mL vials containing 40 mg/mL methylprednisolone acetate and 10 mg/mL lidocaine hydrochloride.

When necessary, pH was adjusted with Sodium Hydroxide and/or Hydrochloric Acid. The pH of the finished product remains within the USP specified range i.e. 3.5 to 7.0.

7 WARNINGS AND PRECAUTIONS

General

DEPO-MEDROL with Lidocaine should not be administered by any route other than those listed under 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING and 1 INDICATIONS. It is critical that, during administration of DEPO-MEDROL with Lidocaine appropriate technique be used and care taken to assure proper route of administration.

Sterile technique is necessary to prevent infections or contamination.

This product contains benzyl alcohol which is potentially toxic when administered locally to neural tissue.

Special Precautions Regarding Use of Lidocaine for Local Anesthesia

Facilities for resuscitation should be available when administering local anesthetics, such as the lidocaine contained in the methylprednisolone with lidocaine solution for injection. Certain local anesthetic procedures may be associated with serious adverse reactions, regardless of the local anesthetic drug used and are usually the result of raised plasma concentrations due to accidental intravascular injection, excessive dosage or rapid absorption from highly vascular areas, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Systemic toxicity mainly involves the central nervous system and/or the cardiovascular system (see 5 OVERDOSAGE and 8 ADVERSE REACTIONS).

As with other local anesthetics, lidocaine should be used with caution in patients with epilepsy, myasthenia gravis, cardiac conduction disturbances, congestive heart failure, hypovolemia, and

bradycardia. Elderly or debilitated patients require smaller doses, commensurate with age and physical status.
Intra-articular injected corticosteroids may be systemically absorbed and may produce systemic as well as local effects. Where parenteral corticosteroid therapy for sustained systemic effect is desired, plain DEPO-MEDROL should be used.

Appropriate examination of any joint fluid present is necessary to exclude a septic process. A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, appropriate antimicrobial therapy should be instituted.
Local injection of a steroid into a previously infected joint is to be avoided.

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).

A metabolite of lidocaine, 2,6-xylidine, has shown weak genotoxic potential in vitro and in vivo and carcinogenic potential (in rats) with unknown clinical relevance in relation to short-term/intermittent use of lidocaine as a local anesthetic (see 16 NON-CLINICAL TOXICOLOGY).

Cardiovascular

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.

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

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.

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

Dizziness, vertigo, visual disturbances and fatigue are possible side effects associated with corticosteroid use, and temporary impairment of mobility and coordination of movement may occur

due to the local anesthetic effect of lidocaine. When outpatient anesthesia affects areas of the body involved in driving or operating machinery, patients should be advised to avoid these activities until normal function is fully restored.

Endocrine and Metabolism

Corticosteroids administration may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency 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, corticosteroid therapy may need to be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid may need to be administered concurrently. If glucocorticoids are withdrawn abruptly, acute adrenal insufficiency leading to a fatal outcome may occur.

Because glucocorticoid therapy can lead to 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.

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

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.

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.

Gastrointestinal

Corticosteroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection, 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.

Glucocorticoid therapy may mask the symptoms of peptic ulcer so that perforation or haemorrhage 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 (acetylsalicylic acid), the risk of developing gastrointestinal ulcers is increased.

Hematologic

Aspirin (acetylsalicylic acid) should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia (see 9 DRUG INTERACTIONS).

Hepatic/Biliary/Pancreatic

There is an enhanced effect of corticosteroids in 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 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 organisms, in any location in the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect cellular immunity, humoral immunity, or neutrophil function. These infections may be mild, but can be severe and at times fatal. With increasing doses of corticosteroids, the rate of occurrence of infectious complications increases. Do not use intrasynovially, intrabursally, or for intratendinous administration for local effect in the presence of acute infection.
Monitor for the development of infection and consider withdrawal of corticosteroids or dosage reduction as needed.

Recent studies suggest that corticosteroids should not be used in septic shock (an unapproved indication), 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).

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 Stronglyoides 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 DEPO-MEDROL with Lidocaine 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.

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 can have a more serious or even fatal course in pediatric and adult patients 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.

Monitoring and Laboratory Tests
Corticosteroids may suppress reactions to skin tests.

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, see 7 WARNINGS AND PRECAUTIONS, Neurologic), or in patients receiving concomitant therapy with

anticholinergics such as neuromuscular blocking drugs (e.g., pancuronium). This acute myopathy is generalized, may involve ocular and respiratory muscles, and may result in quadriparesis. Elevations of creatine kinase may occur. Cases of rhabdomyolysis have been reported. Clinical improvement or recovery after stopping corticosteroids may require weeks to years.

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 large doses of glucocorticoid.

Neurologic

Results from one multicenter, randomized, placebo-controlled study with IV methylprednisolone hemisuccinate, showed an increase in early (at 2 weeks) and late (at 6 months) mortality in patients with cranial trauma. Therefore, systemic corticosteroids, including DEPO-MEDROL with Lidocaine, are not indicated for, and therefore should not be used to treat, traumatic brain injury.

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

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

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

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 corneal perforation. Corticosteroids should not be used in active ocular herpes simplex.

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

Psychiatric

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Potentially severe psychiatric adverse reactions may occur with systemic steroids. 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

- **Fertility**

  Steroids may increase or decrease motility and number of spermatozoa in some patients (see 2 CONTRAINDICATIONS, 7.1.1 Pregnant Women)

Sensitivity/Resistance

Allergic reaction 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 patients have a history of allergy to any drug.

Skin

While crystals of adrenal steroids in the dermis suppress inflammatory reactions, their presence may cause disintegration of the cellular elements and physicochemical changes in the ground substance of the connective tissue. The resultant infrequently occurring dermal and/or subdermal changes may form depressions in the skin at the injection site.

The degree to which this reaction occurs will vary with the amount of adrenal steroid injected. Regeneration is usually complete within a few months or after all crystals of the adrenal steroid have been absorbed.

7.1 Special Populations

7.1.1 Pregnant Women

Corticosteroids readily cross the placenta. Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to human dose. Animal studies in which corticosteroids have been given to pregnant mice, rats, and rabbits, have yielded an increase incidence of cleft palate in the off-spring (see 16 NON-CLINICAL TOXICOLOGY, Reproductive and Developmental Toxicology).

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

Lidocaine and benzyl alcohol can cross the placenta.

There are no known effects of corticosteroids on labour and delivery. The use of local anesthetics such as lidocaine during labor and delivery may be associated with adverse effects on mother and fetus.

Since adequate human reproductive studies have not been done with methylprednisolone, lidocaine or benzyl alcohol, 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.

7.1.2 Breast-feeding

Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants.

Lidocaine is excreted in breast milk.

Because of the potential for serious adverse reactions in nursing infants, 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 (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of DEPO-MEDROL with Lidocaine in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use.

DEPO-MEDROL with Lidocaine is contraindicated for use in premature infants. Benzyl alcohol, a component of this product, has been associated with serious adverse events including death, particularly in pediatric patients, including the "gasping syndrome" in neonate and low-birth weight infants. The "gasping syndrome" is characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine. Additional symptoms may include gradual neurological deterioration, seizures, intracranial

hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse. The minimum amount of benzyl alcohol at which toxicity may occur is not known. Premature and low-birth-weight infants, as well as patients receiving high dosages (>90 mg/kg/day), may be more likely to develop toxicity. Practitioners administering this and other medications containing benzyl alcohol should consider the combined daily metabolic load of benzyl alcohol from all sources.

Growth may be suppressed in children receiving long-term, daily divided-dose glucocorticoid therapy. The use of such a regimen should be restricted to those most serious indications. 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

Geriatrics (>65 years of age): 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, increased risk for osteoporosis and fluid retention (with possible resultant hypertension) and of concomitant disease or other drug therapy.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

The following adverse reactions have been reported with (A) DEPO-MEDROL or other corticosteroids products and (B) Lidocaine:

In common with other local anesthetics, adverse reactions to lidocaine are rare and are usually the result of raised plasma concentrations due to accidental intravascular injection, excessive dosage or rapid absorption from highly vascular areas, or may result from a hypersensitivity, idiosyncrasy or diminished tolerance on the part of the patient. Systemic toxicity mainly involves the central nervous system and/or the cardiovascular system. Neurological signs of systemic toxicity include dizziness or light-headedness, nervousness, tremor, circumoral paraesthesia, tongue numbness, drowsiness, convulsions, coma. Cardiovascular reactions are depressant and may manifest as hypotension,

bradycardia, myocardial depression, cardiac arrhythmias, and possibly cardiac arrest or circulatory collapse. Blurred vision, diplopia, and transient amaurosis may be signs of lidocaine toxicity.

A. DEPO-MEDROL (methylprednisolone acetate) with Lidocaine and other corticosteroid products

MedDRA (v15) System Organ Class	Undesirable Effect
Blood and lymphatic system disorders	Leukocytosis
Cardiac disorders	Cardiac failure (in susceptible patients); bradycardia; tachycardia; cardiac arrest; cardiac arrhythmias; cardiac enlargement; circulatory collapse; fat embolism; flushing; hypertrophic cardiomyopathy in premature infants; myocardial rupture following recent myocardial infarction; pulmonary oedema; syncope; thromboembolism; thrombophlebitis; vasculitis
Ear and labyrinth disorders	Vertigo; tinnitus (for lidocaine only)
Endocrine disorders	Cushingoid; hypothalamic-pituitary-adrenal axis suppression (particularly in times of stress, as in trauma, surgery, or illness); moon face; weight gain; abnormal fat deposits; glycosuria; hypertrichosis 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.
Eye disorders	Cataract; glaucoma; exophthalmos; increased intraocular pressure; central serous chorioretinopathy; diplopia (for lidocaine only); vision blurred (for lidocaine only)
Gastrointestinal disorders	Peptic ulcer (with possible subsequent peptic ulcer perforation and peptic ulcer haemorrhage); gastric haemorrhage; intestinal perforation (particularly in patients with inflammatory bowel disease); pancreatitis; oesophagitis ulcerative ; oesophagitis; abdominal pain; abdominal distension; diarrhoea; dyspepsia; nausea; bowel/bladder dysfunction (after intrathecal administration); increased appetite; peritonitis (peritonitis may be the primary presenting sign or symptom of a gastrointestinal disorder such as perforation, obstruction or pancreatitis); vomiting (for lidocaine only)
General disorders and administration site conditions	Impaired healing; oedema peripheral; injection site reaction; fatigue; malaise; oedema (for lidocaine only); feeling hot (for lidocaine only); feeling cold (for lidocaine only)

MedDRA (v15) System Organ Class	Undesirable Effect
Hepatic disorders	Hepatomegaly; elevation in serum liver enzyme levels (usually reversible upon discontinuation)
Immune system disorders	Drug hypersensitivity; anaphylactic reaction; anaphylactoid reaction
Infections and infestations	Infection; opportunistic infection; injection site infections (following non-sterile technique); decreased resistance to infection
Injury, poisoning and procedural complications	Tendon rupture
Investigations	Blood potassium decreased; alanine aminotransferase increased; aspartate aminotransferase increased; blood alkaline phosphatase increased; carbohydrate tolerance decreased; urine calcium increased; suppression of reactions to skin tests; blood urea increased
Metabolism and nutrition disorders	Sodium retention; fluid retention; glucose tolerance impaired; increased requirements for insulin (or oral hypoglycemic agents in diabetics); alkalosis hypokalaemic; dyslipidemia; increased appetite (which may result in weight increased); lipomatosis; metabolic acidosis; nitrogen balance negative (due to protein catabolism)
Musculoskeletal and connective tissue disorders	Growth retardation; osteoporosis; muscular weakness; osteonecrosis; pathological fracture; muscle atrophy; myopathy; rhabdomyolysis; arthralgia; myalgia; calcinosis (following intra-articular or intralesional use); Charcot-like arthropathy; post injection flare (following intra-articular use, periarticular, and tendon sheath injections); spinal compression fracture; neuropathic arthropathy; muscle twitching (for lidocaine only)
Nervous system disorders	Intracranial pressure increased (with papilledema [idiopathic intracranial hypertension] usually following discontinuation of treatment); convulsion; amnesia; cognitive disorder, dizziness; headache; neuritis; neuropathy; paresthesia, epidural lipomatosis; loss of consciousness (for lidocaine only); hypoaesthesia (for lidocaine only); tremor (for lidocaine only); somnolence (for lidocaine only); light-headedness (for lidocaine only); numbness (for lidocaine only)
Psychiatric disorders	Affective disorder (including depressed mood, euphoric mood); mood swings; abnormal behaviour; insomnia; affective disorder (including affect lability, drug dependence, suicidal ideation); psychotic disorder (including mania, delusion, hallucination, schizophrenia); confusional state; mental disorder; anxiety; personality change; emotional instability; irritability; euphoric mood (for lidocaine only); nervousness (for lidocaine only)

MedDRA (v15) System Organ Class	Undesirable Effect
Reproductive system and breast disorders	Menstruation irregular; increased or decreased motility and number of spermatozoa
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism; hiccups; Bronchospasm; Dyspnoea; respiratory arrest (for lidocaine only); respiratory depression (for lidocaine only)
Skin and subcutaneous disorders	Ecchymoses; acne; angioedema; Face oedema; petechiae; skin atrophy; skin striae; skin hyperpigmentation; skin hypopigmentation; hirsutism; rash; erythema; pruritus; urticaria; hyperhidrosis; allergic dermatitis; cutaneous and subcutaneous atrophy; dry scaly skin; sterile abscess; thinning scalp hair; post-injection flare – following intrasynovial use; Kaposi's sarcoma; skin lesion (for lidocaine only); skin reaction (for lidocaine only)
Vascular disorders	Hypertension; thrombosis; hypotension; cardiac arrest (for lidocaine only); circulatory collapse (for lidocaine only)

B. Lidocaine

MedDRA (v15) System Organ Class	Undesirable Effect
Cardiac disorders	Bradycardia
Ear and labyrinth disorders	Tinnitus
Eye disorders	Diplopia; vision blurred
Gastrointestinal disorders	Vomiting
General disorders and administration site conditions	Oedema; feeling hot; feeling cold
Immune system	Anaphylactic reaction
Musculoskeletal and connective tissue disorders	Muscle twitching
Nervous system disorders	Loss of consciousness; convulsion; hypoaesthesia; tremor; somnolence; dizziness; light-headedness; numbness
Psychiatric disorders	Confusional state; euphoric mood; nervousness; anxiety
Respiratory, thoracic and mediastinal disorders	Respiratory arrest; respiratory depression
Skin and subcutaneous disorders	Skin lesion; urticaria; skin reaction
Vascular disorders	Hypotension; cardiac arrest; circulatory collapse

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Methylprednisolone

Methylprednisolone is a cytochrome P450 enzyme (CYP) substrate and is mainly metabolized by the CYP3A 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. Many other compounds are also substrates of CYP3A4, some of which (as well as other drugs) have been shown to alter glucocorticoid metabolism by induction (upregulation) or inhibition of the CYP3A4 enzyme.

CYP3A4 INHIBITORS – Drugs that inhibit CYP3A4 activity generally decrease hepatic clearance and increase the plasma concentration of CYP3A4 substrate medications, such as methylprednisolone. In the presence of a CYP3A4 inhibitor, the dose of methylprednisolone may need to be titrated to avoid steroid toxicity.

CYP3A4 INDUCERS – Drugs that induce CYP3A4 activity 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.

CYP3A4 SUBSTRATES – 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.

NON-CYP3A4-MEDIATED EFFECTS – Other interactions that may occur with methylprednisolone are described in the table below.

9.4 Drug-Drug Interactions

Drug Class or Type **- DRUG or SUBSTANCE**	**Interaction or Effect**
Aminoglutethimide	Aminoglutethimide may lead to a loss of corticosteroid-induced adrenal suppression.
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

Drug Class or Type - DRUG or SUBSTANCE	Interaction or Effect
Anticoagulants (oral)	The effect of methylprednisolone on oral anticoagulants, including vitamin K antagonists (e.g. warfarin, acenocoumarol, fluindione), is variable. There are reports of enhanced as well as diminished effects of anticoagulants when given concurrently with corticosteroids. Therefore, coagulation indices should be monitored to maintain the desired anticoagulant effects. 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 effect.
Anticonvulsant - CARBAMAZEPINE	CYP3A4 INDUCER (and SUBSTRATE)
Anticonvulsants - PHENOBARBITAL - PHENYTOIN	CYP3A4 INDUCERS
Anticholinergics -NEUROMUSCULAR BLOCKERS	Corticosteroids may influence the effect of anticholinergics. 1) An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs. (See 7 WARNINGS AND PRECAUTIONS - Musculoskeletal, for additional information.) 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	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. Steroids may reduce the effects of anticholinesterases in myasthenia gravis.
Antidiabetics	Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.
Antiemetic - APREPITANT - FOSAPREPITANT	CYP3A4 INHIBITORS (and SUBSTRATES)
Antifungal - ITRACONAZOLE - KETOCONAZOLE	CYP3A4 INHIBITORS (and SUBSTRATE)
Antitubercular drugs	Serum concentrations of isoniazid may be decreased.

Drug Class or Type - DRUG or SUBSTANCE	Interaction or Effect
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 inhibitor - AMINOGLUTETHIMIDE	Aminoglutethimide-induced adrenal suppression may exacerbate endocrine changes caused by prolonged glucocorticoid treatment.
Calcium Channel Blocker - DILTIAZEM	CYP3A4 INHIBITOR (and SUBSTRATE)
Cholestyramine	Cholestyramine may increase the clearance of oral corticosteroids
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. Convulsions have been reported with concurrent use. Mutual inhibition of metabolism occurs with concurrent use of cyclosporine and methylprednisolone, therefore it is possible that adverse events associated with the individual use of either drug may be more apt to occur**.**
Immunosuppressant - CYCLOPHOSPHAMIDE - TACROLIMUS	CYP3A4 SUBSTRATE
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.
Macrolide Antibacterial - CLARITHROMYCIN - ERYTHROMYCIN	CYP3A4 INHIBITOR (and SUBSTRATE) Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.
Macrolide Antibacterial - TROLEANDOMYCIN	CYP3A4 INHIBITOR Macrolide antibiotics have been reported to cause a significant decrease in corticosteroid clearance.

Drug Class or Type - DRUG or SUBSTANCE	Interaction or Effect
NSAIDs (nonsteroidal anti-inflammatory drugs) - high-dose ASPIRIN (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 aspirin, which can lead to decreased salicylate serum levels, which could lead to an increased risk of salicylate toxicity. 3) Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with concurrent use of corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.
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, 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.
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, Vaccinations).

Lidocaine

Drugs which inhibit the metabolism of lidocaine (e.g., cimetidine) may cause potentially toxic plasma concentrations when lidocaine is given repeatedly in high doses over long periods of time. Such interactions have no clinical relevance during short-term treatment with lidocaine in recommended doses. Lidocaine should be used with caution in patients receiving other local anesthetics or class Ib antiarrhythmic drugs, as the toxic effects are additive.

9.5 Drug-Food Interactions

Grapefruit juice is a CYP3A4 inhibitor. See 9.2 DRUG INTERACTIONS OVERVIEW, 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

10.2 Pharmacodynamics

Methylprednisolone

Methylprednisolone is an anti-inflammatory steroid. Estimates of the relative potencies of methylprednisolone and prednisolone range from 1.13 to 2.1 with an average of 1.5. While the effect of parenterally administered methylprednisolone acetate is prolonged, it has the same metabolic and anti-inflammatory actions as orally administered drug.

Cortisol and its synthetic analogues, such as methylprednisolone acetate, exert their action locally by preventing or suppressing the development of local heat, redness, swelling and tenderness by which inflammation is recognized at the gross level of observation. At the microscopic level, such compounds inhibit not only the early phenomena of the inflammatory process (edema, fibrin deposition, capillary dilatation, migration of phagocytes into the inflamed area and phagocytic activity), but also the later manifestations (capillary proliferation, fibroblast proliferation, deposition of collagen and still later cicatrization). These compounds inhibit inflammatory response whether the inciting agent is mechanical, chemical or immunological.

Lidocaine

Lidocaine is a potent local anesthetic agent widely used both for topical and injection anaesthesia. Lidocaine prevents both the generation and the conduction of the nerve impulse. Its main site of action is the cell membrane, and there is seemingly little action of physiological importance on the axoplasm. The exact mechanism whereby a local anesthetic influences the permeability of the membrane is unknown. As a general rule, small nerve fibers are more susceptible to the action of local anaesthetics than are large fibers.

10.3 Pharmacokinetics

No pharmacokinetic studies have been performed with the combination product of methylprednisolone and lidocaine, however, data are provided from pharmacokinetic studies performed with the individual product components methylprednisolone and lidocaine.

Absorption:

Methylprednisolone

One in-house study of eight volunteers determined the pharmacokinetics of a single 40 mg intramuscular dose of DEPO-MEDROL. The average of the individual peak plasma concentrations was 14.8 ± 8.6 ng/mL, the average of the individual peak times (t_{max}) was 7.25 ± 1.04 hours, and the average area under the curve (AUC) was 1354.2 ± 424.1 ng/mL x hrs (Day 1-21).

Lidocaine

Pharmacokinetics of lidocaine after synovial absorption following intra-articular bolus injection in patients with knee joint arthroscopy was studied with different maximum concentration (C_{max}) values reported. The C_{max} values are 2.18 µg/mL at 1 hour (serum) and 0.63 µg/mL at 0.5 hour (plasma) following administration of lidocaine doses of 7 mg/kg and 400 mg, respectively. Other reported serum Cmax values are 0.69 µg/mL at 5 minutes and 0.278 µg/mL at 2 hours following administration of lidocaine doses of 25 mL of 1% and 20 mL of 1.5%, respectively.

Pharmacokinetic data of lidocaine after intra-bursa and intra-cyst administrations for local effect are not available.

Distribution:

Methylprednisolone

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 1.4 L/kg. The plasma protein binding of methylprednisolone in humans is approximately 77%.

Lidocaine

The plasma protein binding of lidocaine is concentration-dependent, and binding decreases as concentration increases. At concentrations of 1 to 5 µg/mL, 60%-80% lidocaine is protein bound. Binding is also dependent on the plasma concentration of the α1-acid glycoprotein.

Lidocaine has a volume of distribution at steady state of 91 L.

Lidocaine readily crosses the placenta, and equilibrium of unbound drug concentration is rapidly reached. The degree of plasma protein binding in the fetus is less than in the mother, which results in lower total plasma concentrations in the fetus.

Metabolism:

Methylprednisolone

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. (For a list of drug interactions based on CYP3A4- mediated metabolism, 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 modulated by P-gp.

Lidocaine

Lidocaine is mainly metabolized by the liver. The main metabolites of lidocaine are monoethylglycine xylidide, glycinexylidide, 2,6-dimethylaniline, and 4-hydroxy-2,6-dimethylaniline. The lidocaine N-dealkylation to monoethylglycine xylidide is considered to be mediated by both CYP1A2 and CYP3A4. The metabolite 2,6-dimethylaniline is converted to 4-hydroxy-2,6-dimethylaniline by CYP2A6 and CYP2E1.

Elimination:

Methylprednisolone
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.

Lidocaine
The clearance of lidocaine in plasma following intravenous bolus administration is 9 to 10 mL/min/kg.

The elimination half-life of lidocaine following intravenous bolus injection is typically 1.5 to 2 hours.

The pharmacological actions of monoethylglycine xylidide and glycinexylidide are similar to but less potent than those of lidocaine. Monoethylglycine xylidide has a half-life of approximately 2.3 hours and glycinexylidide has a half-life of about 10 hours and may accumulate after long-term administration.

Only 3% of lidocaine is excreted unchanged by the kidneys. About 73% of lidocaine appears in the urine as 4-hydroxy-2,6-dimethylaniline metabolite.

Special Populations and Conditions

Methylprednisolone
No pharmacokinetic studies have been performed for methylprednisolone in special populations.

Lidocaine

- **Hepatic insufficiency**

  Following intravenous administration, the half-life of lidocaine has approximately 3-fold increase in patients with liver impairment. Pharmacokinetic data of lidocaine after intra-articular, intra-bursa and intra-cyst administrations for local effect are not available in hepatic impairment.

- **Renal insufficiency**
  Mild to moderate renal impairment (Clcr 30-60 mL/min) does not affect lidocaine pharmacokinetics but may increase the accumulation of glycinexylidide metabolite following intravenous administration. However, lidocaine clearance decreases about half and its half-life is approximately doubled with increased accumulation of glycinexylidide metabolite in patients with severe renal impairment (Clcr <30 mL/min).

The pharmacokinetics of lidocaine and its main metabolite of monoethylglycine xylidide are not altered significantly in haemodialysis patients who receive an intravenous dose of lidocaine.

11 STORAGE, STABILITY AND DISPOSAL

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

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

DEPO-MEDROL

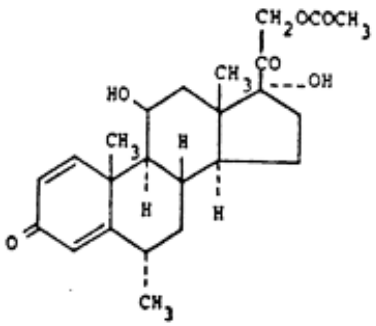
Drug Substance

Proper name: methylprednisolone acetate

Chemical name: (1) Pregna-1,4-diene-3,20-dione,21 (acetyloxy)-11,17-di-hydroxy-6- methyl, (6∞, 11β-;(2)11β,17,21- trihydroxy-6∞-methylpregna-1,4- diene 3,20-dione 21-acetate

Molecular formula and molecular mass: $C_{24}H_{32}O_6$, 416.51

Structural formula:



Physicochemical properties: Methylprednisolone acetate is the 6-methyl derivative of prednisolone. It is a white or practically white, odorless, crystalline powder which melts at about 215°C with some decomposition. It is soluble in dioxane, sparingly soluble in acetone, in alcohol, in chloroform, and in methanol, and slightly soluble in ether. It is practically insoluble in water.

Lidocaine

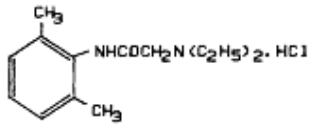
Drug Substance

Proper name: lidocaine hydrochloride

Chemical name: (1) Acetamide, 2-(diethylamino)-N-(2,6- dimethylphenyl)-, monohydrochloride, monohydrate;(2)2-(Diethylamino)-2',6'- acetoxylidide monohydrochloride monohydrate

Molecular formula and molecular mass: $C_{14}H_{23}ClN_2O,H_2O$, 234.34

Structural formula:



Physicochemical properties: Lidocaine hydrochloride is very soluble in water, alcohol; soluble in chloroform and insoluble in ether. The melting point is between 74°C to 79°C. Lidocaine has a pKa of 7.68 and a partition coefficient of 1.65 at pH 7.4.

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

General Toxicology:

Methylprednisolone

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.

Methylprednisolone plus Lidocaine

Acute Toxicity: The LD_{50} of lidocaine alone given intraperitoneally to albino mice was found to be 126 ± 4.6 mg/kg. Pretreatment of similar mice with as high as 0.5 mg/kg of methylprednisolone did not significantly alter the acute toxicity of lidocaine.

Repeat-dose toxicity: A six week parenteral toxicity study in rats to characterize the systemic subacute toxicity of a combination of methylprednisolone acetate and lidocaine was performed. No findings other than those attributable to the glucocorticoid content of the product were found, nor were there any histological changes found in these animals which could not be attributed to treatment with either methylprednisolone or lidocaine alone.

Local tolerance: Acute intra-articular irritation studies were performed in albino rabbits using 0.25 mL of each of methylprednisolone acetate and lidocaine hydrochloride, methylprednisolone acetate alone or saline. Four days after the injection of one of these materials, no significant abnormalities of synovial fluid, synovial membranes or articulating surfaces of these joints could be found.

Genotoxicity, Carcinogenicity and Reproductive and Developmental Toxicology studies were not conducted with the methylprednisolone and lidocaine combination.

Carcinogenicity:

Methylprednisolone

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.

Lidocaine

Long-term studies in animals have not been performed to evaluate the carcinogenic potential of lidocaine. In a carcinogenicity study in rats, the lidocaine metabolite 2,6-xylidine was administered in the diet to rats of both sexes before breeding, through pregnancy, and through the lactation period and to the male and female offspring through their lifetime at doses of 15, 50 and 150 mg/kg/day. Tumors in the nasal cavity, subcutaneous tumors and liver tumors were observed in the offspring at high doses. The clinical relevance of this finding is unknown.

Genotoxicity:

Methylprednisolone

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.

Lidocaine

Genotoxicity tests with lidocaine showed no evidence of mutagenic potential. A metabolite of lidocaine, 2,6-xylidine, showed weak genotoxic potential in vitro and in vivo.

Reproductive and Developmental Toxicology:

Methylprednisolone

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.

Lidocaine

A study was conducted on male and female rats administered orally 30 mg/kg body weight (bw) of lidocaine daily for 8 months. During that period, 3 matings were conducted and reproductive parameters were analyzed for each gestation, as well as offspring development up to weaning. No effects could be detected.

Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]DEPO-MEDROL WITH LIDOCAINE

methylprednisolone acetate and lidocaine hydrochloride injectable suspension

This patient medication information is written for the person who will be given **DEPO-MEDROL with Lidocaine**. 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 **DEPO-MEDROL with Lidocaine**, talk to a healthcare professional.

What DEPO-MEDROL with Lidocaine is used for:
DEPO-MEDROL with Lidocaine is used as an additional treatment in adults to treat acute or worsening inflammation of joints and tendons.

How DEPO-MEDROL with Lidocaine works:
- DEPO-MEDROL with Lidocaine contains methylprednisolone acetate and lidocaine hydrochloride.
- Methylprednisolone belongs to a group of medicines called corticosteroids hormones. It decreases the body's immune response to certain diseases and reduces inflammation.
- Lidocaine is a local anesthetic. It numbs the area of the body where it is used and reduces pain and inflammation.

The ingredients in DEPO-MEDROL with Lidocaine are:
Medicinal ingredients: methylprednisolone acetate and lidocaine hydrochloride.
Non-medicinal ingredients: benzyl alcohol, myristyl-gamma-picolinium chloride, polyethylene glycol 3350, sodium chloride and water for injection.

DEPO-MEDROL with Lidocaine comes in the following dosage forms:
Suspension: 40 mg/mL methylprednisolone acetate and 10 mg/mL lidocaine hydrochloride.

Do not use DEPO-MEDROL with Lidocaine if:
- you have allergies to:
    - methylprednisolone acetate;
    - any other steroid medicine;
    - lidocaine or any similar local anesthetics;
    - any of the other ingredients in DEPO-MEDROL with Lidocaine.
- you have any fungal infection or any untreated infection;
- you have a blood condition called idiopathic thrombocytopenic purpura if DEPO-MEDROL with Lidocaine is given to you through an injection into your muscle. This is a condition when you have a low blood platelet count;
- you have recently received a type of vaccine called a live or live-attenuated vaccine. Do not receive this vaccine during treatment with DEPO-MEDROL with Lidocaine;

- you have viral diseases including cowpox (vaccinia), chicken pox (varicella), and herpes simplex of the eye;
- you have unstable joints when DEPO-MEDROL with Lidocaine is injected into the joint.

DEPO-MEDROL with Lidocaine should not be injected into your muscles, your veins or your spine.

DEPO-MEDROL with Lidocaine should NOT be given to premature infants because it contains the preservative benzyl alcohol.

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

- have an infection (such as herpes simplex, chicken pox, tuberculosis, threadworm);
- have recently had or are about to have any vaccine;
- recently had any heart problems such as a heart attack, heart failure, heart rate or rhythm disorders or heart disease;
- have a condition where your body has lost fluid (such as blood or water, due to a recent trauma or severe dehydration)
- have bleeding or blood clotting problems;
- have brittle bone disease (osteoporosis);
- have high blood pressure;
- have water retention (edema);
- have epilepsy, seizures or other nervous system problems;
- have thyroid problems;
- have muscle pain or weakness (such as myasthenia gravis);
- have a tumour of the adrenal glands (pheochromocytoma)
- have certain eye diseases such as glaucoma, cataracts, herpes infection or any problems with the retina;
- have kidney disease;
- 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 blood potassium or calcium;
- have Cushing's disease (caused by an excess of cortisol hormone);
- have a weak immune response. Tell your healthcare professional if you suspect an infection has occurred, as corticosteroids (such as DEPO-MEDROL with Lidocaine) can make infections more likely and may mask their signs;
- have diabetes or high blood sugar;
- have a condition known as systemic sclerosis, in which your body makes too much of a protein called collagen
- had prior use of DEPO-MEDROL with Lidocaine.

Other warnings you should know about:

DEPO-MEDROL with Lidocaine can cause serious and potentially fatal reactions. Your healthcare professional will give you DEPO-MEDROL with Lidocaine in a medical setting that allows for immediate treatment if serious reactions occur.

DEPO-MEDROL with Lidocaine can cause serious side effects, including:

- **Kaposi's sarcoma** (skin cancer): Kaposi's sarcoma have been reported with corticosteroid therapy, such as DEPO-MEDROL with Lidocaine. Stopping treatment of DEPO-MEDROL with Lidocaine may result in signs of the cancer going away.
- **Pheochromocytoma** (tumour of the adrenal glands): This tumour has been reported with corticosteroid therapy, such as DEPO-MEDROL with Lidocaine. 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.

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

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 DEPO-MEDROL with Lidocaine 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.
- You should tell your healthcare professional if you are breast feeding or planning to breastfeed as small amounts of corticosteroid medicines (such as DEPO-MEDROL with Lidocaine) may get into breast milk.

Male fertility:
Taking DEPO-MEDROL with Lidocaine may affect male fertility.

Stopping treatment:
Talk to your healthcare professional before stopping DEPO-MEDROL with Lidocaine.

If you suddenly stop taking DEPO-MEDROL with Lidocaine, 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.

Immune system:

- If you are exposed to measles or chickenpox during treatment with DEPO-MEDROL with Lidocaine, contact your healthcare professional immediately. Serious or fatal side effects can

occur if you have not already had these infections or been immunized/vaccinated for these infections previously.
- DEPO-MEDROL with Lidocaine may:
  - hide symptoms of infection;
  - worsen symptoms of existing infections;
  - cause new infections due to lowered body resistance.

Skin:
- Dents/holes may appear at the site of injection.
- Tell your healthcare professional you are taking DEPO-MEDROL with Lidocaine since it can affect the results of skin tests.

Driving and using machines:
DEPO-MEDROL with Lidocaine may cause dizziness, vertigo, vision problems, fatigue, temporary mobility and movement problems. 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 DEPO-MEDROL with Lidocaine:

Medicines used to:
- treat glaucoma and epilepsy such as acetazolamide
- prevent or treat nausea and vomiting associated with cancer chemotherapy treatment such as aprepitant or fosaprepitant
- treat cancer such as cyclophosphamide
- treat Cushing's syndrome, breast or ovarian cancer (aromatase inhibitors) such as aminoglutethimide
- "thin" the blood or prevent blood clotting (anticoagulants) such as acenocoumarol, 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, rifampicin and rifabutin
- treat inflammation such as aspirin and non-steroidal anti-inflammatory medicines (also called NSAIDs) such as ibuprofen
- treat epilepsy such as barbiturates, carbamazepine, phenobarbital, phenytoin and primidone
- treat heartburn and acid indigestion such as cimetidine
- prevent organ rejection such as cyclosporine or tacrolimus
- treat heart problems or high blood pressure such as digoxin and diltiazem
- reduce extra fluid in the body (diuretics, also known as "water pills")
- hormone replacement therapy or hormonal oral contraceptives such as ethinyl estradiol and norethindrone
- treat HIV infections such as indinavir or ritonavir
- to block signals between nerves and muscles in surgery (neuromuscular blocking agents) such as pancuronium or vecuronium

- vaccines. Tell your healthcare professional if you have recently had, or are about to have any vaccinations.
- treat diabetes
- treat tuberculosis such as isoniazid
- treat high cholesterol such as cholestyramine
- treat pain and inflammation such as other local anesthetics
- treat heart rhythm disorders or irregular heartbeat

Do not eat grapefruit or drink grapefruit juice while taking DEPO-MEDROL with Lidocaine.

How DEPO-MEDROL with Lidocaine is given:

- DEPO-MEDROL with Lidocaine will be given to you by your healthcare professional. It will be give as an injection into the joint or the tendon (intra-articular, intrasynovial, intrabursal or periarticular).
- Your healthcare professional will decide on the site of injection, as well as how much of the medicine and how many injections you will receive.
- Your healthcare professional will prescribe the lowest possible dose for the minimum period of time.

Usual dose:

The dose you will receive depends on:

- the condition you are being treated for;
- the severity of your condition;
- your response to treatment; and
- your exposure to physical stress like infection, surgery or injury.

Overdose:

If you think you, or a person you are caring for, have been given too much DEPO-MEDROL with Lidocaine, 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.

Possible side effects from using DEPO-MEDROL with Lidocaine:

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

Side effects of DEPO-MEDROL with Lidocaine may include:

- facial blushing;
- skin problems such as reddish spots containing blood that appear in your skin, red or tender bumps on your skin, acne, rash, redness, itchy skin, dry and scaly skin, increased sweating, lightening or darkening of an area of skin, abscess (pocket of pus), thinning of hair, and stretch marks;
- abnormal hair growth;

- gastrointestinal problems such as nausea, vomiting, diarrhea, altered sense of taste, abdominal pain, bloating, abnormal appetite, and indigestion;
- loss of muscle mass and muscle weakness;
- muscle cramps and spasms;
- nervous system problems (including nerve inflammation and damage) such as headache, pain, tenderness, impaired sensation, strength and reflexes, sensation of heat, cold, numbness, sensation of tingling, tickling, prickling, or burning of a person's skin, vertigo, dizziness, forgetfulness, twitching, drowsiness, ringing in ears, and tremors;
- abnormal behaviour such as anxiety, nervousness, confusion, euphoria (intense feelings of well-being, elation, happiness, excitement and joy), personality changes, irritability, mood swings/emotional instability, mania (feeling high), drug dependence, and trouble sleeping;
- irregular periods;
- memory loss.

DEPO-MEDROL with Lidocaine can cause abnormal blood test results. Your healthcare professional will decide when to perform the tests and interpret the results.

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			
Abnormal (high or low) blood pressure: headaches, dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up), racing pulse, or heart palpitations.		**√**	
Allergic reactions: rash, hives, swelling of the face, lips, tongue, or throat, itching, difficulty swallowing, difficulty breathing, drop in blood pressure, dizziness, fainting, wheezing, nausea, or vomiting.			**√**
Arrhythmia (abnormal heart rhythms): fast, slow, pounding, or irregular heartbeat.		**√**	
Aseptic necrosis (tissue death): progressive or persistent pain, limited range of motion in a joint or limb, joint pain, swelling, tenderness, weakness, or joint stiffness.			**√**

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Bladder problems: not reaching the bathroom in time, or having to pee multiple times during the night.		√	
Bleeding, poor wound healing	√		
Blood clots: swelling, pain or tenderness, usually in the arm or leg, tingling, numbness, pale skin, muscle pain, or muscle spasms.			√
Breathing problems or breathing stops			√
Cardiac arrest (heart stops beating suddenly): fatigue, loss of consciousness, dizziness, nausea, chest pain, shortness of breath, or pounding heart beat.			√
Charcot joint disease (foot and ankle issues due to nerve-related problems): joint swelling, foot pain, or heat or redness over the joint.		√	
Coma (deep loss of consciousness)			√
Cushingoid syndrome (increased cortisol levels): weight gain, rounded "moon" face, thin and fragile skin, easy bruising, fatigue, headache, or weak muscles.	√		
Depression (sad mood that won't go away): difficulty sleeping, sleeping too much, changes in appetite or weight, feelings of worthlessness, guilt, regret, helplessness or hopelessness, withdrawal from social situations, family, gatherings and activities with friends, or reduced libido (sex drive).	√		
Diabetes (high blood sugar) **or decreased sugar tolerance:** increased thirst, increased urination, increased appetite, or have blurry vision.		√	
Edema (swelling or fluid retention): unusual swelling of the arms, hands, legs, feet and ankles, face or airway passages.		√	
Epidural lipomatosis (fat build-up around the spine): back pain,		√	

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
weakness, loss of sensation, or reflexes that are too slow or too fast.			
Eye problems including cataracts: retina pulled away from normal position, double vision, blurry vision, eye pain, increased pressure in the eyes, blindness in one or both eyes, or bulging eyes.			√
Flare up of a previous tuberculosis: cough that does not go away, fever, loss of weight, coughing blood, or pain in the chest.			√
Fractures (broken bones): pain, bruising, swelling over the broken bone, or sudden pain that is worse when walking or standing.		√	
Heart attack: pressure or squeezing pain between the shoulder blades, in the chest, jaw, left arm or upper abdomen, shortness of breath, dizziness, fatigue, light-headedness, clammy skin, sweating, indigestion, anxiety, feeling faint, or irregular heartbeat.			√
Heart failure: dizziness, fatigue, weakness, shortness of breath, fainting, irregular heart rate, or fast pounding heart beat.			√
Increased intracranial pressure (pressure within the skull with swelling)			√
Infections: symptoms of an existing infection worsen, reactivation of a dormant infection, persistent fever, cough, feeling unwell, sore throat, painful urination, eye pain, eye discharge.			√
Injection site infections/reactions: blistering, pain, skin changes or depressions, tenderness, warmth in the area around the injection, or inflammation.	√		
Kaposi's sarcoma (cancer that causes tumours in the blood vessels and skin):			√

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
slightly elevated purple, pink, brown, black, blue, or red blotches or bumps anywhere on the skin or in the mouth and/or throat.			
Liver problems including liver injury and hepatitis (inflammation of the liver): yellowing of the skin or whites of eyes, urine turns dark, nausea, vomiting, lower stomach pain, fatigue, fever, light-coloured stool, or unusual tiredness.		√	
Meningitis (infection of membranes that surround brain and spinal cord): fever, nausea, vomiting, headache, stiff neck, extreme sensitivity to bright light, confusion, seizures, sleepiness, difficulty waking, no appetite or thirst, or skin rash.			√
Metabolic acidosis (high level of acid in the blood): fatigue, abdominal pain, confusion, dizziness, loss of appetite, headache, nausea, vomiting, weakness, or increased heart rate.			√
Osteoporosis (thin, fragile bones): broken bones, joint pain, bone pain, or back pain that gets worse when standing or walking.		√	
Pancreatitis or esophagitis (inflammation of the pancreas or esophagus): abdominal pain, nausea, vomiting, hard or painful swallowing, heartburn, fever, rapid heart beat, or tenderness when touching the abdomen.			√
Perforation of the bowel (a hole in the intestines): abdominal pain, feeling bloated, nausea, vomiting, chills, or fever.			√
Peritonitis (inflammation of the stomach lining): severe abdominal pain that is worse when you move, feeling sick to your stomach or throwing up, fever, or swollen belly.			√

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Pheochromocytoma (adrenal gland tumour): high blood pressure, sweating, rapid heartbeat, pale appearance, or headache.			√
Rhabdomyolysis (breakdown of damaged muscle): muscle pain that you cannot explain, muscle tenderness or weakness, dark urine.		√	
Schizophrenia or worsening of schizophrenia: hallucinations (feeling, seeing, or hearing things which do not exist), delusions, disorganized or incoherent thinking, feeling paranoid, suspicious, or scared.		√	
Seizures (fits): loss of consciousness with uncontrollable shaking.			√
Skin cancer (unusual skin growth): blotches of skin that may be red, purple, brown or black and may be raised.			√
Stomach ulcers (burst or bleeding ulcers): stomach pain, bleeding from the rectum, black or bloodstained stools, vomiting blood, loss of appetite, or weight loss.			√
Suicidal thoughts or actions			√
Suppression of hypothalamic pituitary-adrenal axis: (body's responses to natural stress do not work properly): fatigue, depression and anxiety, difficulty sleeping, weakness, or loss of muscle mass.		√	
Tendon rupture (particularly of the Achilles tendon): a snap or popping sound with severe pain at the site of the break, bruising, or inability to use the arm or leg with the break.			√
Thinning of skin, fragile skin	√		
Tumour lysis syndrome (sudden, rapid death of cancer cells due to the treatment): life-threatening kidney failure and heart problems, nausea, shortness of breath, irregular			√

Frequency/Side Effect/Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
heartbeat, heart rhythm disturbances, lack of urination, clouding of urine, muscle spasms, muscle twitching, tiredness, joint pain, severe muscle weakness, or seizures.			

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 between 15°C and 30°C. Protect from freezing. Keep out of reach and sight of children.

If you want more information about DEPO-MEDROL with Lidocaine:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database 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.

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