

- Glucocorticoids should be used cautiously in patients with ocular herpes simplex for fear of corneal perforation
- Increased intraocular pressure
- Exophthalmos
- **Metabolic**
 - Negative nitrogen balance due to protein catabolism
- **Immune system**
 - Masking of infections
 - Latent infections becoming active
 - Opportunistic infections
 - Hypersensitivity reactions including anaphylaxis
 - May suppress reactions to skin tests
- ***In situ* administration**
 - In situ* administration can cause dermal and subdermal atrophy. While crystals of adrenal steroids in the dermis suppress inflammatory reactions, their presence may cause disintegration of the cellular elements and physiochemical 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 (see SPECIAL PRECAUTIONS). Regeneration is usually complete within a few months or after all crystals of the adrenal steroid have been absorbed.
- **The following additional reactions are related to parenteral corticosteroid therapy**
 - Rare instances of blindness associated with intralesional therapy around the face and head
 - Anaphylactic or allergic reactions
 - Hyperpigmentation or hypopigmentation
 - Subcutaneous and cutaneous atrophy
 - Sterile abscess
 - Postinjection flare, following intrasynovial use
 - Charcot-like arthropathy
 - Injection site infections following non-sterile technique

B. Adverse reactions related to lidocaine hydrochloride

- **Central nervous system**
 - Lightheadedness or dizziness
 - Nervousness
 - Apprehension
 - Euphoria
 - Confusion
 - Drowsiness
 - Tinnitus
 - Blurred or double vision
 - Vomiting
 - Sensation of heat, cold, numbness
 - Twitching
 - Tremors
 - Convulsions
 - Loss of consciousness
 - Respiratory depression
 - Respiratory arrest
- **Cardiovascular system**
 - Bradycardia
 - Hypotension
 - Cardiovascular collapse
 - Cardiac arrest
- **Allergic reactions**
 - Cutaneous lesions
 - Urticaria
 - Edema
 - Anaphylactic reactions

C. Adverse reactions reported with some non-recommended routes of administration

- **Intrathecal/epidural**
 - Arachnoiditis, meningitis, paraparesis/paraplegia, sensory disturbances, bowel/bladder dysfunction, headache, seizures
- **Intranasal**
 - Temporary/permanent visual impairment including blindness, allergic reactions, rhinitis
- **Ophthalmic**
 - Temporary/permanent visual impairment including blindness, increased intraocular pressure, ocular and periocular inflammation including allergic reactions, infection, residue or slough at injection site
- **Miscellaneous injection sites (scalp, tonsillar fauces, sphenopalantine ganglion)**
 - Blindness

SPECIAL PRECAUTIONS

Special risk groups

Patients belonging to the following special risk groups should be under strict medical surveillance and should be treated during an as short as possible period:

- **Children:** 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.
- **Diabetics:** manifestations of latent diabetes mellitus or increased requirements for insulin or oral hypoglycemic agents.
- **Hypertensive patients:** aggravation of arterial hypertension.
- **Patients with psychiatric antecedents:** existing emotional instability or psychotic tendencies may be aggravated by glucocorticoids.
- Since 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.

Intra-articular use

Following intra-articular corticosteroid 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. 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.

If a local anesthetic is used prior to injection of DEPO-MEDROL™ with Lidocaine, the anesthetic package insert should be read carefully and all the precautions observed.

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 intrasynovial injection should include precautions against injection or leakage into the dermis.

Appropriate measures must be taken to avoid intravascular injections.

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

Corticosteroids may mask some signs of infection and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used. Do not use intrasynovial, intrabursal or intratendinous administration for local effect in the presence of acute infection.

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.

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

Allergic skin reactions have been reported apparently related to the excipients. Rarely has skin testing demonstrated a reaction to methylprednisolone acetate, *per se*.

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

Caution must also be used in diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis and myasthenia gravis, when steroids are used as direct or adjunctive therapy.

No evidence exists showing that corticosteroids are carcinogenic, mutagenic or impair fertility.

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

Benzyl alcohol has been reported to be associated with a fatal "gasping syndrome" in premature infants.

The following additional precautions apply for parenteral corticosteroids

- intrasynovial injection of a corticosteroid may produce systemic as well as local effects;
- 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;
- corticosteroids should not be injected into unstable joints. Sterile technique is necessary to prevent infections or contamination.

Multidose use

Multidose use of DEPO-MEDROL™ with Lidocaine 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, should be observed if intrasynovial use is intended. There is some evidence that benzalkonium chloride is not an adequate antiseptic for sterilizing DEPO-MEDROL™ with Lidocaine multidose vials. A povidone-iodine solution or a similar product is recommended to cleanse the vial top prior to aspiration of contents.

Multidose use of DEPO-MEDROL™ with Lidocaine vials is not recommended for intrasynovial injection.

INCOMPATIBILITIES

Because of possible physical incompatibilities DEPO-MEDROL™ with Lidocaine should not be diluted or mixed with other solutions.

PREGNANCY AND LACTATION

Some animal studies have shown that corticosteroids, when administered to the mother at high doses, may cause fetal malformations.

Adequate human reproduction studies have not been done with corticosteroids or lidocaine. Therefore the use of this drug in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential hazards to the mother and embryo or fetus. Corticosteroids should be used in pregnancy only if clearly needed. Corticosteroids and lidocaine diffuse across the placenta.

Newborn infants born of mothers who have received substantial doses of glucocorticosteroids during pregnancy, should be carefully observed and evaluated for signs of adrenal insufficiency. Corticosteroids are excreted in breast milk. It is not known whether lidocaine is excreted in human breast milk. The use of local anesthetics such as lidocaine during labor and delivery may be associated with adverse effects on mother and fetus. There are no known effects of corticosteroids on labor and delivery.

INTERACTIONS

Undesired interactions

- Corticosteroids may increase renal clearance of salicylates.
- This could lead to a decrease in salicylate serum levels or increase the risk of salicylate toxicity when corticoids are withdrawn.
- Drugs such as troleandomycin and ketoconazole may inhibit the metabolism of corticoids.
- Therefore the dose of corticoid should be titrated to avoid overdosage.
- Concurrent administration of barbiturates, phenylbutazone, phenytoin or rifampicin may enhance the metabolism and reduce the effects of corticoids.
- There are reports of enhanced as well as diminished effects of anticoagulant when given concurrently with corticosteroids. Therefore coagulation indices should be monitored to maintain the desired anticoagulant effect.
- 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 on high doses, because of possible hazards of neurological complications and lack of antibody response.
- Glucocorticoids may increase the requirements for insulin or oral hypoglycemic agents in diabetics.
- Combination of glucocorticoids with thiazid-diuretics increases the risk of glucose intolerance.
- Concurrent use of ulcerogenic drugs (e.g. salicylates, NSA1 drugs) may increase the risk of gastrointestinal ulceration.
- Aspirin should be used cautiously in conjunction with corticosteroids in patients suffering from hypoprothrombinemia.
- Convulsions have been reported with concurrent use of methylprednisolone and cyclosporin.
- Mutual inhibition of metabolism occurs with concurrent use of cyclosporin and methylprednisolone; therefore it is possible that convulsions and other adverse events associated with the individual use of either drug may be more apt to occur.
- No additional benefit derives from the IM administration of DEPO-MEDROL™ with Lidocaine.
- Where parenteral corticosteroid therapy for sustained systemic effect is desired, plain DEPO-MEDROL™ should be used.

OVERDOSAGE

There is no clinical syndrome of acute overdosage with methylprednisolone acetate. Repeated frequent doses (daily or several times per week) over a protracted period may result in a Cushingoid state and other complications of chronic steroid therapy. Overdosage of lidocaine hydrochloride may produce convulsions, bradycardia, hypotension and respiratory arrest.

STORAGE

Store at controlled room temperature (20°-25°C).
The expiry date (month/year) is mentioned on the package after "EXP:." (EXP. = expiry date).

Dispensing in the country of origin: On medical prescription only.

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