יולי 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

חברת מרק שארפ ודוהם (ישראל-1996) בע"מ (MSD ישראל) מבקשת ליידע על הוספת עלון חדש לצרכן ועדכון העלון לרופא ושל התכשיר:

Diprospan Injection

ההתוויה הרשומה לתכשיר בישראל:

Produces anti-inflammatory, anti-rheumatic and anti-allergic action and is indicated for systemic and local therapy of acute and chronic corticosteroid-responsive disorders.

בהודעה זו מצוינים ומוארים ברקע צהוב רק שינויים מהותיים בעלון לרופא. בעלון לרופא בוצעו עדכונים נוספים שאינם נכללים בהודעה זו.
למידע מלא ולהוראות מתן מפורטות יש לעיין בעלון לרופא ובעלון החדש לצרכן המאושרים על ידי משרד הבריאות.
העלון לרופא והעלון לצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלם מודפסים על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.

Diprospan Injection מופץ ע"י חברת נובולוג בע"מ.

בברכה,

עלמה שימן
רוקחת ממונה
MSD ישראל

<u>עדכונים מהותיים בעלון לרופא</u>:

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4.4 Special warnings and precautions for use

Diprospan cannot be used for intravenous or subcutaneous administration.
Serious neurologic events, some resulting in death, have been reported with epidural injection of corticosteroids. Specific events reported include, but are not limited to, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, and stroke. These serious neurologic events have been reported with and without use of fluoroscopy. The safety and effectiveness of epidural administration of corticosteroids have not been established, and corticosteroids are not approved for this use.
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Eliminating or abruptly reducing administration during chronic use (at very high doses, after only a short time), or when an increase in corticosteroid requirements (following stress: infection, trauma, surgery) may precipitate adrenal insufficiency. It is therefore necessary to reduce the dose gradually. In stressful situations, it is sometimes necessary to administer corticosteroids again or to increase the dose.

The dose reduction should be achieved under close medical supervision and it is sometimes necessary to monitor the patient for up to 1 year after cessation of prolonged or high-dose treatment.

The symptoms of adrenal insufficiency are: discomfort, muscle weakness, mental disorders, lethargy, muscle and bone pain, desquamation of the skin, dyspnea, anorexia, nausea, vomiting, fever, hypoglycemia, hypotension, dehydration, and even death following abrupt discontinuation of the treatment. Treatment of adrenal insufficiency consists in administering corticosteroids, mineralocorticoids, water, sodium chloride and glucose.

Rapid intravenous injection of high doses of corticosteroids can cause cardiovascular collapse; this is why the injection has to be administered over a 10-minute period.

Rare instances of anaphylactoid/anaphylactic reactions with a possibility of shock have occurred in patients receiving parenteral corticosteroid therapy. Appropriate precautionary measures should be taken with patients who have a history of allergic reactions to corticosteroids.

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Specific groups at risk

In diabetics, betamethasone may be used only for a short period and only under close medical supervision, given its glucocorticoid properties (transformation of glucose into proteins).

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The use of Diprospan in ocular herpes simplex should be avoided, given the possibility of perforation of the cornea.

Caution is advised in case of:

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- acute psychoses;
- viral and bacterial infections;
- Cushing's syndrome;
- diabetes;
- heart failure;
- difficult-to-treat epilepsy;
- thromboembolism or thrombophlebitis tendencies;

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Corticosteroids may mask certain signs of infection or make the detection of infection more difficult. Due to a decrease in resistance, new infections can occur during use.

Prolonged use can lead to a posterior subcapsular cataract (especially in children) or to glaucoma, which can damage the optic nerves and may exacerbate secondary ocular infections due to fungi or viruses. In case of prolonged treatment (over 6 weeks), it is necessary to undergo regular ophthalmological examinations.

PATIENTS ON CORTICOTHERAPY CANNOT RECEIVE THE FOLLOWING TREATMENTS:

- SMALLPOX VACCINATION;
- OTHER METHODS OF IMMUNIZATION (ESPECIALLY AT HIGH DOSE) BECAUSE OF THE RISK OF NEUROLOGICAL COMPLICATIONS AND INADEQUATE ANTIBODY RESPONSE.

However, patients receiving corticosteroids as replacement therapy may be immunized (e.g., Addison's disease).

Patients, especially children, receiving immunosuppressive doses of corticosteroids should be warned to avoid exposure to chickenpox or measles.

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If corticosteroids are indicated in patients with latent tuberculosis or reacting to tuberculin, strict monitoring is necessary because disease reactivation can occur. During prolonged corticosteroid therapy, patients should receive chemoprophylaxis.

If using rifampicin in a chemoprophylaxis program, its enhancing effect on the metabolic hepatic clearance of corticosteroids must be remembered; it may be necessary to adjust the dose of the corticosteroid.

As corticosteroids can disturb the growth of infants and children and inhibit the endogenous production of corticosteroids, it is important to monitor their growth and development carefully in the event of prolonged treatment.

Diprospan contains benzyl alcohol, which may cause toxic reactions and anaphylactoid reactions in infants and children up to 3 years. Do not administer to premature babies or newborns at term.

Diprospan contains methylparaben (methyl parahydroxybenzoate) and propylparaben (propyl parahydroxybenzoate)
which may cause allergic reactions (possibly delayed) and exceptionally, bronchospasm.

Visual disturbance

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

4.5 Interaction with other medicinal products and other forms of interaction

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The combination with diuretics such as thiazides may increase the risk of glucose intolerance.

Patients simultaneously receiving a corticosteroid and an estrogen must be monitored for excessive corticosteroid effects.
The simultaneous use of corticosteroids and coumarin-type anticoagulants may increase or decrease the anticoagulant effects, which may require a dosage adjustment. In patients taking anticoagulants in combination with glucocorticoids, the possibility of gastrointestinal ulceration induced by corticosteroids, or increased risk of internal bleeding, must be considered.

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Corticosteroids may decrease the concentration of salicylates in the blood. When lowering the dose of corticosteroids or discontinuing treatment, patients should be checked for the presence of salicylism. The combination of glucocorticoids with salicylates may increase the frequency and severity of a gastrointestinal ulcer

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Co-treatment with CYP3A inhibitors, including cobicistat-containing products, is expected to increase the risk of systemic side-effects. The combination should be avoided unless the benefit outweighs the increased risk of systemic corticosteroid side-effects, in which case patients should be monitored for systemic corticosteroid side-effects.

4.7 Effects on ability to drive and use machines

Caution should be exercised concerning the central effects when administered at high doses (euphoria, insomnia) and with regard to the vision disorders that can occur with prolonged treatment.

4.8 Undesirable effects

Fluid and electrolyte disorders:
Sodium retention - Potassium loss - Hypokalemic alkalosis - Fluid retention - Congestive heart failure in susceptible patients - Hypertension;

Musculoskeletal disorders:

Muscular weakness - Loss of muscle mass - Aggravation of myasthenic symptoms in myasthenia gravis
- Osteoporosis with sometimes severe bone pain and spontaneous fractures (vertebral compression fractures) - Aseptic bone necrosis (femoral and humeral head) - Tendon rupture - Steroid myopathy - Pathological fractures - Joint instability;

Skin disorders:
Skin atrophy - Delayed healing - Thin and fragile skin - Petechiae - Bruising - Allergic dermatitis - Angioneurotic edema - Facial erythema - Increased sweating - Urticaria;

Digestive disorders:
Gastric ulcer with bleeding and possible perforation - Pancreatitis - Abdominal distension - Intestinal perforation - Ulcerative esophagitis - Nausea - Vomiting;

Neurological disorders:
Seizures - Vertigo - Headache - Migraines - Increased intracranial pressure (pseudotumor cerebri);

Psychiatric disorders:
Euphoria - Mood Disorders - Personality changes and severe depression - Hyperirritability - Insomnia - Psychotic reactions especially in patients with a psychiatric history - Depression;

Ophthalmic disorders:
Increased intraocular pressure (pseudotumor cerebri: see neurological); Glaucoma - Posterior subcapsular cataract - Exophthalmos - Vision blurred (see also section 4.4).

Endocrine disorders:
Clinical symptoms of Cushing's syndrome - Menstrual disorders - Increased need for insulin or oral antidiabetic agents in diabetics - Inhibition of fetal child growth - Reduced tolerance to carbohydrates - Signs of latent diabetes mellitus - Secondary inhibition of the pituitary and the adrenal cortex, especially harmful in case of stress (such as trauma, surgery and disease);

Metabolic disorders:
Negative nitrogen balance with protein degradation - Lipomatosis - Weight gain;

Immunity disorders:
Corticosteroids can cause an inhibition of skin tests, mask the symptoms of infection and active a latent infection. They can also decrease resistance to infection, especially when due to mycobacteria, tuberculosis, Candida albicans or viruses.

Other:
Anaphylactic or allergic reactions, hypotensive reactions or reactions related to shock.

THE FOLLOWING ADVERSE REACTIONS MAY BE OBSERVED DURING PARENTERAL CORTICOTHERAPY:
Rare cases of blindness associated with intralesional treatment of the face and head - Hyperpigmentation or hypopigmentation - Subcutaneous and cutaneous atrophy - Sterile abscess - Post-injection exacerbation (after intra-articular use) - Charcot arthropathy.

After repeated intra-articular administration, joint damage may occur. There is a risk of contamination.

References:
DIPROSPAN INJECTION-Heb-PIL-06-2021
DIPROSPAN-INJECTION-SPC-06-2021