פייזר פי אף אי פרמצבטיקה ישראל בע"מ
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יוני 2020

רופא/ה, רוקח/ת נכבד/ה,

חב' פייזר פי אף אי מבקשת להודיע על עדכון בעלונים לרופא ולצרכן של התכשיר **DEPO MEDROL+LIDOCAINE**

המרכיבים הפעילים בתכשיר:

METHYLPREDNISOLONE ACETATE 40 mg/ mL
LIDOCAINE (AS HYDROCHLORIDE) 10 MG/ML

התוויה רשומה:

Indicated for:
Depo-Medrol with Lidocaine is indicated as adjunctive therapy for short-term 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.

להלן העדכונים העיקריים בעלון לרופא:

2. Qualitative and Quantitative Composition

Methylprednisolone acetate with lidocaine (as hydrochloride): (40 mg, 10 mg)/ml

4.1 Therapeutic Indications

Depo-Medrol may be used by any of the following routes: Intra-articular, Intrabursal, Intrasynovial Cyst and Tendon Sheath injection.
It must not be used by the intrathecal or intravenous routes (see section 4.3 Contraindications) The following routes of administration are not recommended; epidural, intranasal, intraocular and any other unapproved route of administration (see section 4.4 Special Warnings and Precautions for Use)

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4.4 Special warnings and precautions for use

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Ocular Effects

Visual disturbance may be reported with systemic and topical 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 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. Central serous chorioretinopathy, may lead to retinal detachment.

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Gastrointestinal Effects

High doses of corticosteroids may produce acute pancreatitis.
There is no universal agreement on whether corticosteroids per se are responsible for peptic ulcers encountered during therapy; however, 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.

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Hepatobiliary Effects

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

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Renal and Urinary Disorders

Caution is required in patients with systemic sclerosis because an increased incidence of scleroderma renal crisis has been observed with corticosteroids, including methylprednisolone. Blood pressure and renal function (s-creatinine) should therefore be routinely checked. When renal crisis is suspected, blood pressure should be carefully controlled.

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

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Other

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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 (see section 4.5).

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4.5 Interaction with other medicinal products and other forms of interaction

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9. Antivirals - HIV protease inhibitors: Indinavir, ritonavir and pharmacokinetic enhancers (cobicistat) (CYP3A4 inhibitors and substrates) may increase plasma concentrations of corticosteroids. Corticosteroids may induce the metabolism of HIV-protease inhibitors resulting in reduced plasma concentrations.

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4.6 Fertility, pregnancy and lactation

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Pregnancy

Methylprednisolone

The ability of corticosteroids to cross the placenta varies between individual drugs, however, methylprednisolone does cross the placenta. One retrospective study found an increased incidence of low birth weights in infants born of mothers receiving corticosteroids. In humans, the risk of low birth weight appears to be dose related and may be minimized by administering lower corticosteroid doses. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and affects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate in man, however, when administered for long periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. Although neonatal adrenal insufficiency appears to be rare in infants who were exposed in utero to corticosteroids, those exposed to substantial doses of corticosteroids must be carefully observed and evaluated for signs of adrenal insufficiency. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential, however, patients with normal pregnancies may be treated as though they were in the non-gravid state. However, corticosteroids do not appear to cause congenital anomalies when given to pregnant women.

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Methylprednisolone acetate with lidocaine

Since adequate human reproductive studies have not been done with methylprednisolone acetate with lidocaine, this medicinal product should be used during pregnancy only after a careful assessment of the benefit-risk ratio to the mother and fetus.

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Breast-feeding

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

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4.8 Undesirable effects

MedDRA System Organ Class	Frequency	Undesirable Effects

MedDRA System Organ Class	Frequency	Undesirable Effects
Infections and infestations	***Not Known***	Opportunistic infection[e]; Infection[e] (including increased susceptibility and severity of infections with suppression of clinical symptoms and signs), Injection site infection; Peritonitis[c,e]; Recurrence of dormant tuberculosis
Blood and lymphatic system disorders	***Not Known***	Leukocytosis[e]
Immune system disorders	***Not Known***	Drug hypersensitivity, Anaphylactic reaction, Anaphylactoid reaction[e]
Endocrine disorders	***Not Known***	Cushingoid[e] Hypopituitarism [e]; Withdrawal symptoms - Too rapid a reduction of corticosteroid dosage following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. However, this is more applicable to corticosteroids with an indication where continuous therapy is given (see section 4.4). A 'withdrawal syndrome' [e]; may also occur including, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight.
Metabolism and nutrition disorders	***Not Known***	Metabolic acidosis[e], Sodium retention[e]; Fluid retention[e], Alkalosis hypokalaemic[e]; Dyslipidaemia[e], Glucose tolerance impaired[e]; Increased requirements for insulin (or oral hypoglycemic agents in diabetics) [a,e], Lipomatosis[e], Increased appetite (which may result in Weight increased)
Psychiatric disorders	***Not Known***	Affective disorder[e] (including Depressed mood[e], Euphoric mood, Affect lability[e], psychological dependence [not a MedDRA PT[e]], Suicidal ideation[e]), Psychotic disorder[e] (including Mania[e], Delusion[e], Hallucination[e], and Schizophrenia[e] [aggravation of]); Confusional state; Mental disorder[e]; Anxiety; Personality change[e]; Mood swings[e]; Abnormal behaviour[e]; Insomnia[e], Irritability[e,], Nervousness[d]
Nervous system disorders	***Not Known***	Epidural lipomatosis[e] , Intracranial pressure increased (with Papilloedema [Benign intracranial hypertension] [e]); Loss of consciousness[d]; Seizure; Amnesia[e]; Cognitive disorder[e]; Tremor[d], Somnolence[d], Hypoaesthesia[d], Dizziness; Headache[e];
Eye disorders	***Not Known***	Exophthalmos[e]; Vision blurred[d] (See also section 4.4); chorioretinopathy [e]; Cataract[e]; Glaucoma[e]; Diplopia[d] ; Rare instances of blindness associated with intralesional therapy around the face and head [not a MedDRA PT]; Corneal or scleral thinning; Exacerbation of ophthalmic viral or fungal disease
Ear and labyrinth disorders	***Not Known***	Vertigo[e], Tinnitus[d]
Cardiac disorders	***Not Known***	Cardiac arrest[d] , Cardiac failure congestive (in susceptible patients) [e] , Bradycardia[d]
Vascular disorders	***Not Known***	Circulatory collapse[d]; Hypertension[e]; Hypotension; Embolism arterial, Thrombotic events[e]
Respiratory, thoracic and mediastinal disorders	***Not Known***	Respiratory arrest[d], Respiratory depression[d], Pulmonary embolism[e], Hiccups[e]
Gastrointestinal disorders	***Not Known***	Peptic ulcer[b,e] (with possible Peptic ulcer perforation and Peptic ulcer haemorrhage) Gastric haemorrhage[e]; Intestinal perforation[e]; Pancreatitis[e]; Oesophagitis ulcerative[e]; Oesophagitis; Oesophageal candidiasis; Abdominal pain[e]; Abdominal distension[e]; Diarrhoea[e]; Dyspepsia[e]; Nausea[e], Vomiting[d]
Hepatobiliary disorders	***Not Known***	Hepatitis, Increase of liver enzymes

MedDRA System Organ Class	Frequency	Undesirable Effects
Skin and subcutaneous tissue disorders	***Not Known***	Angioedema[e]; Petechiae; Ecchymosis[e]; Skin atrophy[e]; Skin striae[e]; Skin hyperpigmentation[e]; Skin hypopigmentation[e]; Hirsutism[e]; Rash[e]; Erythema[e]; Pruritus[e]; Urticaria; Acne[e]; Hyperhidrosis[e] Skin lesion[d]
Musculoskeletal and connective tissue disorders	***Not Known***	Muscular weakness[e],Osteonecrosis[e]; Osteoporosis[e]; Pathological fracture[e]; Muscle atrophy[e]; Myopathy[e]; Neuropathic arthropathy[e]; Growth retardation[e]; Arthralgia; Myalgia[e]; Muscle twitching[d]
Reproductive system and breast disorders	***Not Known***	Menstruation irregular
General disorders and administration site conditions	***Not Known***	Impaired healing[e]; Oedema peripheral[e]; Injection site reaction[e]; Abscess sterile[e]; Fatigue[e]; Malaise[e]; Feeling cold[d], Feeling hot[d]
Investigations	***Not Known***	Intraocular pressure increased[e], Alanine aminotransferase increased[e]; Aspartate aminotransferase increased; Blood alkaline phosphatase increased[e]; Blood potassium decreased[e] ; Carbohydrate tolerance decreased[e]; Urine calcium increased[e]; suppression of reactions to skin tests [not a MedDRA PT]; Blood urea increased[e]; Nitrogen balance negative (due to protein catabolism); Suppression of reactions to skin tests[a,e]
Injury, poisoning and procedural complications	***Not Known***	Tendon rupture[e] (particularly of the Achilles tendon); Spinal compression fracture[e]. Systemic corticosteroids are not indicated for, and therefore should not be used to treat, traumatic brain injury.

[a] Not a MedDRA Preferred term.
[b] Peptic ulcer perforation and Peptic ulcer haemorrhage.
[c] Peritonitis may be the primary presenting sign or symptom of a gastrointestinal disorder such as perforation, obstruction or pancreatitis (see section 4.4).
[d] Reported for lidocaine only.
[e] Reported for methylprednisolone acetate only.

CERTAIN SIDE EFFECTS REPORTED WITH SOME NON RECOMMENDED ROUTES OF ADMINISTRATION:
Intrathecal/Epidural: Usual systemic corticoid adverse reactions, headache, meningismus, meningitis, paraparesis/paraplegia, spinal fluid abnormalities, nausea, vomiting, sweating, arachnoiditis, functional gastrointestinal disorder/bladder dysfunction, Seizure, sensory disturbances.

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השינויים המודגשים בצהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע (טקסט מחוק מסומן בקו חוצה) ועדכוני נוסח שאינם מהווים החמרה.

העלונים המעודכנים נשלחו למשרד הבריאות לצורך פרסומם במאגר התרופות שבאתר משרד הבריאות:
https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h

לחילופין, לקבלת עלונים מלאים מודפסים ניתן לפנות לחברת פייזר פי אף אי פרמצבטיקה ישראל בע"מ
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בברכה,
עידית שלם-אבידר
רוקחת ממונה

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