הודעה על החמרה (מידע בטיחות) בעלון לרופא

תאריך 15.02.2016

שם התכשיר באנגלית ומספר הרישום Depo-Medrol with Lidocaine (045 97 23829 00)

שם בעל הרישום Pfizer PFE Pharmaceuticals Israel LTD

טופס זה מיועד לפרוט ההחמרות בלבד!

ההחמרות המבוקשות		
טקסט חדש	**טקסט נוכחי**	**פרק בעלון**
Depo-Medrol with Lidocaine vials are intended for single dose use only. (see section 4.4 **Special warnings and precautions for use**).	when multidose vials are used, special care to prevent contamination of the contents is essential	**Posology and Method of Administration**
Depo-Medrol with Lidocaine is contra-indicated where there is known hypersensitivity to components or to any local anesthetics of the amide type and in systemic infection unless anti-infective therapy is employed.	Methylprednisolone acetate with Lidocaine is contraindicated : • in patients who have systemic fungal infections	**Contraindications**
1. Undesirable effects may be minimised by using the lowest effective dose for the minimum period. Frequent patient review is required to appropriately titrate the dose against disease activity (see Dosage and administration). 3. Depo-Medrol with Lidocaine vials are intended for single dose use only. Any multidose use of the product may lead to contamination. 4. Due to the absence of a true tendon sheath, the Achilles tendon should not be injected with Depo-Medrol with Lidocaine. 5. 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 and the possibility of depigmentation. 6. Systemic absorption of methylprednisolone occurs following intra-articular injection of Depo-Medrol with Lidocaine. Systemic as well as local effects can therefore be expected. 7.Intra-articular corticosteroids are associated with a substantially increased	While crystals of adrenal steroids in the dermis suppress inflammatory reaction, 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.	**Special warnings and precautions for use**

risk of inflammatory response in the joint, particularly bacterial infection introduced with the injection. Charcot-like arthropathies have been reported particularly after repeated injections. Appropriate examination of any joint fluid present is necessary to exclude any bacterial infection, prior to injection. 8.Following a single dose of Depo-Medrol with Lidocaine, plasma cortisol levels are reduced and there is evidence of hypothalamic-pituitary-adrenal axis (HPA) suppression. This suppression lasts for a variable period of up to 4 weeks. The usual dynamic tests of HPA axis function can be used to diagnose evidence of impaired activity (e.g. Synacthen test). 9.Adrenal cortical atrophy develops during prolonged therapy and may persist for months after stopping treatment. In patients who have received more than physiological doses of systemic corticosteroids (approximately 6 mg methylprednisolone) for greater than 3 weeks, withdrawal should not be abrupt. How dose reduction should be carried out depends largely on whether the disease is likely to relapse as the dose of systemic corticosteroids is reduced. Clinical assessment of disease activity may be needed during withdrawal. If the disease is unlikely to relapse on withdrawal of systemic corticosteroids, but there is uncertainty about HPA suppression, the dose of systemic corticosteroid may be reduced rapidly to physiological doses. Once a daily dose of 6 mg methylprednisolone is reached, dose reduction should be slower to allow the HPA-axis to recover. Abrupt withdrawal of systemic corticosteroid treatment, which has continued up to 3 weeks is appropriate if it considered that the disease is unlikely to relapse. Abrupt withdrawal of doses up to 32 mg daily of methylprednisolone for 3 weeks is unlikely to lead to clinically relevant HPA-axis suppression, in the majority of patients. In the following patient groups, gradual withdrawal of systemic corticosteroid therapy should be *considered* even after courses lasting 3 weeks or less: • Patients who have had repeated courses of systemic corticosteroids, particularly if taken for greater than 3 weeks.		

• When a short course has been prescribed within one year of cessation of long-term therapy (months or years). • Patients who may have reasons for adrenocortical insufficiency other than exogenous corticosteroid therapy. • Patients receiving doses of systemic corticosteroid greater than 32 mg daily of methylprednisolone. • Patients repeatedly taking doses in the evening. 10. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently. 12. Corticosteroids may mask some signs of infection, and new infections may appear during their use. Suppression of the inflammatory response and immune function increases the susceptibility to fungal, viral and bacterial infections and their severity. The clinical presentation may often be atypical and may reach an advanced stage before being recognised. 13. Chickenpox is of serious concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunization with varicella/zoster immunoglobin (VZIG) is needed by exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased. 14. Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.	Corticosteroids may increase susceptibility to infection, may mask some signs of infection, and new infections may appear during their use. Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids.	

17. Care should be taken for patients receiving cardioactive drugs such as digoxin because of steroid induced electrolyte disturbance/potassium loss (see Side-effects). Special precautions: Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary. 3. Existing or previous history of severe affective disorders (especially previous steroid psychosis). 8. Liver failure or cirrhosis. 10. Epilepsy. 13. Predisposition to thrombophlebitis. 20. Patients and/or carers should be warned that potentially severe psychiatric adverse reactions may occur with systemic steroids (see section 4.8). Symptoms typically emerge within a few days or weeks of starting treatment. Risks may be higher with high doses/systemic exposure (see also section 4.5 Interaction with Other Medicaments and Other Forms of Interaction that can increase the risk of side effects), although dose levels do not allow prediction of the onset, type, severity or duration of reactions. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients/carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected. Patients/carers should be alert to possible psychiatric disturbances that may occur either during or immediately after dose tapering/withdrawal of systemic steroids, although such reactions have been reported infrequently. Particular care is required when considering the use of systemic corticosteroids in patients with existing or previous history of severe affective disorders in themselves or in their first degree relatives. These would include depressive or manic-depressive illness and previous steroid psychosis.	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.	

Use in children: Corticosteroids cause growth retardation in infancy, childhood and adolescence which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. *Use in the elderly:* The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threning reactions	Use in Children: Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed. Growth may be suppressed in children receiving long-term, daily-divided dose glucocorticoid therapy and use of such a regimen should be restricted to those most serious indications. Infants and children on prolonged corticosteroid therapy are at special risk from raised intracranial pressure. High doses of corticosteroids may produce pancreatitis in children	
2. Drugs that induce hepatic enzymes, such as rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone, and aminoglutethimide enhance the metabolism of corticosteroids and its therapeutic effects may be reduced. 4. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. The desired effects of hypoglycaemic agents (including insulin), anti-hypertensives and diuretics are antagonised by corticosteroids, and the hypokalaemic effects of acetazolamide, loop diuretics, thiazide diuretics and carbenoxolone are enhanced.		**Interaction with other medicaments and other forms of interaction**
Pregnancy The ability of corticosteroids to cross the placenta varies between individual drugs, however, methylprednisolone does cross the placenta. 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,	Pregnancy Some animal studies have shown that corticosteroids, when administered to the mother at high doses, may cause fetal malformations. Adequate human reproductive studies have not been done with corticosteroids or Lidocaine. Therefore the use of this drug in pregnancy, nursing mothers, or women of child bearing potential requires that the benefits of the drug be carefully weighed against the	**Pregnancy and lactation**

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. 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. The use of local anaesthetics such as lidocaine during labour and delivery may be associated with adverse effects on mother and foetus. Lidocaine readily crosses the placenta. <u>Lactation</u> Corticosteroids are excreted in small amounts in breast milk, however, doses of up to 40 mg daily of methylprednisolone are unlikely to cause systemic effects in the infant. Infants of mothers taking higher doses than this may have a degree of adrenal suppression, but the benefits of breastfeeding are likely to outweigh any theoretical risk. It is not known whether lidocaine is excreted in human breast milk.	potential risk to the mother and embryo or fetus. Since there is inadequate evidence of safety in human pregnancy, this drug should be used in pregnancy only if clearly needed. Corticosteroids and Lidocaine readily cross the placenta. One retrospective study found an increased incidence of low birth weights in infants born of mothers receiving corticosteroids. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy must be carefully observed and evaluated for signs of adrenal insufficiency. 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. 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 Cataracts have been observed in infants born to mothers treated with long-term corticosteroids during pregnancy. <u>Lactation</u> Corticosteroids are excreted in breast milk. Corticosteroids distributed into breast milk may suppress growth and interfere with endogenous glucocorticoid production in nursing infants. Since adequate reproductive studies have not been performed in humans with glucocorticoids, these drugs should be administered to nursing mothers only if the benefits of therapy are judged to	

	outweigh the potential risks to the infant It is not known whether lidocaine is excreted in human breast milk.	
The incidence of predictable undesirable side-effects associated with the use of corticosteroids, including hypothalamic-pituitary-adrenal suppression correlates with the relative potency of the drug, dosage, timing of administration and duration of treatment (See other special warnings and precautions). Side-effects for the Depo-Medrol component may be observed including: PARENTERAL CORTICOSTEROID THERAPY - Anaphylactic reaction or allergic reactions, hypopigmentation or hyperpigmentation, subcutaneous and cutaneous atrophy, sterile abscess, post injection flare (following intra-articular use), charcot-like arthropathy. GASTRO-INTESTINAL - Dyspepsia, peptic ulceration with perforation and haemorrhage, abdominal distension, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis, perforation of bowel. Increases in alanine transaminase (ALT, SGPT) aspartate transaminase (AST, SGOT) and alkaline phosphatase have been observed following corticosteroid treatment. These changes are usually small, not associated with any clinical syndrome and are reversible upon discontinuation. ANTI-INFLAMMATORY AND IMMUNOSUPPRESSIVE EFFECTS - Increased susceptibility and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, may suppress reactions to skin tests, recurrence of dormant tuberculosis (see Other special warnings and precautions). MUSCULOSKELETAL - Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, aseptic necrosis, muscle weakness. FLUID AND ELECTROLYTE DISTURBANCE - Sodium and water		**Undesirable effects**

retention, potassium loss, hypertension, hypokalaemic alkalosis, congestive heart failure in susceptible patients. DERMATOLOGICAL - Impaired healing, petechiae and ecchymosis, thin fragile skin, skin atrophy, bruising, striae, telangiectasia, acne. ENDOCRINE/METABOLIC - Suppression of the hypothalamo-pituitary-adrenal axis; growth suppression in infancy, childhood and adolescence; menstrual irregularity and amenorrhoea. Cushingoid facies, hirsutism, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, negative nitrogen and calcium balance. Increased appetite. NEUROPSYCHIATRIC - A wide range of psychiatric reactions including affective disorders (such as irritable, euphoric, depressed and labile mood psychological dependence and suicidal thoughts), psychotic reactions (including mania, delusions, hallucinations and aggravation of schizophrenia), behavioural disturbances, irritability, anxiety, sleep disturbances, and cognitive dysfunction including confusion and amnesia have been reported for all corticosteroids. . Reactions are common and may occur in both adults and children. Psychological effects have been reported on withdrawal of corticosteroids; the frequency is unknown. Increased intra-cranial pressure with papilloedema in children (pseudotumour cerebri) has been reported, usually after treatment withdrawal of methylprednisolone. OPHTHALMIC - Increased intra-ocular pressure, glaucoma, papilloedema, cataracts with possible damage to the optic nerve, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease, exophthalmos. GENERAL - Leucocytosis, hypersensitivity including anaphylaxis, thrombo-embolism, nausea, vertigo. 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 Other special warnings and precautions).		

A 'withdrawal syndrome' may also occur including, fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful itchy skin nodules and loss of weight. Side-effects for the Lidocaine component include: CENTRAL NERVOUS SYSTEM - Lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, 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, oedema, anaphylactic reactions. *CERTAIN SIDE-EFFECTS REPORTED WITH SOME NON RECOMMENDED ROUTES OF ADMINISTRATION:* *Intrathecal (contra-indicated route of administration):*Usual systemic corticoid adverse reactions, headache, meningismus, meningitis, paraplegia, spinal fluid abnormalities, nausea, vomiting, sweating, arachnoiditis, convulsions. *Extradural:* Wound dehiscence, loss of sphincter control. *Intranasal:* Permanent/temporary blindness, allergic reactions, rhinitis. *Ophthalmic (Subconjunctival):* Redness and itching, abscess, slough at injection site, residue at injection site, increased intra-ocular pressure, decreased vision - blindness, infection. Miscellaneous: Scalp, tonsillar fauces, sphenopalatine ganglion: blindness.		
There is no clinical syndrome of acute overdosage with Depo-Medrol with Lidocaine. Following overdosage the possibility of adrenal suppression should be guarded against by gradual diminution of dose levels over a period of time. In such event the patient may require to be	Reports of acute toxicity and/or death following overdosage of corticosteroids are rare. In the event of overdosage, no specific antidote is available; treatment is supportive and symptomatic. Methylprednisolone is dialyzable.	**Overdose**

supported during any further traumatic episode.		

מצ"ב העלון שבו מסומנים ההחמרות המבוקשות על רקע צהוב.
שינויים שאינם בגדר החמרות סומנו (בעלון) בצבע שונה (טקסט ירוק). יש לסמן רק תוכן מהותי ולא שינויים במיקום הטקסט.