הודעה על החמרה (מידע בטיחות) בעלון לרופא

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תאריך: 03/2017

שם תכשיר באנגלית ומספר הרישום:

Depo-Medrol with Lidocaine 045-97-23829

שם בעל הרישום: פייזר פי אף אי פרמצבטיקה בע"מ

! פרוט ההחמרות בלבד

ההחמרות המבוקשות		
פרק בעלון	**טקסט נוכחי**	**טקסט חדש**
Contraindications	----------	Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids.
Special warnings and precautions for use	Because rare instances of skin reactions and anaphylactic/ anaphylactoid 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 drug allergy. 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). --------- ---------	**Immune System Effects** Allergic reactions 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 patient has a history of drug allergy. **Endocrine Effects** Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration, and duration of glucocorticoid therapy. ... 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. Because glucocorticoids can produce or aggravate Cushing’s syndrome, glucocorticoids should be avoided in patients with Cushing’s disease. There is an enhanced effect of corticosteroids on patients with hypothyroidism. **Metabolism and Nutrition** Corticosteroids, including methylprednisolone, can increase blood glucose, worsen pre-existing

diabetes, and predispose those on long-term corticosteroid therapy to diabetes mellitus. ... There have been reports of epidural lipomatosis in patients taking corticosteroids, typically with long-term use at high doses. **Ocular Effects** Prolonged use of corticosteroids may produce posterior subcapsular 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. Corticosteroids should be used cautiously in patients with ocular herpes simplex, because of possible corneal perforation. Corticosteroid therapy has been associated with central serous chorioretinopathy, which may lead to retinal detachment. **Cardiac Effects** Adverse effects of glucocorticoids on the cardiovascular system, such as dyslipidaemia 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. Systemic corticosteroids should be used with caution, and only if strictly necessary, in cases of congestive heart failure. **Vascular Effects** Corticosteroids should be used with caution in patients with hypertension. 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. **Gastrointestinal Effects** 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. In combination with NSAIDs, the risk of developing gastrointestinal ulcers is increased.	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. …. Ocular herpes simplex, for fear of corneal perforation. Hypertension or congestive heart failure. Peptic ulceration.	

Corticosteroids should be used with caution in nonspecific 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, when steroids are used as direct or adjunctive therapy. **Hepatobiliary Effects** Drug induced liver injury including acute hepatitis or liver enzyme increase can result from cyclical pulsed IV methylprednisolone (usually at initial dose ≥ 1 g / day). Rare cases of hepatotoxicity have been reported. The time to onset can be several weeks or longer. In the majority of case reports resolution of the adverse events has been observed after treatment was discontinued. Therefore, appropriate monitoring is required. High doses of corticosteroids may produce acute pancreatitis. Corticosteroids should be used with caution in patients with liver failure or cirrhosis. **Musculoskeletal Effects** An acute myopathy has been reported with the use of high doses of corticosteroids, most often occurring in patients with disorders of neuromuscular transmission (e.g. myasthenia gravis), 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. Clinical improvement or recovery after stopping corticosteroids may require weeks to years. … **Injury, Poisoning and Procedural Complications** Systemic corticosteroids are not indicated for, and therefore should not be used to treat, traumatic brain injury, a multicenter study revealed an increased mortality at 2 weeks and 6 months after injury in patients administered methylprednisolone sodium succinate compared to placebo. A causal association with methylprednisolone sodium succinate treatment has not been established. **Investigations** Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion	Liver failure or cirrhosis. ---------- ----------	

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. **Other** … Aspirin and nonsteroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids. Pheochromocytoma crisis, which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation. **Paediatric population** Intravenous administration of the preservative benzyl alcohol has been associated with serious adverse event, and death in paediatric patients including neonates characterized by central nervous system depression, metabolic acidosis, gasping respirations, cardio-vascular failure and haematological anomalies ("gasping syndrome"). The minimum amount of benzyl alcohol at which toxicity may occur is not known. Use only if it is necessary and if there are no alternatives possible. If given in high volumes, should be used with caution and preferably for short term treatment in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis) Premature and low-birth weight infants may be more likely to develop toxicity. Benzyl Alcohol containing products should not be used in pre-term or full-term neonates unless strictly necessary Corticosteroids cause growth retardation in infancy, childhood and adolescence which may be irreversible. Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed. Treatment should be limited to the minimum dosage for the shortest possible time. The 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	---------- ---------- ---------- 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.	

pancreatitis in children.		
3. Antibiotics/Antimycotics - Drugs such as erythromycin (macrolide antibacterial CYP3A4 inhibitor and substrate), itraconazole and ketoconazole antifungal CYP3A4 inhibitors and substrates) may inhibit the metabolism of corticosteroids and thus decrease their clearance. Troleandomycin (CYP3A4 inhibitor), as well as clarithromycin, erythromycin, itraconazole and ketoconazole (CYP3A4 inhibitors and substrates) increase the effects and the side effects of methylprednisolone. The acetylation rate and clearance of isoniazid (CYP3A4 inhibitor), an antibacterial drug, can be increased by methylprednisolone. 4. Steroids may reduce the effects of anticholinesterases in myasthenia gravis. An acute myopathy has been reported with the concomitant use of high doses of corticosteroids and anticholinergics, such as neuromuscular blocking drugs (see section 4.4). ... 5. The effect of methylprednisolone on oral anticoagulants is variable. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding and to maintain the desired anticoagulant effects. There are also reports of diminished effects of anticoagulants when given concurrently with corticosteroids. … 7. Antidiabetics - Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required. 8. Antiemetics - Aprepitant and fosaprepitant (CYP3A4 inhibitors and substrates). 9. Antivirals - HIV protease inhibitors: Indinavir and ritonavir (CYP3A4 inhibitors and substrates) may increase plasma concentrations of corticosteroids. Corticosteroids may induce the metabolism of HIV-protease inhibitors resulting in reduced plasma concentrations. 10.Calcium channel blocker - Diltiazem (CYP3A4 inhibitor and substrate). 11. Contraceptives (oral) - Ethinylestradiol/norethindrone (CYP3A4 inhibitors and substrate). 12.Other immunosuppressants like cyclophosphamide and tacrolimus are substrates of CYP3A4. 13. Potassium-depleting agents - When corticosteroids are administered concomitantly with potassium-depleting agents (i.e. diuretics), patients should be observed closely for	3. Drugs such as erythromycin and ketoconazole may inhibit the metabolism of corticosteroids and thus decrease their clearance. 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. 5. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy and close monitoring of the INR or prothrombin time is required to avoid spontaneous bleeding. 6. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Salicylates and non-steroidal anti-inflammatory agents should be used cautiously in conjunction with corticosteroids in hypothrombinaemia. 7. Steroids have been reported to interact with neuromuscular blocking agents such as pancuronium with partial reversal of the neuromuscular block.	**Interaction with other medicinal products and other forms of interaction**

development of hypokalaemia. There is also an increased risk of hypokalaemia with concurrent use of corticosteroids with amphotericin B, xanthenes, or beta2 agonists. 14. Grapefruit juice - CYP3A4 inhibitor.		
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. 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. Cataracts have been observed in infants born to mothers treated with long-term corticosteroids during pregnancy. *Lidocaine* Adequate human reproductive studies have not been done with Lidocaine. 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. Benzyl alcohol can cross the placenta	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, 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. Lactation 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.	**Fertility, pregnancy and lactation**

	It is not known whether lidocaine is excreted in human breast milk.	
Effects on ability to drive and use machines The effect of corticosteroids on the ability to drive or use machinery has not been systematically evaluated. Undesirable effects, such as dizziness, vertigo, visual disturbances, and fatigue are possible after treatment with corticosteroids. If affected, patients should not drive or operate machinery.	None stated.	
Infections and infestations: ***common:*** Infection (including increased susceptibility and severity of infections with suppression of clinical symptoms and signs) ***Not known:*** Injection site infection; Peritonitis… ***Endocrine disorders:*** ***Common:*** Cushingoid ***Metabolism and nutrition disorders:*** ***Common*** Glucose tolerance impaired; Increased requirements for insulin (or oral hypoglycemic agents in diabetics)… ***Not Known***: Dyslipidaemia;Epidural lipomatosis… ***Psychiatric disorders:*** ***Common:*** Affective disorder (including Depressed mood, Euphoric mood). Mood swings; Abnormal behaviour; Insomnia ***Not Known***: Mental disorder; Personality change… ***Nervous system disorders***: ***Not Known***: Convulsion; Dizziness; Headache… ***Eye disorders:*** ***Common***: Cataract; Glaucoma ***Not Known:*** chorioretinopathy; Rare instances of blindness associated with intralesional therapy around the face and head… ***Cardiac disorders:*** ***Not Known:*** Cardiac failure congestive (in susceptible patients) ***Vascular disorders:*** ***Common:*** Hypertension ***Not Known:*** Hypotension… ***Respiratory, thoracic and mediastinal disorders:*** ***Not Known:*** Pulmonary embolism, Hiccups ***Gastrointestinal disorders:*** ***Common:*** Peptic ulcer (with possible Peptic ulcer perforation and Peptic ulcer haemorrhage) ***Not Known:*** Intestinal perforation; Oesophagitis; Abdominal pain; Diarrhoea; Nausea…	----------	**Undesirable effects**

Hepatobiliary disorders: ***Not known:*** Hepatitis.. ***Skin and subcutaneous tissue disorders:*** ***Common:*** Ecchymosis; Acne ***Not Known:*** Angioedema; Rash; Erythema; Pruritus; Urticaria; Hyperhidrosis.. ***Musculoskeletal and connective tissue disorders:*** ***Common:*** Growth retardation; Osteoporosis; Muscular weakness ***Not Known:*** Pathological fracture; Muscle atrophy; Neuropathic arthropathy; Arthralgia; Myalgia… ***General disorders and administration site conditions*** ***Common:*** Oedema peripheral… ***Not Known:*** Injection site reaction; Fatigue; Malaise… ***Investigations*** ***Common*** Blood potassium decreased ***Not Known***: Urine calcium increased; Blood urea increased.. ***Injury, poisoning and procedural complications: Not Known***: Spinal compression fracture. Side effects for the Lidocaine component include: ***Psychiatric disorders: Common:*** Anxiety.. ***Nervous System disorders: Common:*** Hypoaesthesia; Somnolence; Dizziness… ***Skin and subcutaneous disorders: Not known:*** Skin lesion… ***Musculoskeletal and connective tissue disorders***: ***Common***: Muscle twitching *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, convulsions, sensory disturbances. The frequency of these adverse reactions is not known.	*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.	