פייזר PFE פרמצבטיקה ישראל בע"מ
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טל: 972-9-9700500 פקס: 972-9-9700501

ספטמבר 2021

רופא/ה, רוקח/ת נכבד/ה,
ברצוננו להודיעך על עדכון בעלון לרופא ובעלון לצרכן של **Depo-Provera® 500 mg/ml** (3.3 mL vial **).**
Depo-Provera® 150 mg /ml :העלון הופרד מעלון התכשיר. (Suspension for intramuscular injection**)** .

<u>המרכיב הפעיל:</u>

MEDROXYPROGESTERONE ACETATE 150 mg / mL

<u>Indicated for:</u>
DEPO-PROVERA® 500 is indicated for: Palliation of inoperable recurrent or metastatic carcinoma of endometrium, breast, ovary and kidney.

<u>להלן העדכונים העיקריים בעלון לרופא:</u>

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

The site of injection should be cleansed using standard methods prior to administration of the injection.

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Long-Term Use

Since loss of bone mineral density (BMD) may occur in pre-menopausal women who use DMPA injection long-term (see Section 4.4 Special warnings and precautions for use and Section 5.1 – Pharmacodynamic properties, Clinical Studies, Bone Mineral Density Studies), a risk/benefit assessment, which also takes into consideration the decrease in BMD that occurs during pregnancy and/or lactation, should be considered .

Use in Children

DMPA IM is not indicated before menarche. Data are available in adolescent females (12 18 years) (see Section 5.1-Pharmacodynamic properties, Clinical Studies, BMD Changes in Adolescent Females (12-18 years). Other than concerns about loss of BMD, the safety and effectiveness of DMPA IM are expected to be the same as for postmenarcheal adolescent and adult females .

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4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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Loss of bone mineral density:

There are no studies on the effect caused by medroxyprogesterone, administered parenterally, on bone mineral density in oncological treatment.

It could be necessary to make an assessment of bone mineral density in patients who are undergoing prolonged treatment with Depo-Provera® (see section 4.2: Loss of bone mineral density).

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A study to assess the BMD effects of Depo-Provera in adolescent females showed that its use was associated with a statistically significant decline in BMD from baseline.
After discontinuing depot medroxyprogesterone acetate intramuscular (DMPA-IM) in adolescents, full recovery of mean BMD required 1.2 years at the lumbar spine, 4.6 years at the total hip, and 4.6 years at the femoral neck (see section 5.1). However, in some participants, BMD did not fully return to baseline during follow-up and the long-term outcome is not known in this group.
A large observational study of predominantly adult female contraceptive users showed that use of DMPA-IM did not increase risk for bone fractures. It should be noted that this study could not determine whether use of

medroxyprogesterone acetate has an effect on fracture rate later in life (see section 5.1 – Relationship between fracture incidence and use of DMPA-IM in women of reproductive age).

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Loss of Bone Mineral Density:

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A study to assess the BMD effects of DMPA -IM (Depo-Provera) in adolescent females showed that its use was associated with a statistically significant decline in BMD from baseline. After discontinuing DMPA-IM in adolescents, return of mean BMD to baseline values required 1.2 years at the lumbar spine, 4.6 years at the total hip and at least 4.6 years at the femoral neck (see section 5.1). However in some participants, BMD did not fully return to baseline during follow-up and the long-term outcome is not known in this group. In adolescents, Depo-Provera may be used, but only after other methods of contraception have been discussed with the patients and considered to be unsuitable or unacceptable.
A large observational study of predominantly adult female contraceptive users showed that use of DMPA-IM did not increase risk for bone fractures. Importantly, this study could not determine whether use of DMPA has an effect on fracture rate later in life (see section 5.1 – Relationship of fracture incidence to use of DMPA-IM by women of reproductive age).

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Breast cancer
After various epidemiological studies, no increase in the risk of breast cancer was found in users of injectable prolonged-release progestogen, when compared to non-users. However, an increase was found in the relative risk (for example 2.0 in one study) in women who used prolonged-release injectable progestogen or had used it in previous years. From these data it is not possible to infer whether the increased rate of diagnoses of breast cancer in women who were users is due to an increase of vigilance, to the biological effects of injectable progestogen or to a combination of both reasons.

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Depo-Provera® can give rise to Cushingoid symptoms.

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This medicine contains methyl parahydroxybenzoate (Methylparaben) and propyl parahydroxybenzoate (Propylparaben). It can cause allergic reactions (possibly delayed), and, exceptionally, bronchial spasm.

This medicine contains sodium. It contains less than 1 mmol sodium (23 mg) per ml, that is to say essentially ‘sodium free’

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4.6 FERTILITY, PREGNANCY AND LACTATION

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Fertility:

Depo-Provera® has a prolonged contraceptive effect. In the event of conception, the average time for this to occur is after 10 months (ranging from 4-31 months) after the last administration, but there is no relation to the duration of the treatment.

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4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Depo-Provera may cause headaches and dizziness. Patients should be advised not to drive or operate machinery if affected.

4.8 UNDESIRABLE EFFECTS

The table below provides a listing of adverse drug reactions with frequency based on all-causality data from 1337 patients who received medroxyprogesterone acetate in 4 pivotal studies that evaluated efficacy and safety of medroxyprogesterone acetate for oncology indications.

System Organ Class	Very Common ≥1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Rare ≥ 1/10,000 to < 1/1000	Frequency Not Known (cannot be estimated from the available data)
Immune system disorders			Angioedema	Drug hypersensitivity	Anaphylactic reaction, Anaphylactoid reaction
Endocrine disorders			Corticoid-like effects		Prolonged anovulation
Metabolism and nutritional disorders		Weight fluctuation, Increased appetite	Diabetes mellitus exacerbated, Hypercalcaemia		
Psychiatric disorders		Insomnia	Depression, Euphoria, Changes in libido	Nervousness	Confusion
Nervous system disorders		Headache, Dizziness, Tremors		Cerebral infarction, Somnolence	Loss of concentration, Adrenergic-like effects
Eye disorders					Retinal embolism and thrombosis, Cataract diabetic, Visual impairment
Cardiac disorders			Cardiac failure congestive	Myocardial infarction	Tachycardia, Palpitations
Vascular disorders			Thrombo phlebitis	Embolism and thrombosis	
Respiratory, thoracic and mediastinal disorders			Pulmonary embolism		
Gastrointestinal disorders		Vomiting, Constipation, Nausea,	Diarrhoea, Dry mouth		
Hepatobiliary disorders				Jaundice	
Skin and subcutaneous tissue disorders		Hyperhidrosis	Acne, Hirsutism	Alopecia, Rash	Lipodystrophy acquired*, Urticaria, Pruritus
Musculoskeletal and connective tissue disorders			Muscle spasms		
Renal and urinary system disorders					Glycosuria

System Organ Class	Very Common ≥1/10	Common ≥ 1/100 to < 1/10	Uncommon ≥ 1/1000 to < 1/100	Rare ≥ 1/10,000 to < 1/1000	Frequency Not Known (cannot be estimated from the available data)
Reproductive system and breast disorders		Erectile dysfunction	Dysfunctional uterine bleeding (irregular, increase, decrease, spotting), Breast pain		Amenorrhoea, Uterine cervical erosions, Cervical discharge, Galactorrhoea
General disorders and administration site conditions		Oedema /fluid retention, Fatigue Injection site reaction*	Injection site pain/tenderness*	Malaise, Pyrexia	Injection site persistent atrophy/indentation/dimpling*, Injection site nodule/lump*
Investigations				Glucose tolerance decreased, Blood pressure increased	Liver function test abnormal, White blood cell count increased, Platelet count increased

* Adverse drug reaction identified post-marketing

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6.4 Special precautions for storage

Store below 25°C.

השינויים המודגשים ברקע צהוב מהווים החמרה. כמו כן, בוצעו שינויים נוספים הכוללים תוספת מידע, השמטת מידע ועדכוני נוסח שאינם מהווים החמרה. העלונים המעודכנים זמינים באתר משרד הבריאות.

https://www.old.health.gov.il/units/pharmacy/trufot/index.asp?safa=h

לחילופין, לקבלת עלון מלא מודפס ניתן לפנות לחברת פייזר PFE פרמצבטיקה ישראל בע"מ, שנקר 9, ת.ד. 12133 הרצליה פיתוח, 46725.

בברכה,
עידית שלם אבידר
רוקחת ממונה