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אוקטובר 2020

רופא/ה, רוקח/ת נכבד/ה,
ב
רצוננו להודיעך על עדכון בעלון לרופא ובעלון לצרכן של **SAYANA** :

<u>המרכיב הפעיל:</u>

MEDROXYPROGESTERONE ACETATE 104 mg / 0.65 mL

<u>Indicated for:</u>
* SAYANA is indicated for long-term female contraception.
Each subcutaneous injection prevents ovulation and provides contraception for at least 13 weeks (+/- 1 week).
However, it should be taken into consideration that the return to fertility (ovulation) may be delayed for up to one year . Since loss of bone mineral density may occur in females of all ages who use SAYANA long-term, a risk/benefit assessment, which also takes into consideration the decrease in bone mineral density that occurs during pregnancy and/or lactation, should be considered.
* Use in Adolescents (12-18 years)
In adolescents, use of SAYANA is only indicated when other contraceptive methods are considered unsuitable or unacceptable, due to unknown long-term effects of bone loss associated with SAYANA during the critical period of bone accretion.
SAYANA has not been studied in women under the age of 18 years but data is available for intramuscular medroxyprogesterone acetate in this population.

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

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 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.

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4. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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<u>BMD Changes in Adult Women</u>

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Table 2. Mean Percent Change (with 95% Confidence Intervals) from Baseline in BMD in Adults by Skeletal Site and Cohort after 5 Years of Therapy with DMPA-IM and after 2 Years Post-Therapy or 7 Years of Observation (Control)

Time in Study	Spine		Total Hip		Femoral Neck	
	DMPA	Control	DMPA	Control	DMPA	Control
5 years*						
n	33	105	21	65	34	106
Mean	-5.4%	0.4%	-5.2%	0.2%	-6.1%	-0.3%
(SD)	(3.57)	(3.27)	(3.60)	(3.18)	(4.68)	(5.22)
95% CI	-6.65; -4.11	-0.20; 1.06	-6.80; -3.52	-0.60; 0.98	-7.75; -4.49	-1.27; 0.73
7 years**						
n	12	60	7	39	13	63
Mean	-3.1%	0.5%	-1.3%	0.9%	-5.4%	-0.0%
(SD)	(3.15)	(3.65)	(4.95)	(3.81)	(2.73)	(5.88)
95% CI	-5.13; -1.13	-0.39; 1.49	-5.92; 3.23	-0.29; 2.17	-7.03; -3.73	-1.51; 1.45

* The treatment group consisted of women who received **DMPA- IM** for 5 years and the control group consisted of women who did not use hormonal contraception for this time period.
** The treatment group consisted of women who received **DMPA-IM** for 5 years and were then followed up for 2 years post-use and the control group consisted of women who did not use a hormonal contraceptive for 7 years.
SD = Standard Deviation
CI = Confidence Interval

BMD Changes in Adolescent Females (12-18 years)

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Table 3: Mean Percent Change (with 95% Confidence Intervals) from Baseline in BMD in Adolescents Receiving ≥4 Injections per 60-week Period, by Skeletal Site

Duration of Treatment	DMPA-IM	
	N	Mean % Change [95 % CI]
Total Hip BMD		
Week 60 (1.2 years)	113	-2. 7 [-3.27; -2.12]
Week 120 (2.3 years)	73	-5.4 [-6.16; -4.65]
Week 180 (3.5 years)	45	-6.4 [-7.38; -5.37]
Week 240 (4.6 years)	28	-6.4 [-8.56; -4.24]
Femoral Neck BMD		
Week 60	113	-2.9 [-3.72; -2.15]
Week 120	73	-5.3 [-6.23; -4.37]
Week 180	45	-6.0 [-7.31; -4.59]
Week 240	28	-5.4 [-7.81; -3.00]
Lumbar Spine BMD		
Week 60	114	-2.5 [-2.95; -1.98]
Week 120	73	-2.7 [-3.57; -1.91]
Week 180	44	-2.7 [-3.99; -1.35]
Week 240	27	-2.1 [-4.16; -0.07]

CI = Confidence Interval

Post-treatment follow-up of adolescent participants from the same study, who received at least 1 DMPA injection and provided at least 1 follow-up BMD measurement after stopping DMPA-IM use is shown in Table 4. The median number of injections received in this cohort during the treatment phase was 9. At the time of the final DMPA injection, BMD % changes from baseline in this cohort were -2.7%, -4.1% and -3.9% at the spine, total hip and femoral neck, respectively. Over time, these mean BMD deficits recovered to baseline after DMPA-IM was discontinued. Recovery to baseline required 1 year at the lumbar spine, 4.6

years at the total hip and 4.6 years at the femoral neck. However, it is important to note that a large number of subjects discontinued from the study, therefore these results are based on a small number of subjects and some subjects still had deficit in total hip BMD after 240 weeks. Longer duration of treatment and smoking were associated with slower recovery. Please refer to Table 4 below.

Table 4: Mean Percentage Changes (with 95% Confidence Intervals) from baseline in BMD in Adolescents after Discontinuation of DMPA

Week after DMPA discontinuation	N	Median Number of injections	Mean % change (SE) from baseline to end of treatment	95% CI	Mean % change (SE) from baseline to post-DMPA visit	95% CI
Total Hip BMD						
0	98	9	-4.1 (0.43)	[-4.95; -3.25]	N/A	
24	74	9	-4.1 (0.53)	[-5.15; -3.04]	-4.0 (0.61)	[-5.25; -2.80]
60	71	8	-3.6 (0.46)	[-4.48; -2.66]	-2.8 (0.56)	[-3.97; -1.72]
120	52	10	-4.3 (0.64)	[-5.56; -2.98]	-1.7 (0.72)	[-3.14; -0.26]
180	39	7	-4.1 (0.72)	[-5.55; -2.63]	-1.2 (0.85)	[-2.96; 0.46]
240	25	9	-3.4 (0.67)	[-4.73; -1.98]	0.1 (0.98)	[-1.95; 2.11]
Femoral Neck BMD						
0	98	9	-3.9 (0.50)	[-4.92; -2.92]	N/A	
24	74	9	-3.8 (0.60)	[-5.01; -2.62]	-4.0 (0.71)	[-5.40; -2.55]
60	71	8	-3.3 (0.56)	[-4.41; -2.18]	-3.6 (0.70)	[-4.99; -2.18]
120	52	10	-3.8 (0.74)	[-5.25; -2.28]	-1.8 (0.82)	[-3.43; -0.13]
180	39	7	-3.9 (0.85)	[-5.62; -2.17]	-1.0 (0.98)	[-3.00; 0.97]
240	25	9	-3.4 (0.80)	[-5.07; -1.78]	-0.7 (1.19)	[-3.20; 1.72]
Lumbar Spine BMD						
0	98	9	-2.7 (0.39)	[-3.45; -1.91]	N/A	
24	74	9	-2.6 (0.43)	[-3.42; -1.69]	-2.5 (0.51)	[-3.52; -1.48]
60	70	8	-2.8 (0.43)	[-3.66; -1.96]	-0.2 (0.60)	[-1.41; 1.01]
120	52	10	-2.7 (0.61)	[-3.96; -1.50]	2.2 (0.73)	[0.74; 3.67]
180	39	7	-3.0 (0.67)	[-4.35; -1.66]	2.8 (0.79)	[1.16; 4.35]
240	25	9	-2.6 (0.80)	[-4.28; -0.99]	4.5 (1.03)	[2.35; 6.61]

SE = Standard Error
CI = Confidence interval
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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,
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