אוגוסט 2021

רופא/ה נכבד/ה
רוקח/ת נכבד/ה

הנדון: PNEUMOVAX 23
<u>פנאומווקס 23</u>

Dosage Form: SOLUTION FOR INJECTION
Composition: PNEUMOCOCCAL VACCINE POLYVALENT 25 MCG / 0.5 ML

חברת מרק שארפ ודוהם (ישראל-1996) בע"מ (MSD ישראל) מבקשת ליידע על עדכון העלון לרופא של PNEUMOVAX 23.

להלן לשון ההתוויה המאושרת לתכשיר:

For vaccination against pneumococcal disease caused by those pneumococcal types included in the vaccine.

למידע מלא ולהוראות מתן מפורטות, יש לעיין בעלון לרופא המאושר על ידי משרד הבריאות.

טקסט מהותי שהתווסף מודגש <u>בקו תחתון</u>.
טקסט מהותי שהוסר מסומן ~~בקו חוצה~~.

<u>עדכונים מהותיים בעלון לרופא:</u>
הפרקים הבאים עברו עידכון:

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5 WARNINGS AND PRECAUTIONS

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<u>5.6 Sodium</u>
<u>This medicinal product contains less than 1 mmol (23 mg) sodium per dosage unit and is considered to be essentially sodium-free.</u>
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6 ADVERSE REACTIONS

The most common adverse reactions, reported in >10% of subjects vaccinated with PNEUMOVAX 23 <u>for the first time in a</u> clinical trial~~s~~<u>,</u> were: injection-site pain/soreness/tenderness (60.0%), injection-site swelling/induration (20.3%), headache (17.6%), injection-site erythema (16.4%), asthenia/fatigue (13.2%), and myalgia (11.9%). *[See Adverse Reactions (6.1).]*

6.1 Clinical Trials Experience

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<u>Sequential Administration of Prevnar 13 and PNEUMOVAX 23</u>
<u>In a randomized, double-blind, placebo-controlled, multicenter study, healthy adults, 50 years of age and older, received Prevnar 13 followed by PNEUMOVAX 23 either 8 weeks later (Group 1) or 26 weeks later (Group 2). Placebo was administered instead of PNEUMOVAX 23 at 26 weeks (Group 1) or 8 weeks (Group 2). Solicited injection site adverse reactions were evaluated during Days 1 through 5 postvaccination. Solicited systemic adverse reactions and any other adverse reactions were evaluated during Days 1 through 14 postvaccination, and any serious adverse events (SAEs) were collected throughout the study period (through Week 30). *[See Clinical Studies (14.2).]*</u>
<u>Overall, subjects were a mean age of 64.2 years (range: 50 to 97 years). There were more females (n=219, 54.8%) than males (n=181, 45.3%). By race, 84.8% of subjects were White, 9.3% were Black or African-American, and 6.1% were other racial groups; the majority of subjects were not Hispanic or Latino (n=322, 80.5%).</u>
<u>Serious Adverse Reactions</u>

There were 24 SAEs reported in 20 subjects (n=9 [4.5%] Group 1; n=11 [5.5%] Group 2). No SAEs were considered related to vaccination.

Solicited Adverse Reactions

Solicited injection site adverse reactions that occurred during Days 1 through 5 postvaccination with PNEUMOVAX 23, solicited systemic adverse reactions that occurred during Days 1 through 14, and fever that occurred during Days 1 through 5 postvaccination with PNEUMOVAX 23 are presented in Table 2. In this study, 81.4% of subjects in Group 1 and 64.0% of subjects in Group 2 reported at least 1 injection site adverse reaction from Days 1 through 5 postvaccination with PNEUMOVAX 23, and 64.9% of subjects in Group 1 and 54.9% of subjects in Group 2 reported at least 1 systemic adverse reaction from Days 1 through 14 postvaccination with PNEUMOVAX 23.

Table 2: Rates (%) of Solicited Injection Site Reactions Occurring on Days 1 to 5 After PNEUMOVAX 23 and Solicited Systemic Adverse Reactions Occurring on Days 1 to 14 After PNEUMOVAX 23

	Group 1* (Prevnar 13 -> PNEUMOVAX 23 -> Placebo)		Group 2† (Prevnar 13 -> Placebo -> PNEUMOVAX 23)	
	n	(%)	n	(%)
Injection Site Adverse Reactions				
Subjects in population with follow-up	188		164	
Any injection site reaction	153	(81.4)	105	(64.0)
Any Injection site pain‡	149	(79.3)	105	(64.0)
Mild	72	(38.3)	65	(39.6)
Moderate	65	(34.6)	36	(22.0)
Severe§	12	(6.4)	4	(2.4)
Any Injection site swelling	95	(50.5)	48	(29.3)
0 to <2.5 cm	28	(14.9)	19	(11.6)
≥2.5 to <5.1 cm	20	(10.6)	9	(5.5)
≥5.1 to <7.6 cm	20	(10.6)	10	(6.1)
≥7.6 to <10.2 cm	15	(8.0)	2	(1.2)
≥10.2 cm§	12	(6.4)	8	(4.9)
Any Injection site erythema	78	(41.5)	48	(29.3)
0 to <2.5 cm	26	(13.8)	20	(12.2)
≥2.5 to <5.1 cm	12	(6.4)	13	(7.9)
≥5.1 to <7.6 cm	12	(6.4)	6	(3.7)
≥7.6 to <10.2 cm	7	(3.7)	3	(1.8)
≥10.2 cm	19	(10.1)	6	(3.7)
Unknown [missing data]	2	(1.1)	0	(0.0)
Systemic Adverse Reactions				
Subjects in population with follow-up	188		164	
Any systemic adverse reaction	122	(64.9)	90	(54.9)
Myalgia	93	(49.5)	70	(42.7)
Fatigue	59	(31.4)	45	(27.4)
Headache	46	(24.5)	30	(18.3)
Arthralgia	37	(19.7)	25	(15.2)
Subjects with temperature data¶	185		161	
Temperature ≥ 100.4°F	1	(0.5)	0	(0.0)

Every subject is counted a single time for each applicable row and column.
A specific adverse reaction appears in this table only if its incidence in one or more of the columns meets the incidence criterion in the table title, after rounding.
*Group 1: 8-week interval between Prevnar 13 and PNEUMOVAX 23.
†Group 2: 26-week interval between Prevnar 13 and PNEUMOVAX 23.
‡Pain was characterized as mild, moderate or severe. (Mild: awareness of sign or symptom, but easily tolerated. Moderate: discomfort enough to cause interference with usual activity. Severe: incapacitating with inability to work or do usual activity).
§One Group 1 subject with severe pain and swelling greater than 10.2 cm after receipt of PNEUMOVAX 23, went to the Emergency Room for medical attention.
¶Percentages are calculated based on number of subjects with temperature data. Oral temperature was solicited on Days 1 to 5 after PNEUMOVAX 23 vaccination.

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6.2 Post-Marketing Experience

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General disorders and administration site conditions

Cellulitis
Malaise
Fever (>38.9°C)

Warmth at the injection site
Decreased limb mobility
Peripheral edema in the injected extremity
Injection-site necrosis

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8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. ~~In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.~~
Available human data from clinical trials of PNEUMOVAX 23 in pregnancy have not established the presence or absence of a vaccine-associated risk.
Developmental toxicity studies have not been conducted with PNEUMOVAX 23 in animals.
~~*Pregnancy Category C:* Animal reproduction studies have not been conducted with PNEUMOVAX 23. It is also not known whether PNEUMOVAX 23 can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. PNEUMOVAX 23 should be given to a pregnant woman only if clearly needed.~~

8.~~3~~2 ~~Nursing Mothers~~Lactation

Risk Summary

It is not known whether ~~this drug~~PNEUMOVAX 23 is excreted in human milk. Data are not available to assess the effects of PNEUMOVAX 23 on the breastfed infant or on milk production/excretion.
The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for PNEUMOVAX 23 and any potential adverse effects on the breastfed child from PNEUMOVAX 23 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to the disease prevented by the vaccine.
~~Because many drugs are excreted in human milk, caution should be exercised when PNEUMOVAX 23 is administered to a nursing woman.~~

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12 CLINICAL PHARMACOLOGY

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14.2 Immunogenicity

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Sequential Administration of Prevnar 13 and PNEUMOVAX 23

In a randomized, double-blind, placebo-controlled, multicenter study, healthy adults, 50 years of age and older, received Prevnar 13 followed by PNEUMOVAX 23 either 8 weeks later (Group 1) or 26 weeks later (Group 2). Four hundred subjects were randomized 1:1 into Group 1 or Group 2, all of whom were initially vaccinated with Prevnar 13; of these, 188 subjects received PNEUMOVAX 23 (Group 1) and 185 subjects received placebo (Group 2) at Week 8, and 172 subjects received placebo (Group 1) and 164 subjects received PNEUMOVAX 23 (Group 2) at Week 26.
Opsonophagocytic activity (OPA) titers were measured at prevaccination, at Week 12 and at Week 30 for the 12 shared serotypes contained in both PNEUMOVAX 23 and Prevnar 13 (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F), 2 of the 11 serotypes unique to PNEUMOVAX 23 (22F and 33F), and 1 serotype unique to Prevnar 13 (6A). OPA testing was performed on evaluable serum samples from all subjects at baseline (Day 1) and Week 12, and on sera from a random subset of subjects (approximately 50% of subjects) at Week 30. Estimated GMTs, GMT ratio, and 95% confidence intervals were obtained from a constrained Longitudinal Data Analysis model[3].
For each of the shared serotypes, Week 12 OPA geometric mean titers (GMTs) in Group 1 were noninferior to those of Group 2, as the lower bounds of the 95% CIs for the OPA GMT ratios were >0.5 for all 12 shared serotypes. For serotypes 22F and 33F, OPA GMTs in Group 1 at Week 12 were superior to those of Group 2 at Week 12, as the lower bounds of the 95% CIs for the OPA GMT ratios were >2.0 for both serotypes.

The OPA GMTs to the 12 shared serotypes and 2 unique serotypes (22F and 33F) when measured 4 weeks after dosing with PNEUMOVAX 23 were generally similar between Group 1 (Week 12) and Group 2 (Week 30 subset).

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בעלון לרופא בוצעו עדכונים נוספים שאינם נכללים בהודעה זו.
העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות, וניתן לקבלו מודפס על ידי פניה לבעל הרישום, חברת MSD, בטלפון 09-9533333.
PNEUMOVAX 23 מופצת ע"י חברת נובולוג בע"מ.

בברכה,

מיכל סרפר
רוקחת ממונה
MSD ישראל

References:
PNEUMOVAX 23_SPC_082021