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## Memorandum

**Date:** April 21, 2021

**To:** Tatiana Claro Da Silva, Ph.D.  
CBER/OVRR/DVRPA/CMC1

Anuja Rastogi, MD, MHS  
CBER/OVRR/DVRPA/CRB1

**From:** Michael Brony, Pharm.D.  
CBER/OCBQ/DCM/APLB

**Through:** Lisa L. Stockbridge, Ph.D.  
CBER/OCBQ/DCM/APLB

**Subject:** Labeling Review  
**VAXNEUVANCE (pneumococcal 15-Valent conjugate vaccine [CRM197 Protein])**  
**STN # 125741/0**

**Sponsor:** Merck Sharp and Dohme Corp.

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**Background:** The sponsor submitted:

New Approval  
 Changes Being Effected (CBE) supplement  
 Prior Approval Supplement (PAS) Amendment  
 Major Amendment

Submission contains:

Prescribing Information (PI)  
 Patient Package Insert (PPI)  
 Package and/or container labels  
 Other (Medication Guide)

Submission Date: November 17, 2020

Action Due Date: July 18, 2021

## APLB Comments/Recommendations

Merck Sharp and Dohme Corp. submitted a Biologics License Application (BLA) for VAXNEUVANCE (pneumococcal 15-Valent conjugate vaccine [CRM197 Protein]) seeking approval for the active immunization for the prevention of invasive pneumococcal disease caused by *Streptococcus pneumoniae* serotypes (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F) in adults 18 years of age and older.

APLB has reviewed the draft PI and labels from a promotional and comprehension perspective and offer the following comments:

### GENERAL COMMENTS

- Use command language or active voice wherever possible (e.g. DOSAGE AND ADMINISTRATION; CLINICAL STUDIES).
- Avoid research terminology (e.g., Phase 1, 2, 3, pivotal), as not all end users are academic researchers. Simply describe the clinically significant data regarding safety and effectiveness.
- Overuse of the vague term, *generally*, hinders readability and comprehension.

### HIGHLIGHTS

- Directly under the heading, **DOSAGE AND ADMINISTRATION**, please include the bolded, sentence case statement “**For intramuscular use only.**”
- In **CONTRAINDICATIONS**, include likely candidate components that could cause a severe hypersensitivity reaction (e.g., aluminum phosphate, polysorbate 20).
- Ensure that at least one warning and precaution is reflected in the **WARNINGS AND PRECAUTIONS** section of the **HIGHLIGHTS**.
- Since this is a new application, please remove *Revised: [date]*.

### FULL PRESCRIBING INFORMATION: CONTENTS

Ensure that the table of contents reflects the sections and regulatory subsections of the **FULL PRESCRIBING INFORMATION**.

### FULL PRESCRIBING INFORMATION (FPI)

#### 2 DOSAGE AND ADMINISTRATION

- Immediately following the heading, **DOSAGE AND ADMINISTRATION**, please bold the statement: **For intramuscular use only.**
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- For consistency with similar biologic product labeling, please organize this section into two or three subsections (see below) and place related information under the correct subheading. For example, the subsection on dosage should not start with “Administer...”

- **2.1 Dose**
- **2.2 Administration**

or

- **2.1 Dose**
- **2.2 Preparation**
- **2.3 Administration**

- For readability and comprehension, revise this section to active voice.

#### 4 CONTRAINDICATIONS

Due to the fact that all stylesheets will not include all sections of the content of labeling, it is advisable that this section include likely candidate components that could cause a severe hypersensitivity reaction (e.g., aluminum phosphate, polysorbate 20) in addition to the cross reference to **11 DESCRIPTION**.

#### 6 ADVERSE REACTIONS

- Directly beneath the section heading restate the most common adverse reactions, along with a cut-off frequency, that is found in the **HIGHLIGHTS**.
- Any event associated or potentially associated with the vaccine is an *adverse reaction*. Subsection 6.1 should not include anything other than adverse reactions. Therefore, there should not be a heading *Serious Adverse Events*. (See 21 CFR §201.57(c)(7) and *Guidance for Industry: Adverse Reactions Sections of Labeling for Human Prescription Drug and Biological Products – Content and Format*)

#### 12 CLINICAL PHARMACOLOGY

Please add the following required subsections:

- 12.2 Pharmacodynamics
- 12.3 Pharmacokinetics

#### 15 REFERENCES

- Limit references to circumstances where labeling must summarize or otherwise rely on recommendations from an authoritative scientific body, standardized methodology, scale, technique, or similar information important to the safe and effective use of the product, that cannot readily be summarized and requires a reference to the source of the information. (See 21 CFR §201.57(c)(16))

- References listed must be cited in the text of the FPI using a numerical superscript.
- List references in numerical order.

## **PATIENT PACKAGE INSERT (PPI)**

### General

Please align the PPI with 21 CFR §208.20 (section and content). The sections are as follows:

- "What is the most important information I should know about (name of drug)?"
- "What is (name of drug)?"
- "Who should not take (name of drug)?"
- "How should I take (name of drug)?"
- "What should I avoid while taking (name of drug)?"
- "What are the possible or reasonably likely side effects of (name of drug)?"

### What is the TRADEMARK?

- The explanation of Pneumococcal disease is not in patient-friendly language and will negatively impact the comprehension of the PPI. We recommend revising this explanation. It is not necessary to go into the disease types in this document.
- The statement, "*These infections are more likely to occur in older people,*" may cause younger patients to reject the vaccine. We recommend revising this statement.

### What are possible side effects of TRADEMARK?

Please delete the following the sentence because it is promotional in tone:

- "These side effects are generally mild and last a short time."

### What if I have other questions?

We recommend deleting this section as it appears to be a means to solicit "unsolicited" contact with Merck.

## **PACKAGE/CONTAINER LABELS**

The proper name should be printed in letters that are at least half as large as the letters of the proprietary name (See 21 CFR §610.62; FD&C Act §502[USC 352](e)(1)(B)).

If you have any questions regarding this review please contact Michael Brony, Pharm.D. at 240-402-8898.

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