CLINICAL UPDATE

Brand Name	Vaxneuvance™
Generic Name	pneumococcal 15-valent Conjugate Vaccine
Drug Manufacturer	Merck Sharp & Dohme Corp.

Clinical Update

TYPE OF CLINICAL UPDATE

New brand

FDA APPROVAL DATE

July 16, 2021

LAUNCH DATE

October 20, 2021

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Biologics License Application (BLA)

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION(S) FOR USE

Vaxneuvance™ is a vaccine indicated for active immunization for the prevention of invasive disease by caused *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.

MECHANISMS OF ACTION

Protection against invasive disease is conferred mainly by opsonophagocytic killing of S. pneumoniae. Vaxneuvance™ induces opsonophagocytic activity against the serotypes contained in the vaccine.

DOSAGE FORM(S) AND STRENGTH(S)

Suspension for injection (0.5 mL dose), supplied as a single-dose prefilled syringe.

DOSE & ADMINISTRATION

For intramuscular use only.
Administer a single 0.5 mL dose.

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EFFICACY

The Vaxneuvance™ Phase 3 program includes a total of 16 trials evaluating its safety, tolerability, and immunogenicity. Vaxneuvance™ was approved based on results from four Phase 3 clinical trials in patients 18 years of age and older. These trials are summarized in Table.

Table: Vaxneuvance ™ Phase 3 Clinical Trials

Trial	Population	Dose/Design	Immunologic Response
Study 1: PNEU-AGE (NCT03950622)	Unvaccinated adults 50 years of age and older in good health with stable chronic conditions*	Single dose of Prevnar 13 (N = 601) or Vaxneuvance™ (N = 604)	Vaxneuvance™ was noninferior to Prevnar 13 for the 13 serotypes common to both vaccines based on OPA GMTs, and superior to Prevnar 13 for serotype 3, 22F, and 33F.
Study 3: PNEU-PATH (NCT03480763)	Unvaccinated adults 50 years of age and older in good health	Single dose of Vaxneuvance™ (N = 327) or Prevnar 13 (N = 325); all patients received Pneumovax 23 vaccine 1 year later	OPA GMTs following the administration of Pneumovax 23 were similar in both groups for the 15 pneumococcal serotypes in Vaxneuvance™. At 1 month following Vaxneuvance™ or Prevnar 13, immune responses were comparable for the 13 serotypes common to both vaccines.
Study 4: PNEU-DAY (NCT03547167)	Unvaccinated adults 18–49 years of age, including those at higher risk of pneumococcal disease due to an underlying medical condition, smoking, or alcohol consumption	Single dose of Vaxneuvance™ (N = 1135) or Prevnar 13 (N = 380); all patients received Pneumovax 23 vaccine 6 months later	Following vaccination with Pneumovax 23, the OPA GMTs for the 15 serotypes in Vaxneuvance™ were numerically similar among all subjects regardless of whether they initially got Vaxneuvance™ or Prevnar 13. OPA GMTs at 30 days post-vaccination with Vaxneuvance™ or Prevnar 13 were comparable in both groups for the 13 serotypes common to both vaccines.
Study 6: PNEU-FLU (NCT03615482)	Adults 50 years of age and older in good health. Chronic conditions were documented to be stable. Patients who had received Pneumovax 23 more than 1 year prior to study enrollment were eligible.	Single dose of Vaxneuvance™ concomitantly administered with an inactivated QIV (Fluarix Quadrivalent) (N = 600) or Vaxneuvance™ administered 30 days after receiving QIV (N = 600)	Pneumococcal vaccine serotype OPA GMTs were evaluated 30 days after administration of Vaxneuvance™ and influenza vaccine strain HAI GMTs were evaluated 30 days after QIV. Noninferiority in GMTs were met for the 15 pneumococcal serotypes in Vaxneuvance™ and for the 4 influenza vaccine strains tested.

In the PNEU-AGE trial, Vaxneuvance™ demonstrated superior immunogenicity for serotype 3 compared with Prevnar 13. Serotype 3 is the leading cause of invasive pneumococcal disease among adult patients in the United

States, despite its inclusion in all FDA-approved pneumococcal vaccines. However, it is worthwhile to note that the PNEU-AGE trial was not designed as a head-to-head trial comparing Vaxneuvance™ to Prevnar 13; therefore, the significance of this result is unclear. Additionally, although increased immunogenicity may be expected to translate to a reduction in clinical illness, this outcome has not been measured in clinical trials to date.

Preliminary results are also available from the Phase 3 PNEU-TRUE trial which demonstrated a consistent immune response to all 15 serotypes across 3 different vaccine lots, and the PNEU-WAY trial (which confirmed that immunogenicity was stimulated to all 15 serotypes in adult patients with human immunodeficiency virus (HIV). The Phase 3 PNEU-STEM trial a study in patients who have undergone hematopoietic stem cell transplant (HSCT), is currently underway. All trials include Prevnar 13 as the comparator.

Safety

Safety was monitored using a Vaccination Report Card (VRC) for up to 14 days following vaccination. Oral body temperature and injection-site reactions were solicited on Days 1–5 after vaccination. Systemic adverse reactions (ARs) were solicited on Days 1–14 post-vaccination. Unsolicited adverse events (AEs) were reported on Days 1–14 following vaccination. Safety follow-up for serious adverse events (SAEs) ranged from 1 to 12 months, depending on the study.

The most frequently reported solicited ARs in patients 18–49 years of age were injection-site pain (76%), fatigue (34%), myalgia (29%), headache (26%), injection-site swelling (22%), injection-site erythema (15%), and arthralgia (13%). In adults 50 years of age and older, the most commonly reported solicited ARs were injection-site pain (67%), myalgia (27%), fatigue (22%), headache (19%), injection-site swelling (15%), injection-site erythema (11%), and arthralgia (8%).

Serious AE rates within 30 days after vaccination were 0.4% for Vaxneuvance™ and 0.7% for Prevnar 13. In the subset of patients followed for 6 months after vaccination, the rate of SAEs was 2.5% for Vaxneuvance™ and 2.4% for Prevnar 13.
The safety profile of Vaxneuvance™ was similar when administered with and without the quadrivalent influenza vaccine (QIV) in the PNEU-FLU trial.

Abbreviations: GMT, geometric mean titer; HAI, hemagglutination inhibition; OPA, opsonophagocytic activity; QIV, quadrivalent influenza vaccine.

*Chronic conditions were considered stable based on the investigator's judgement.