

Category

Best Biotechnology Product

Drug / Device Name

VAXNEUVANCE Suspension for Intramuscular injection

Compound/ Tech Name

VAXNEUVANCE (Pneumococcal 15-valent Conjugate Vaccine)

Trade Name

VAXNEUVANCE

Date of Approval

2022-06-17

Indications

Vaxneuvance™ is indicated for active immunization for the prevention of invasive disease caused by *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F in individuals 6 weeks of age and older.

Therapeutic Categories

Vaccine for the prevention of pneumococcal disease

Background information and need for drug/device

Streptococcus pneumoniae remains a major cause of vaccine-preventable disease worldwide despite the significant public health impact of currently available pneumococcal vaccines. After the implementation of universal vaccination of children <5 years of age with pneumococcal conjugated vaccines (PCV) in the US and other countries, the distribution of pneumococcal serotypes has evolved. With the exception of serotype 3, which is included in Prevnar 13™, the overall incidence of pneumococcal disease (PD) due to serotypes included in currently licensed pediatric PCVs has decreased significantly in all age groups in countries and regions where PCVs are routinely used in infant immunization schedules. However, PCV introduction has led to an increase in the absolute and proportional burden of disease due to non-vaccine serotypes. Because of the severity of invasive PD and the health-care burden of residual disease, prevention of pneumococcal disease remains an unmet medical need.

New PCVs are needed to address the evolving serotype landscape and improve on the public health benefit worldwide. There are several critical characteristics for new pneumococcal vaccines: a) they must maintain disease suppression at current levels in order to prevent increase in breakthrough disease caused by serotypes already included in these vaccines, especially in vulnerable infants under 1 year of age (the target population for PCV vaccination), b) they must address limitations in the effectiveness of licensed PCVs against disease caused by serotypes included in these vaccines, such as serotype 3, and lastly, c) they must also address emergence of pneumococcal disease caused by

prevalent serotypes not included in licensed PCVs.

Vaxneuvance™ addresses these key factors based on its serotype composition and clinical immunogenicity and safety profiles. Vaxneuvance™ is composed of the 13 serotypes included in the licensed Prevnar 13™ (PCV13), which is currently the standard-of-care (SOC) in US infants, plus serotypes 22F and 33F. These additional serotypes have been associated with serious clinical outcomes (including meningitis, bacteremia, sepsis, bacteremic pneumonia and septic arthritis), which indicate their relatively high degree of severity in comparison to other serotypes not currently covered by licensed PCVs. Moreover, serotypes 22F and 33F have demonstrated resistance to several important classes of antibiotics. Furthermore, Vaxneuvance™ induces substantially higher immune responses than Prevnar 13™ against serotype 3, a notoriously poor immunogen. Serotype 3 is a key contributor to pneumococcal disease burden in the post-PCV era and as such is a serotype of great public health importance. Notably, despite its inclusion in Prevnar 13™, serotype 3 has persisted with little change in disease incidence in many countries who have implemented Prevnar 13™ into infant immunization programs.

History of the development of the drug/device

Vaxneuvance™ was judiciously designed to address the current unmet medical need in the burden of pneumococcal disease prevention by maintaining robust protection against disease caused by *S. pneumoniae* serotypes already included in Prevnar 13™, improving immune responses to the recalcitrant serotype 3 (shared with Prevnar 13™), and expanding coverage to 2 serotypes (22F and 33F) of substantial public health importance.

Clinical development of Vaxneuvance™ was initiated in 2009. Seven early phase (Phase 1/2, Phase 2) studies were conducted to evaluate different formulations of Vaxneuvance™. Although safety and immunogenicity profiles of an earlier formulation of Vaxneuvance™ were acceptable in adults (V114-002), immune responses of the same formulation in infants (V114-003) were significantly lower than the licensed Prevnar 13™ for some shared serotypes, underscoring a need to optimize the vaccine formulation. Several modifications were made to the drug substance manufacturing process for a subset of serotypes and final formulation of the drug product to improve the clinical performance of the investigational PCV in infants, which was successfully achieved (V114-005) and later confirmed in larger Phase 2 studies (V114-008 in children and V114-006 in older adults). The safety and immunogenicity profiles of the new and improved vaccine formulation were subsequently evaluated in 16 pediatric and adult Phase 3 clinical trials to support the licensure of Vaxneuvance™. The adult indication was approved by US-FDA on 16-Jul-2021 and the pediatric on 17-Jun-2022, with additional approvals in more than 50 countries globally to date. Notably, Vaxneuvance™ was the first PCV licensed in over a decade since Prevnar 13™ was introduced in 2009, potentially strengthening global supply and access.

The Vaxneuvance™ Pediatric Phase 3 Program was designed to generate a robust safety and immunogenicity profile to comprehensively characterize the vaccine's performance in pediatric populations with the greatest burden of PD for whom vaccination is indicated, specifically infants <1 year of age and individuals at increased risk for pneumococcal disease due to immunocompromising medical conditions. The program includes immunogenicity and safety data from 9 key studies, comprised of >8500 participants: 3 pivotal studies in infants, evaluating 3+1 dosing (V114-029) and 2+1 dosing (V114-025, V114-026); 3 supportive studies, evaluating PCV-switch in infants (V114-027) and catch-up vaccination (V114-024), which are important to advise health-care personnel incorporating Vaxneuvance™ into their practice, as well as the large safety study in infants (V114-031); and 3 studies in special populations at increased risk for invasive pneumococcal disease: children with Sick Cell

Disease (V114-023), children living with HIV (V114-030), and hematopoietic-stem-cell-transplant recipients (V114-022). The clinical program also included over 300 infants born before term (<37 weeks gestational age at birth) as these infants are at increased risk for PD given their immunological immaturity and vulnerability to infections. Additionally, an ongoing study is evaluating the efficacy of V114 in the prevention of acute otitis media (V114-032).

The conclusions of the pediatric program are that Vaxneuvance™ is well tolerated, robustly immunogenic to all 15 serotypes, and superior to Prevnar 13™ for the shared serotype 3, and as such is expected to confer protection against all 15 vaccine serotypes. Importantly, immune responses in infancy, when children are most vulnerable to deadly invasive pneumococcal diseases, were robust in comparison to Prevnar 13™, without significant loss of immunogenicity for the 13 shared serotypes. Therefore, Vaxneuvance™ has the potential to significantly address the burden of remaining pneumococcal disease due to vaccine-types and leading non-vaccine types in children.

Why this drug or device is innovative, the broad implications for future research, and/or how it will improve the human condition

For the last two decades, PCVs from only one manufacturer have been licensed in the US. Development of Vaxneuvance™ represents a bold and innovative conception in the manufacturing process of glycoconjugates. The goal was for Vaxneuvance™ to display a safety profile comparable to the SOC, and to induce robust immune responses to all 15 vaccine serotypes, at levels comparable to Prevnar 13™ for shared serotypes while also improving immunogenicity against serotype 3. Availability of a well-tolerated and effective PCV, like Vaxneuvance™, provides an opportunity to further decrease the burden of pneumococcal disease worldwide in a cost-effective way, particularly for vulnerable populations at risk for serious disease and poor outcomes, such as infants. A health economic model in children developed by the CDC demonstrated that Vaxneuvance™ is cost saving as compared to the SOC, Prevnar 13™, meaning, total costs are reduced, and health outcomes are improved with Vaxneuvance™ as compared to the routine use of Prevnar 13™ in the US. Moreover, if indirect effects from the vaccinated cohort to older individuals is included, then total societal benefits would be even greater. Another health economic model demonstrated that a pediatric Vaxneuvance™ vaccination program in the US was cost saving and may be associated with additional disease prevention compared with the SOC during a 100-year time horizon. In this model, Vaxneuvance™ was associated with prevention of additional 185,711 cases of invasive pneumococcal disease (IPD), 987,727 cases of pneumonia, 11,151,473 cases of acute otitis media, 3,592 cases of post-meningitis sequelae, 20,197 cases of IPD deaths, and 41 cases of pneumonia deaths, as compared with Prevnar 13™. Additional life-years saved was estimated at 371,219 compared with an existing Prevnar 13™ program. With the expectation that Vaxneuvance™ will further reduce pneumococcal disease incidence in children and adolescents, the CDC Advisory Committee on Immunization Practices recommended use of Vaxneuvance™ as an option for pediatric and adolescent pneumococcal vaccination on 22-Jun-2022.

The aforementioned health economic models assume equal protection against shared serotypes, including serotype 3, for Vaxneuvance™ and Prevnar 13™. However, a model predicting the effectiveness of Vaxneuvance™ against invasive PD in a US pediatric population based on immunogenicity results demonstrated that while protection would be largely comparable to that of Prevnar™/Prevnar 13™ for the shared serotypes, a higher overall benefit would be gained from increased serotype 3 effectiveness with Vaxneuvance™, leading to fewer cases of breakthrough disease.

As the distribution of pneumococcal serotypes causing disease is dynamic, especially in response to

the introduction of new PCVs, continued vaccine innovation will remain important to address future prevention needs. Development of Vaxneuvance™ will help in designing new vaccines that could address the continued morbidity and mortality associated with pneumococcal disease in children and adults. Translating basic science advances into effective vaccines will continue to be challenging. Building on knowledge, experience, and capabilities of Vaxneuvance™ and other PCVs may enable development of new vaccines in the future.

Please provide appropriate references (ie Pubmed links)

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