Pneumococcal 21-valent conjugate vaccine (CAPVAXIVE) Monograph
November 2024

VA Pharmacy Benefits Management Services, Medical Advisory Panel, and VISN Pharmacist Executives

Abbreviations: MOA=mechanism of action n=number of patients; TBD=to be determined; VANF=VA National Formulary; GBS=Guillain-Barre syndrome

FDA Approval	**Description/MOA**	CAPVAXIVE (PCV21) is a 21-valent conjugate pneumococcal vaccine, of purified capsular polysaccharides from 21 serotypes (ST) of *Streptococcus pneumoniae,* which induces an immune response against those vaccine serotypes, measured as opsonophagocytic activity (OPA). An OPA titer predictive of protection has not been established for any pneumococcal conjugate vaccine.
	Indication(s) Under Review	Approved by FDA on 6/17/24 the prevention of invasive pneumococcal disease (IPD) and pneumonia caused by serotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F, and 35B in individuals 18 years of age and older
	Dosage Form(s)	Supplied as a single-dose prefilled syringe (refrigerated)

Clinical Evidence	**Study/Design**	**PCV21 was approved using immunobridging data from several studies, comparing immune responses, as OPA geometric mean antibody titers (GMTs) and proportion of individuals achieving ≥ 4-fold rise in OPA responses at 30 days post-vaccination compared with other pneumococcal vaccines. All studies were randomized, blinded active-controlled trials. No clinical efficacy data are available.** **ACIP completed a GRADE review in February 2024 of 6 studies (STRIDE-3/4/5/6/7 and 1 phase 2 trial).** **Phase 2:** immunogenicity/safety PCV21 vs. PPSV23 in **508 vaccine-naive adults ≥ 50 years** **STRIDE-3:** Immunogenicity/safety PCV21 or 20-valent pneumococcal conjugate vaccine (PCV20) in 2356 vaccine naïve adults ≥ 50 years (cohort 1) or and 300 18-49 years old (cohort 2). *This was the pivotal study supporting the FDA indication for IPD and pneumonia*. **STRIDE-4:** Immunogenicity/safety/lot consistency PCV21 vs. PPSV23 in **2162 adults 18-49 years old with underlying chronic conditions that increase risk of IPD** **STRIDE-5:** Immunogenicity/safety concomitant PCV21 and Influenza vaccine in 1080 adults ≥ 50 yrs **STRIDE-6**: Immunogenicity/safety in **717 Adults ≥50 years old who previously received at least one prior pneumococcal vaccine**. Subject were randomized to 3 cohorts based on prior pneumococcal vaccine. Cohort 1 = prior PPSV23 comparing PCV21 vs. PCV15, cohort 2 was prior PCV13 and compared PCV21 to PPSV23 and cohort 3 received open label PCV21 (had prior exposure to any prior pneumococcal vaccine(s) other than PPSV23 alone). **STRIDE 7:** Immunogenicity/safety PCV21 vs. PCV15 + PPSV23 in **313 adults living with HIV**. Other trials are available or ongoing but were not included in the ACIP analysis (STRIDE-8, 9 and 10)
	Demographics	Across all studies, mean age 54 years; male (43%); race (76% white, 10% black, 10% Asian) 34% had at least 1 prespecified comorbidity that is known to increase risk of pneumococcal disease (diabetes, renal disorders, chronic heart disease, chronic lung disease, chronic liver disease, alcoholism)
	Results	**Across all trials, PCV21 consistently had comparable OPA GMTs for shared vaccine ST, and higher OPA GMTs for the vast majority of ST unique to PCV21 in both PCV vaccine naïve and previously vaccinated subjects, meeting criteria for non-inferiority. STRIDE 3 was the primary trial the FDA used for approval of PCV21. In that trial** **GRADE review in those who were recommended to receive PCV:** - PCV21 noninferior for 9/9 shared and superior in 12/12 unique ST vs. PPSV23 - PCV21 noninferior for 10/10 shared and 10/11 unique ST vs. PCV20 - PCV21 noninferior for 1-4/6 shared and all unique ST vs. PCV15 **Similar results noted when looking at other populations, including** - **Adults 50-64 without risk based indication** - **Adults 19-49 without risk based indication**
	Limitations	Lack of clinical data, and the antibody response that is protective is unknown, although this applies to all Pneumococcal conjugate vaccines (PCV13, PCV15, PCV20 and PCV21).

		Some serotypes of current vaccines not included, most notably serotype 4, which has been found in higher rates in some populations, such as homeless adults (100-300 times higher serotype 4 IPD) and adults in Alaska (88-fold increase in serotype 4 incidence in 2019-2020 compared with 2011-2018)
	Summary	PCV21 was shown to be noninferior to PCV20 by immunobridging for all shared strains and superior to PCV20 for all serotypes unique to PCV21 with the exception of 1 (15C). Data from the CDC from 2018-2022 noted that PCV21 covered 85% coverage of serotypes responsible for IPD compared to 54% with PCV20 in those aged ≥ 65 years. In those 19-64 with a risk based indication, coverage for IPD strains was 81% with PCV21 versus 58% with PCV20.

Safety	**Boxed Warnings**	None
	Contraindications	History of severe allergic reaction to any component of the CAPVAXIVE or diphtheria toxoid
	Warnings/ Precautions	Prevention and management of allergic reactions, syncope (after administration) Those who are immunocompromised may have a diminished response
	Adverse reactions (AE)	Solicited AEs were similar between CAPVAXIVE and comparators. Injection site pain, fatigue and headache were the most commonly reported AEs. Rates and severity of solicited AEs was similar with or without concomitant influenza vaccine. No cases of Guillain Barre syndrome reported in the clinical trials

Alternatives	Status	Clinical Guidance	Other Considerations
PCV21 (CAPVAXIVE)	TBD	FDA approved single dose to prevent against 21 serotypes of *S.pneumo* Covers more serotypes associated with IPD in adults and pneumonia in recent surveillance	Adverse events similar other PCV vaccines Lacks coverage for serotype 4, which is more common in certain populations (homeless and Alaska natives)
PCV20 (PREVNAR 20)	F	FDA approved single dose to protect against 20 serotypes of *S.pneumo.* Coverage for serotype 4, which is more common in certain populations	Adverse events – expected local AEs primarily Only covers around 50% of strains of IPD vs. 85% for PCV21
PCV15 (VAXNEUVANCE)	F	FDA approved single dose, followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23) to protect against 15 serotypes of *S.pneumo.* Coverage for serotype 4, which is more common in certain populations	Requires a follow-up dose of PPSV23 for complete coverage Adverse events – expected local AEs

Conclusions/Projected Place in Therapy

- **Current ACIP recommendations, as of October 2024, ACIP recommend ALL adults ≥ 50 years old, regardless of underlying conditions get a single dose of PCV20, PCV21 or PCV15 (the latter followed by a dose of PPSV23), with no preference.**
- PCV21 is not PCV20 + 1 additional serotype. It was developed specifically to cover IPD serotypes that cause disease in adults, versus a variation of a pediatric vaccine. PCV20 and PCV21 cover 10 common serotypes, with 11 unique to PCV21 and 10 unique to PCV20. PCV21 covers 85% of ST associated with adult IPD vs. 54% for PCV20.
    - For situations where high incidence of ST 4 is suspected (> 30% of IPD cases), PCV15 or PCV20 may be preferred,. CDC's Active Bacterial Core Surveillance (ABC) noted high percentages of ST 4 in Alaska, Colorado, the Navajo Nation, New Mexico and Oregon. Other areas (midwestern, eastern and southern regions) have not detected significant percentages of ST4). CDC surveillance is ongoing and will be updated at a future time.
- The GRADE review presented to ACIP in February 2024 documented that PCV21 met non-inferiority criteria for shared serotypes and superiority for nearly all unique serotypes when compared with PCV20. Similar results were noted compared with PCV15. Adverse events appear to be largely similar across all 3 PCV vaccines.

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