AHP & MHA Clinical Spotlight: Prevnar 20™ (pneumococcal 20-valent conjugate vaccine), Wyeth Pharmaceuticals, a subsidiary of Pfizer, Inc.

Overview of Prevnar 20™

Prevnar 20™ was FDA-approved via an accelerated approval pathway and is indicated to prevent invasive disease and pneumonia from 20 different serotypes of *Streptococcus pneumoniae* (*S. pneumoniae*) in adults 18 years of age and older.

Overview of Pneumococcal Disease

Pneumococcal disease is categorized as invasive (ie, meningitis, bacteremia, bacteremic pneumonia) or non-invasive (ie, non-bacteremic pneumonia, acute otitis media, sinusitis).[1] Invasive pneumococcal disease most commonly presents as bacteremic pneumococcal pneumonia, characterized by abrupt onset of febrile illness accompanied by symptoms including productive cough, dyspnea, productive cough with rusty sputum, hypoxia, and weakness.[1] These symptoms overlap with symptoms of pneumonia from other causes.

Pneumococcal pneumonia can affect patients of all ages. However, it poses a greater risk for morbidity and mortality in patients who are 65 years of age and older, 2 years of age and younger, immunocompromised, have pre-existing medical conditions (ie, cardiovascular disease, chronic obstructive pulmonary disease [COPD], liver disease, diabetes, cerebrospinal fluid leaks), have cochlear implants, and smoke cigarettes.[1] The mortality risk following hospitalization from community-acquired pneumonia (as opposed to hospital-acquired pneumonia) can remain increased for more than ten years.[1]

Community-acquired pneumonia negatively impacts quality of life, even after recovery from illness, particularly in the older population. For example, mobility may be compromised up to six months following active illness. In addition, patients with chronic respiratory disease, such as emphysema or COPD, tend to take longer to return to baseline productivity levels (up to 60 days).[1] In addition to the burden on the quality of life, pneumonia presents an economic burden with projected healthcare costs, mainly fueled by hospitalizations, to increase by $2.5 billion each year.[1] Indirect costs associated with community-acquired pneumonia are also significant and include time off from work and loss of productivity.

Three-quarters of pneumococcal pneumonia cases are non-bacteremic. However, in cases of invasive pneumococcal disease, *S. pneumoniae* is the pathogen responsible for up to half of cases with known etiology. Although there are over 95 serotypes of *S. pneumoniae*, ten are responsible for more than 60% of invasive pneumococcal disease cases.[1] *S. pneumoniae* is carried primarily by young children; however, *S. pneumoniae* can be found in the nasopharynx of up to 90% of healthy people.[1] The transmission of this pathogen is through respiratory tract droplets, and its spread is related to crowds, season, and the presence of upper respiratory infection.[1]

Prevention of pneumococcal pneumonia and invasive disease is through the usual infection control measures (such as hand washing, surface disinfecting, and containing coughs and sneezes), and also via vaccination. There are two types of pneumococcal vaccines: the pneumococcal polysaccharide vaccine (PPSV23), which contains polysaccharide antigen from 23 types of pneumococcal bacteria, and pneumococcal conjugate vaccines (PCVs), which are conjugated to a nontoxic variant of the diphtheria toxin.[2] PCVs cover a certain number of *S. pneumoniae* serotypes. PCV-7 became available in 2000, followed by PCV-13 in 2010 (replacing PCV-7), PCV-20 (Prevnar 20™) in June 2021, and PCV-15 in July 2021.[1,3] PPSV23 and PCV-13 are approved for use in children and adults; PCV-15 and Prevnar 20™ are FDA-approved for use in adults only.[3] The additional serotypes addressed by Prevnar 20™ (ie, not included in PCV13 or CV15) are responsible for up to 18% of cases of invasive pneumococcal disease.[1]

Prevnar 20™: Place in Therapy

Prevnar 20™ was developed to provide broader coverage among the currently marketed PCVs. To that end, the Center for Disease Control's Advisory Committee on Immunization Practices (ACIP) recently issued its recommendations on the role of Prevnar 20™ as well as other pneumococcal vaccines. Table 1 summarizes the recommendations, published in *Morbidity and Mortality Weekly Report* (https://www.cdc.gov/mmwr/volumes/71/wr/mm7104a1.htm?s_cid=mm7104a1_w).

Table 1: Place in Therapy – Pneumococcal Vaccines[1]

Product	ACIP Guideline Recommendations	For use in Children (Y/N)?	*S. pneumoniae* Serotypes covered
Prevnar 20™ (PCV20)	Adults ≥ 65 years of age who have not been vaccinated with a pneumococcal conjugate vaccine (or with unknown vaccination history): either PCV15 or Prevnar 20™. (Patients who receive PCV15 should then receive a dose of PPSV23, usually ≥ 1 year later) Adults ≥ 19 years of age with risk factors or medical conditions warranting vaccination for pneumococcal disease who have not been vaccinated with a pneumococcal conjugate vaccine (or with unknown vaccination history): either PPV15 or Prevnar 20™. (Patients who receive PCV15 should then receive a dose of PPSV23, usually ≥ 1 year later) Adults with previous PPSV23 only: Adults who have only received PPSV23 may receive a PCV (either PCV20 or PCV15) ≥1 year after their last PPSV23 dose. When PCV15 is used in those with history of PPSV23 receipt, it need not be followed by another dose of PPSV23. Adults with previous PCV13: The incremental public health benefits of providing PCV15 or PCV20 to adults who have received PCV13 only or both PCV13 and PPSV23 have not been evaluated. These adults should complete the previously recommended PPSV23 series. (For adults who have received PCV13 but have not completed their recommended pneumococcal vaccine series with PPSV23, one dose of PCV20 may be used if PPSV23 is not available.)	No	1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F
PPSV23		Yes	1, 2, 3, 4, 5, 6B, 7F, 8, 9N, 9V, 10A, 11A, 12F, 14, 15B, 17F, 18C, 19F, 19A, 20, 22F, 23F, and 33F
PCV15		No	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 22F, and 33F
PCV13	Not included in recommendations	No	1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

(ACIP: Center for Disease Control's Advisory Committee on Immunization Practices)

Prevnar 20™: Clinical Studies

Study 1[1,4]: Prevnar 20™ in pneumococcal vaccine-naïve adults

This phase 3, randomized, double-blinded study was conducted to investigate the immunogenicity and safety of Prevnar 20™ compared to PCV13 and PPSV23. The primary endpoint was immune responses as measured by opsonophagocytic activity (OPA) assay (which measured functional antibodies to *S. pneumoniae*). The study population included healthy and immunocompetent adults. Patients with unstable medical conditions, defined as a condition requiring significant change in therapy in the previous six weeks or any hospitalization for worsening disease in the previous 12 weeks, were excluded from the trial.[4] Other exclusion criteria included prior vaccination for pneumococcal disease.

Researchers randomized pneumococcal vaccine-naïve patients (within three cohorts based on age: 18–49 years [N = 448], 50–59 [N = 445], and over 60 years of age [N = 3,009]). Study participants in the 60 years and older group were randomized 1:1 to Prevnar 20™ followed one month later with saline placebo or control (PCV13 followed one month later with PPSV23) while participants in the other two groups were randomized 3:1 to Prevnar 20™ or PCV13.[1] Immune responses in patients within the Prevnar 20™ group were then assessed compared with responses in a subset of the 60 years and older cohort (ie, ages 60 to 64).

Investigators found that after one-month post-vaccination in the over 60 years of age cohort, the primary study objective of immunologic non-inferiority for Prevnar 20™'s 20 serotypes was met for all overlapping serotypes in Prevnar® 13 and six of the seven additional serotypes versus PPSV23. One of the seven serotypes (type 8) missed the criterion for non-inferiority. However, the response was consistent with that of PCV13.[1] Researchers also found that Prevnar 20™ produced serotype-specific responses to each of the 20 vaccine serotypes in the 18–49 years and 50–59 years subgroups. In addition, the responses were nearly twice that of the corresponding serotype-specific responses in the 60–64 age range.

Study 6[4]: Prevnar 20™ in adults previously vaccinated with pneumococcal vaccine

Investigators conducted a randomized, open-label clinical trial to determine immune responses to Prevnar 20™ in adults 65 years of age and older who were previously vaccinated with PPSV23 (1–5 years prior to study enrollment; "PPSV23 group"), previously immunized with PCV13 (≥6 months prior to study enrollment, "PCV13 group"), or previously vaccinated with PCV13 followed by PPSV23 (at least one year prior to study enrollment, "PCV13-PPSV23 group"). OPA geometric mean titers (GMTs) were compared between these three study groups. Study results were as follows: patients in the PPSV23 group had diminished OPA GMTs versus those in the PCV13 group and PCV13-PPSV23 group.

Table 2: Prevnar 20™ (pneumococcal 20-valent conjugate vaccine), Wyeth Pharmaceuticals, a subsidiary of Pfizer, Inc.[4]

FDA Approved Indications, Dosage and Administration	Safety Considerations, Storage, Available Forms
Indications: for active immunization for the prevention of pneumonia and invasive disease caused by *Streptococcus pneumoniae* (*S. pneumoniae*) serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F in adults ≥18 years of age. **Dosage/Administration:** single dose. Each 0.5 mL dose is to be injected intramuscularly using a sterile needle attached to the supplied pre-filled syringe. Special populations: *Immunocompromised patients:* Safety and immunogenicity data on Prevnar 20™ are not available for immunocompromised patients. Based on experience with pneumococcal vaccines, individuals with altered immunocompetence may have reduced immune responses to Prevnar 20™. Consider vaccination on an individual basis. Prevnar 20™ recipients 70 through 79 years of age and ≥80 years of age had lower opsonophagocytic activity (OPA) geometric mean titers (GMTs) for all pneumococcal serotypes compared to Prevnar 20™ recipients 18 through 49 years, 50 through 59, and 60 through 64 years of age.	**Adverse Events:** In adults 18 through 59 years of age, the most commonly reported queried adverse reactions >10% were pain at the injection site (>70%), muscle pain (>50%), fatigue (>40%), headache (>30%), and arthralgia and injection site swelling (>10%). In adults ≥60 years of age, the most commonly reported queried adverse reactions >10% were pain at the injection site (>50%), muscle pain and fatigue (>30%), headache (>20%), and arthralgia (>10%). **Contraindications:** Severe allergic reaction (eg, anaphylaxis) to any component of Prevnar 20™ or diphtheria toxoid. **Drug Interactions:** Do not mix Prevnar 20™ with other vaccines/products in the same syringe. Individuals with impaired immune responsiveness due to the use of immunosuppressive therapy (including irradiation, corticosteroids, antimetabolites, alkylating agents, and cytotoxic agents) may not respond optimally to Prevnar 20™. **Storage:** After shipping, Prevnar 20™ may arrive at temperatures between 2˚C to 25˚C (36˚F to 77˚F). Upon receipt, store refrigerated at 2˚C to 8˚C (36˚F to 46˚F). Syringes should be stored in the refrigerator horizontally to minimize the resuspension time. Do not freeze. Discard if the vaccine has been frozen. Prevnar 20™ should be administered as soon as possible after removing from refrigeration. Prevnar 20™ can be administered as long as cumulative multiple excursion time out of refrigeration (at temperatures between 8˚C and 25˚C) does not exceed 96 hours. Cumulative multiple excursions between 0˚C and 2˚C are also permitted as long as the total time between 0˚C and 2˚C does not exceed 72 hours. **Available Forms:** 0.5 mL suspension for intramuscular injection, supplied in a single-dose pre-filled syringe.

FDA Approved Indications, Dosage and Administration	Safety Considerations, Storage, Available Forms
	Vaccine is a sterile suspension of saccharides of the capsular antigens of *S. pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F,23F, and 33F, individually linked to non-toxic diphtheria CRM197 protein. Each serotype is grown in soy peptone broth. The pre-filled syringe's tip cap and plunger stopper are not made with natural rubber latex.

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References

1. Prevnar 20 formulary submission dossier. December 2021.
2. About pneumococcal vaccines. https://www.cdc.gov/vaccines/vpd/pneumo/hcp/about-vaccine.html. Accessed January 19, 2022.
3. Epidemiology and prevention of vaccine-preventable diseases. Pneumoccal disease. https://www.cdc.gov/vaccines/pubs/pinkbook/pneumo.html#pneumococcal-vaccines. Accessed January 19, 2022.
4. Prevnar 20 [package insert]. Philadelphia, PA: Wyeth Pharmaceuticals; 2021.