



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein] (Pevnar-13™)

Effective Date 6/15/2011
Next Review Date 6/15/2012
Coverage Policy Number 1014

Table of Contents

Coverage Policy	1
General Background	1
Coding/Billing Information	3
References	3
Policy History	4

Hyperlink to Related Coverage Policies

[Routine Immunizations](#)

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

Immunizations are covered under most CIGNA medical plans which include a Preventive Benefit. Please refer to the applicable benefit plan document to determine benefit availability and the terms and conditions of coverage. Many benefit plans specifically exclude immunizations that are for the purpose of travel or to protect against occupational hazards and risks.

If coverage is available under the benefit plan, the following conditions of coverage apply:

CIGNA covers pneumococcal 13-valent conjugate vaccine [Diphtheria CRM197 Protein] (Pevnar-13™) as medically necessary in children 6 weeks through 5 years of age as recommended by the Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices (ACIP) for the prevention of invasive disease and otitis media caused by *Streptococcus pneumoniae*.

General Background

FDA Approved Indications

Pevnar 13 is a vaccine approved for use in children 6 weeks through 5 years of age (prior to the 6th birthday). Pevnar 13 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 and 23F. Pevnar 13 is also indicated for the prevention of otitis media caused by *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F. No otitis media efficacy data are available for serotypes 1, 3, 5, 6A, 7F, and 19A.

FDA Recommended Dosing

The four-dose immunization series consists of a 0.5 mL intramuscular injection administered at 2, 4, 6, and 12-15 months of age.

Drug Availability

Pre-filled syringe with 1 Dose (10 per package).

Pharmacology

Prevnar 13, Pneumococcal 13-valent Conjugate Vaccine (Diphtheria CRM197 Protein) is a sterile suspension of saccharides of the capsular antigens of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F, individually linked to non-toxic diphtheria CRM197 protein. Each serotype is grown in soy peptone broth. The individual polysaccharides are purified through centrifugation, precipitation, ultrafiltration, and column chromatography. The polysaccharides are chemically activated to make saccharides, which are directly conjugated by reductive amination to the protein carrier CRM197, to form the glycoconjugate. CRM197 is a nontoxic variant of diphtheria toxin isolated from cultures of *Corynebacterium diphtheriae* strain C7 (β 197) grown in a casamino acids and yeast extract-based medium. CRM197 is purified through ultrafiltration, ammonium sulfate precipitation, and ion-exchange chromatography. The individual glycoconjugates are purified by ultrafiltration and column chromatography and analyzed for saccharide to protein ratios, molecular size, free saccharide, and free protein. The individual glycoconjugates are compounded to formulate Pevnar 13. Potency of the formulated vaccine is determined by quantification of each of the saccharide antigens and by the saccharide to protein ratios in the individual glycoconjugates. Each 0.5 mL dose of the vaccine is formulated to contain approximately 2.2 μ g of each of *Streptococcus pneumoniae* serotypes 1, 3, 4, 5, 6A, 7F, 9V, 14, 18C, 19A, 19F, 23F saccharides, 4.4 μ g of 6B saccharides, 34 μ g CRM197 carrier protein, 100 μ g polysorbate 80, 295 μ g succinate buffer and 125 μ g aluminum as aluminum phosphate adjuvant.

Guidelines

The ACIP recommends PCV13 for all children 2 through 59 months of age and for children 60 through 71 months who have underlying medical conditions that increase their risk of pneumococcal disease or complications.

Clinical Efficacy

The safety of Pevnar 13 was evaluated in 13 clinical trials in which 4,729 infants and toddlers received at least one dose of Pevnar 13 and 2,760 infants and toddlers received at least one dose of Pevnar active control. Safety data for the first three doses are available for all 13 infant studies; dose 4 data are available for 10 studies; and data for the 6-month follow-up are available for 7 studies. The vaccination schedule and concomitant vaccinations used in these infant trials were consistent with country-specific recommendations and local clinical practice. There were no substantive differences in demographic characteristics between the vaccine groups. By race, 84.0% of subjects were White, 6.0% were Black or African-American, 5.8% were Asian and 3.8% were of 'Other' race (most of these being biracial). Overall, 52.3% of subjects were male infants. Three studies in the U.S. evaluated the safety of Pevnar 13 when administered concomitantly with routine U.S. pediatric vaccinations at 2, 4, 6, and 12-15 months of age. Solicited local and systemic adverse events were recorded daily by parents/guardians using an electronic diary for 7 consecutive days following each vaccination. For unsolicited adverse events, study subjects were monitored from administration of the first dose until one month after the infant series, and for one month after the administration of the toddler dose. Information regarding unsolicited and serious adverse events, newly diagnosed chronic medical conditions, and hospitalizations since the last visit were collected during the clinic visit for the fourth-study dose and during a scripted telephone interview 6 months after the fourth-study dose. Serious adverse events were also collected throughout the study period. Overall, the safety data show a similar proportion of Pevnar 13 and Pevnar subjects reporting serious adverse events. Among U.S. study subjects, a similar proportion of Pevnar 13 and Pevnar recipients reported solicited local and systemic adverse reactions as well as unsolicited adverse events.

Acute Otitis Media (AOM)

The efficacy of Pevnar against otitis media was assessed in two clinical trials: a trial in Finnish infants at the National Public Health Institute and the pivotal-efficacy trial in U.S. infants at Northern California Kaiser Permanente (NCKP). The Finnish Otitis Media (FinOM) trial was a randomized, double-blind trial in which 1,662 infants were equally randomized to receive either Pevnar or a control vaccine Recombivax HB (Hepatitis B

vaccine (Recombinant) [Hep B]) at 2, 4, 6, and 12-15 months of age. In this study, conducted between December 1995 and March 1999, parents of study participants were asked to bring their children to the study clinics if the child had respiratory infections or symptoms suggesting acute otitis media (AOM). If AOM was diagnosed, tympanocentesis was performed, and the middle-ear fluid was cultured. If *S. pneumoniae* was isolated, serotyping was performed; the primary endpoint was efficacy against AOM episodes caused by vaccine serotypes in the perprotocol population. In the NCKP trial, the efficacy of Prevnar against otitis media was assessed from the beginning of the trial in October 1995 through April 1998. The otitis media analysis included 34,146 infants randomized to receive either Prevnar (N=17,070), or the control vaccine (N=17,076), at 2, 4, 6, and 12-15 months of age. In this trial, no routine tympanocentesis was performed, and no standard definition of otitis media was used by study physicians. The primary otitis media endpoint was efficacy against all otitis media episodes in the per-protocol population. The vaccine efficacy against AOM episodes due to vaccine serotypes assessed in the Finnish trial, was 57% (95% CI: 44%-67%) in the per-protocol population and 54% (95% CI: 41%-64%) in the intent-to-treat population. The vaccine efficacy against AOM episodes due to vaccinerelated serotypes (6A, 9V, 18B, 19A, 23A), also assessed in the Finnish trial, was 51% (95% CI: 27, 67) in the per-protocol population and 44% (95% CI: 20, 62) in the intent-to-treat population. There was a nonsignificant increase in AOM episodes caused by serotypes unrelated to the vaccine in the per-protocol population, compared to children who received the control vaccine, suggesting that children who received Prevnar appeared to be at increased risk of otitis media due to pneumococcal serotypes not represented in the vaccine. However, vaccination with Prevnar reduced pneumococcal otitis media episodes overall. In the NCKP trial, in which the endpoint was all otitis media episodes regardless of etiology, vaccine efficacy was 7% (95% CI: 4%-10%) and 6% (95% CI: 4%-9%), respectively, in the per-protocol and intent-to-treat analyses. Several other otitis media endpoints were also assessed in the two trials. Recurrent AOM, defined as 3 episodes in 6 months or 4 episodes in 12 months, was reduced by 9% in both the per-protocol and intent-to-treat populations (95% CI: 3%-15% in per-protocol and 95% CI: 4%-14% in intent-to-treat) in the NCKP trial; a similar trend was observed in the Finnish trial. The NCKP trial also demonstrated a 20% reduction (95% CI: 2, 35) in the placement of tympanostomy tubes in the per-protocol population and a 21% reduction (95% CI: 4, 34) in the intent-to-treat population. Data from the NCKP trial accumulated through an extended follow-up period to April 20, 1999, in which a total of 37,866 children were included (18,925 in Prevnar group and 18,941 in MnCC control group), resulted in similar otitis media efficacy estimates for all endpoints.

Adverse Reactions

The most commonly reported adverse events are bronchiolitis, gastroenteritis, and pneumonia for Prevnar 13 and Prevnar respectively.

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT ^{®*} Codes	Description
90670	Pneumococcal conjugate vaccine, 13 valent, for intramuscular use

ICD-9-CM Diagnosis Codes	Description
V03.82	Need for prophylactic vaccination and inoculation against streptococcus pneumoniae [pneumococcus]

*Current Procedural Terminology (CPT[®]) © 2010 American Medical Association: Chicago, IL.

References

1. Centers for Disease Control (CDC) Morbidity and Mortality Weekly Report (MMWR). Prevention of Pneumococcal Disease Among Infants and Children — Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine Recommendations of the Advisory Committee on Immunization Practices (ACIP): December 10, 2010;59 No.RR-11). Accessed May 11, 2011. Available at <http://www.cdc.gov/mmwr/pdf/rr/rr5911.pdf>
2. GK, ed. AHFS 2011 Drug Information. Bethesda, MD: American Society of Health-Systems Pharmacists, Inc; 2011.
3. Wyeth Pharmaceuticals, Inc. Prevnar 13 (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein]) Prescribing Information. Philadelphia, PA: Wyeth Pharmaceuticals, Inc. April 2011. Accessed May 11, 2011. Available at <http://labeling.pfizer.com/showlabeling.aspx?id=501>

Policy History

<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	5-15-2010	1014	Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM197 Protein] (Prevnar-13™)

Great-West Healthcare

“CIGNA”, “CIGNA HealthCare” and the “Tree of Life” logo are registered service marks of CIGNA Intellectual Property, Inc., licensed for use by CIGNA Corporation and its operating subsidiaries. All products and services are provided by such operating subsidiaries and not by CIGNA Corporation. Such operating subsidiaries include Connecticut General Life Insurance Company, CIGNA Health and Life Insurance Company, CIGNA Behavioral Health, Inc., CIGNA Health Management, Inc., and HMO or service company subsidiaries of CIGNA Health Corporation and CIGNA Dental Health, Inc. In Arizona, HMO plans are offered by CIGNA HealthCare of Arizona, Inc. In California, HMO plans are offered by CIGNA HealthCare of California, Inc. In Connecticut, HMO plans are offered by CIGNA HealthCare of Connecticut, Inc. In North Carolina, HMO plans are offered by CIGNA HealthCare of North Carolina, Inc. In Virginia, HMO plans are offered by CIGNA HealthCare Mid-Atlantic, Inc. All other medical plans in these states are insured or administered by Connecticut General Life Insurance Company or CIGNA Health and Life Insurance Company.