Diphtheria, Tetanus, and Pertussis Vaccines

- Clinical Policy Bulletins
- Medical Clinical Policy Bulletins

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Scope of Policy

This Clinical Policy Bulletin addresses diphtheria, tetanus, and pertussis vaccines.

1. **Medical Necessity**

   Aetna considers the following vaccines medically necessary:

   1. Diphtheria, tetanus toxoid, and whole-cell or acellular pertussis vaccines as preventive services according to the recommendations of the Advisory Committee on Immunization Practices (ACIP);
   2. Combination vaccination with diphtheria-tetanus-acellular pertussis (DTaP), inactivated polio, and hepatitis B (Pediarix®, GlaxoSmithKline) as an acceptable alternative to these individual vaccines for the doses that are generally administered at 2 months, 4 months, and 6 months of age;
   3. Combination vaccination with diphtheria and tetanus toxoids and acellular pertussis, inactivated poliovirus and Haemophilus influenzae type b (Pentacel®, Sanofi Pasteur, Inc.) as an acceptable alternative to these individual vaccines in children 6 weeks through 4 years of age (prior to 5 years of age) for administration as a 4-dose series at 2 months, 4 months, 6 months, and 15 - 18 months of age;
   4. Combination vaccination with diphtheria, tetanus, acellular pertussis, and inactivated poliovirus (Kinrix™, GlaxoSmithKline) as the fifth dose in the DTaP vaccine series and the fourth dose in the inactivated poliovirus vaccine (IPV) series in children 4 through 6 years of age whose previous DTaP vaccine doses have been with Infanrix® and/or Pediarix® for the first three doses and Infanrix® for the fourth dose;
   5. Combination vaccination with diphtheria, tetanus, acellular pertussis and inactivated poliovirus (Quadracel®, Sanofi Pasteur) as the fifth dose in the DTaP vaccine series and as a fourth or fifth dose in the inactivated poliovirus vaccine (IPV) series in children 4 through 6 years of age who have received four doses of Pentacel (Sanofi Pasteur) and/or Daptacel (Sanofi Pasteur) vaccine;
   6. Combination vaccination with diphtheria, tetanus, acellular pertussis, inactivated poliovirus, Haemophilus b conjugate and hepatitis B (Vaxelis™, Sanofi Pasteur) as an acceptable alternative to these individual vaccines in children 6 weeks through 4 years of age (prior to 5 years of age) for administration as a 3-dose series at 2 months, 4 months, and 6 months of age;
   7. Boostrix (GlaxoSmithKline), a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) as a preventive service for active booster immunization against tetanus, diphtheria, and pertussis as a single dose in individuals 10 years of age and older;
   8. Adacel (Sanofi Pasteur, Inc.), a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap), as a preventive service for active booster immunization against tetanus, diphtheria, and pertussis as a single dose in individuals 10 through 64 years of age. Adacel may be used as an alternative to tetanus and diphtheria toxoids (Td) booster immunization for individuals in this age group;
   9. The Tdap vaccine

      1. As a preventive service for immunization against tetanus, diphtheria, and pertussis as a single dose in all individuals 65 years of age and older and in pregnant women regardless of prior vaccination history, or in women immediately postpartum if not administered during pregnancy;
      2. As a preventive service for immunization against tetanus, diphtheria, and pertussis as a single dose in children 7 through 10 years of age with incomplete or unknown pertussis vaccine history;

   10. A tetanus toxoid-containing immunization (e.g., DT, DTaP, Td, or Tdap) for treatment of contaminated wounds;

11. Preservative-free tetanus and diphtheria toxoids (Td) (Tenivac®, Sanofi Pasteur, Inc.) as an acceptable alternative to standard Td for medically necessary indications.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

Code	Code Description

Diphtheria, tetanus toxoid, and whole-cell or acellular pertussis vaccines (Boostrix, Adacel):

CPT codes covered if selection criteria are met:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)
+ 90472	each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)
90700	Diphtheria, tetanus toxoids, and acellular pertussis vaccine (DTaP), when administered to individuals younger than 7 years, for intramuscular use
90715	Tetanus, diphtheria toxoids and acellular pertussis vaccine (Tdap), when administered to individuals 7 years or older, for intramuscular use

ICD-10 codes covered if selection criteria are met:

Z23	Encounter for immunization

Combination vaccination with diphtheria-tetanus-acellular pertussis, and inactivated polio (DTaP-IPV) (Kinrix™, GlaxoSmithKline) (Quadracel®, Sanofi Pasteur):

CPT codes covered if selection criteria are met:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)
+ 90472	each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)
90696	Diphtheria, tetanus toxoids, acellular pertussis vaccine and inactivated poliovirus vaccine (DTaP-IPV), when administered to children 4 through 6 years of age, for intramuscular use

ICD-10 codes covered if selection criteria are met:

Z23	Encounter for immunization

Combination vaccination with DTaP, IPV, Haemophilus b conjugate and hepatitis B (VaxelisTM, Sanofi Pasteur):

CPT codes covered if selection criteria are met:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)
+ 90472	each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)
90697	Diphtheria, tetanus toxoids, acellular pertussis vaccine, inactivated poliovirus vaccine, Haemophilus influenzae type b PRP-OMP conjugate vaccine, and hepatitis B vaccine (DTaP-IPV-Hib-HepB), for intramuscular use

ICD-10 codes covered if selection criteria are met:

Z23	Encounter for immunization

Code	Code Description

***Combination vaccination with diphtheria-tetanus-acellular pertussis (DTaP), inactivated polio, and hepatitis B (Pediatrix®, GlaxoSmithKline)*:**

CPT codes covered if selection criteria are met:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)
+ 90472	each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)
90723	Diphtheria, tetanus toxoids, acellular pertussis vaccine, Hepatitis B, and poliovirus vaccine, inactivated (DtaP-HepB-IPV), for intramuscular use

ICD-10 codes covered if selection criteria are met:

Z23	Encounter for immunization

***Immunization with DTaP, DTP, tetanus toxoid (TT), or tetanus and diphtheria toxoids (Td), Tenivac® (Sanofi Pasteur)*:**

CPT codes covered if selection criteria are met:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)
+ 90472	each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)
90702	Diphtheria and tetanus toxoids adsorbed (DT) when administered to individuals younger than 7 years, for intramuscular use
90714	Tetanus and diphtheria toxoids adsorbed (Td), preservative free, when administered to individuals 7 years or older, for intramuscular use

ICD-10 codes covered if selection criteria are met:

S00.00x+ - S00.97x+ S10.0xx+ - S10.97x+ S20.00x+ - S20.91x+ S30.0xx+ - S30.98x+ S40.011+ - S40.929+ S50.00x+ - S50.919+ S60.00x+ - S60.949+ S70.00x+ - S70.929+ S80.00x+ - S80.929+ S90.00x+ - S90.936+	Superficial injury
S01.00x+ - S01.95x+ S11.011+ - S11.95x+ S21.001+ - S21.95x+ S31.000+ - S31.839+	Open wound

Code	Code Description
S41.001+ - S41.159+ S51.001+ - S51.859+ S61.001+ - S61.559+ S71.001+ - S71.159+ S81.001+ - S81.859+ S91.001+ - S91.359+	
S02.0xxB	Fracture of vault of skull, open
S02.10xB - S02.19xB	Fracture of base of skull, open
S02.2xxB	Fracture of nasal bones, open
S02.600B - S02.69xB	Fracture of mandible, open
S02.8xxB - S02.92xB	Fractures of other specified and unspecified skull and facial bones, open
S03.00x+ - S03.03x+	Dislocation of jaw [open] [Code for open wound must be included]
S06.0X0A - S06.A1XS, S06.0XAA - S06.9XAS	Intracranial injury [open] [Code for open wound must be included]
S12.000B - S12.691B S22.000B - S22.089B S32.000B - S32.19xB	Fracture of vertebral column, open
S12.8xx+, S22.20xB - S22.49xB	Fracture of rib(s), sternum, larynx, and trachea, open
S13.100+ - S13.181+ S23.100+ - S23.171+ S33.100+ - S33.39x+	Dislocation of vertebra [open] [Code for open wound must be included]
S21.301+ - S21.95x+ S31.600+ - S31.659+	Internal injury of thorax, abdomen, and pelvis [open] [Code for open wound must be included]
S22.9xxB	Fracture of bony thorax, part unspecified, open
S23.420+ - S23.429+	Dislocation of sternum [open] [Code for open wound must be included]
S32.301B - S32.9xxB	Fracture of pelvis, open
S42.001B - S42.92xB S52.001B - S52.92xB S62.001B - S69.92xB	Fracture of upper limb, open
S43.001+ - S43.396+ S53.001+ - S53.196+	Dislocation of upper limb [open] [Code for open wound must be included]

Code	Code Description
S63.001+ - S63.299+ S72.001B - S72.92xB S82.001B - S82.92xB S92.001B - S92.919B	Fracture of lower limb, open
S73.001+ - S73.199+ S83.001+ - S83.196+ S93.01x+ - S93.336+	Dislocation of lower limb [open] [Code for open wound must be included]
T20.00x+ - T32.99	Burns
Z23	Encounter for immunization

Combination vaccination with diphtheria-tetanus toxoids-acellular pertussis, inactivated poliovirus and Haemophilis influenza type b (DTaP-Hib-IPV) (Pentacel®, Sanofi Pasteur, Inc.):

CPT codes covered if selection criteria are met:

90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); one vaccine (single or combination vaccine/toxoid)
+ 90472	each additional vaccine (single or combination vaccine/toxoid) (List separately in addition to code for primary procedure)
90698	Diphtheria, tetanus toxoids, acellular pertussis vaccine, Haemophilus influenzae type b, and inactivated poliovirus vaccine (DTaP-IPV/Hib), for intramuscular use

ICD-10 codes covered if selection criteria are met:

Z23	Encounter for immunization

Background

Vaccines are available to help protect individuals against diphtheria, tetanus and pertussis (whooping cough).

The following are the types of vaccines available for diphtheria, tetanus, and pertussis (CDC, 2020a):

- DT (generic) and Td (Tenivac® and generic) which provide protection against diphtheria and tetanus;
- DTaP (Daptacel®, Infanrix®, Kinrix®, Pediarix®, Pentacel®, Quadracel®, and Vaxelis™) provides protection against diphtheria, tetanus, and whooping cough;
- Tdap (Adacel® and Boostrix®) provides protection against tetanus, diphtheria, and whooping cough.

Some of the vaccines above include protection against other diseases as well, including polio, *Haemophilus influenzae* type b disease, and hepatitis B. Note that the abbreviations used to denote diphtheria, tetanus and pertussis include upper-case letters which means the vaccine has full-strength doses of that part of the vaccine. The lower-case “d” and “p” in Td and Tdap means these vaccines use smaller (reduced) doses of diphtheria and pertussis. The “a” in DTaP and Tdap stands for “acellular,” meaning that the pertussis component contains only parts of the bacteria instead of the whole bacteria (CDC, 2020).

DTP was a vaccine that consisted of diphtheria, tetanus, and whole-cell pertussis (whooping cough). DTP has been replaced with acellular pertussis toxin (DTaP) (CDC, 2020a). Fewer side effects have been reported with the diphtheria-tetanus-acellular pertussis (DTaP) vaccines than with diphtheria-tetanus-whole-cell pertussis vaccines (DTP), thus DTaP vaccines are recommended by ACIP for all five doses in the vaccination schedule.

The routine diphtheria, tetanus, and pertussis vaccination schedule for children aged less than 7 years comprises five doses of vaccine containing diphtheria, tetanus, and pertussis antigens. Three (primary) doses should be administered during the first year of life, generally at ages 2, 4, and 6 months. To maintain adequate immunity during preschool years, U.S. Advisory

Committee on Immunization Practices (ACIP) recommends the fourth (first booster) dose for children aged 15 to 18 months. ACIP recommends the fifth (second booster) dose for children aged 4-6 years to confer continued protection against disease during the early years of schooling.

In 2019, ACIP concluded that in light of the higher cost of Tdap relative to Td and uncertainty about the impact that receipt of multiple Tdap doses would have on pertussis control and transmission, there was insufficient evidence to preferentially recommend that Tdap replace Td. However, given the reassuring safety profile and evidence of widespread use of Tdap in place of Td, to allow providers more flexibility, either Tdap or Td was recommended for use in situations when previously only Td was recommended. For 2020, ACIP recommends that either Td or Tdap be used for the decennial Td booster, tetanus prophylaxis for wound management, and for additional required doses in the catch-up immunization schedule if a person has received at least 1 Tdap dose (Havers et al., 2020).

If persons aged 7-18 years have never been vaccinated against pertussis, tetanus, or diphtheria, these persons should receive a series of three tetanus and diphtheria toxoid-containing vaccines, which includes at least 1 Tdap dose. The preferred schedule is 1 dose of Tdap, followed by 1 dose of either Td or Tdap ≥4 weeks afterward, and 1 dose of either Td or Tdap 6 - 12 months later. Persons aged 7-18 years who are not fully immunized against tetanus and diphtheria should receive 1 dose of Tdap, preferably as the first dose in the catch-up series; if additional tetanus toxoid-containing doses are required, either Td or Tdap may be used. The vaccination series does not need to be restarted for those with incomplete DTaP history, regardless of the time that has elapsed between doses (Havers et al., 2020).

For persons aged 7 - 9 years who receive a dose of Tdap as part of the catch-up series, an adolescent Tdap dose should be administered at age 11 - 12 years. If a Tdap dose is administered at age ≥10 years, the Tdap dose may count as the adolescent Tdap dose (Havers et al., 2020).

If persons aged ≥19 years have never been vaccinated against pertussis, tetanus, or diphtheria, these persons should receive a series of three tetanus and diphtheria toxoid-containing vaccines, which includes at least 1 Tdap dose. The preferred schedule is 1 dose of Tdap, followed by 1 dose of either Td or Tdap at least 4 weeks afterward, and 1 dose of either Td or Tdap 6 - 12 months later. Persons aged ≥19 years who are not fully immunized against tetanus and diphtheria should receive 1 dose of Tdap, preferably as the first dose in the catch-up series; if additional tetanus toxoid–containing doses are required, either Td or Tdap may be used (Havers et al., 2020).

In January, 2020 ACIP published general recommendations which include the following (Havers et al., 2020):

- Persons aged 11 - 18 years should receive a single dose of Tdap, preferably at a preventive care visit at age 11 - 12 years. To ensure continued protection against tetanus and diphtheria, 1 booster dose of either Td or Tdap should be administered every 10 years throughout life.
- Persons aged ≥19 years, regardless of the interval since their last tetanus or diphtheria toxoid-containing vaccine, who have never received a dose of Tdap should receive 1 dose of Tdap. To ensure continued protection against tetanus and diphtheria, booster doses of either Td or Tdap should be administered every 10 years throughout life.
- For pregnant women, no change was made to the recommendations for routine Tdap immunization during pregnancy. Pregnant women should receive 1 dose of Tdap during each pregnancy, irrespective of their history of receiving the vaccine. Tdap should be administered at 27 - 36 weeks' gestation, preferably during the earlier part of this period, although it may be administered at any time during pregnancy.

A tetanus toxoid-containing vaccine is indicated for wound management when >5 years have passed since the last tetanus toxoid-containing vaccine dose. If a tetanus toxoid-containing vaccine is indicated for persons aged ≥11 years, Tdap is preferred for persons who have not previously received Tdap or whose Tdap history is unknown. If a tetanus toxoid-containing vaccine is indicated for a pregnant woman, Tdap should be used. For nonpregnant persons with documentation of previous Tdap vaccination, either Td or Tdap may be used if a tetanus toxoid-containing vaccine is indicated (Havers et al., 2020).

Wound management for tetanus prevention includes assessing the type of wound and provide appropriate wound care, evaluate immunization status, and assess the need for administering human tetanus immune globulin (TIG) for prophylaxis. TIG provides temporary immunity by directly providing antitoxin. TIG can help remove unbound tetanus toxin but cannot neutralize toxin that is already bound to nerve endings. Persons who have contaminated and dirty wounds and are either unvaccinated or have not received a primary series of tetanus toxoid-containing vaccines should receive TIG for prophylaxis. The dose of TIG for prophylaxis is 250 IU administered intramuscularly. Persons with HIV infection or severe immunodeficiency who have contaminated wounds (including minor wounds) should also receive TIG, regardless of their history of tetanus immunizations (CDC, 2020b; Liang, 2018).

DT and Td Vaccines

DT (diphtheria and tetanus toxoid, adsorbed) is administered in a 5-shot series to babies and children 6 weeks through 6 years old. Healthcare proividers only use this vaccine for children who should not get whooping cough vaccines (CDC, 2020a).

Td (tetanus and diphtheria toxoids, adsorbed) (e.g., TDVAX, MassBiologics) is administered every 10 years as a booster injection to people 7 years or older. Healthcare providers may also give it as part of a 3-shot series to people 7 years or older

who have not previously gotten any tetanus and diphtheria vaccines. Healthcare providers may also use this vaccine to complete the childhood vaccine series for tetanus and diphtheria in people 7 years or older (CDC, 2020a).

Tenivac is a vaccine administered every 10 years as a booster injection to people 7 years or older. Healthcare providers may also give it as part of a 3-shot series to people 7 years or older who have not previously gotten any tetanus and diphtheria vaccines. Healthcare providers may also use this vaccine to complete the childhood vaccine series for tetanus and diphtheria in people 7 years or older (CDC, 2020a).

Decavac (Sanofi Pasteur, Inc.) was a preservative free formulation of tetanus and diphtheria toxoids (Td). It was approved by the U.S. Food and Drug Administration (FDA) for active immunization of persons 7 years of age or older for prevention of tetanus and diphtheria. Decavac was supplied as preservative-free prefilled syringes, and according to the manufacturer, contained only trace amounts of thimerosal (mercury derivative) from the manufacturing process. In 2012, Decavac was replaced with Tenivac (Sanofi Pasteur), a preservative free formulation of Td indicated for the prevention of tetanus and diphtheria in persons 7 years of age and older.

Tdap Vaccines

Adacel (Tdap) (Sanofi Pasteur, Inc.), is a combination tetanus toxoid (T), reduced diphtheria toxoid (d) and acellular pertussis vaccine (ap), and has been approved by the FDA as a booster immunization against pertussis in combination with tetanus and diphtheria as a single dose in persons 10 through 64 years of age. Adacel is not approved for use in individuals 65 years of age and older. Adacel contains the same components as Daptacel, a DTaP vaccine indicated for infants and children manufactured by Sanofi Pasteur; however, the diphtheria toxoid and one of the pertussis components are in reduced quantities. Clinical studies submitted for FDA approval compared the antibody responses of adolescents and adults who received it with the antibody responses of infants who had received Daptacel. The antibody responses of the adolescents and adults who received a single dose of Adacel were at least as good as those observed in the infants following three doses of Daptacel. For diphtheria and tetanus, the antibody responses following Adacel were comparable to those following immunization with a U.S. licensed Td vaccine. In January 2019, FDA approved Adacel for a second Tdap dose if administered ≥8 years after the first Tdap dose and for use for tetanus prophylaxis when indicated for wound management if ≥ 5 years have elapsed since the previous receipt of any tetanus toxoid-containing vaccine. In light of the new indication for a second dose of Adacel and evidence of Tdap being used frequently in place of Td, ACIP reassessed current Tdap recommendations. In October 2019, ACIP recommended that either Tdap or Td vaccines could be used in situations where only Td vaccine had been recommended previously (Havers et al, 2020).

Healthcare providers administer a single injection of Adacel to preteens and teens, as well as adults who need it. Healthcare providers administer to pregnant women during each pregnancy. Healthcare providers also give it as part of a 3-shot series to people 7 years or older who have not previously gotten any tetanus, diphtheria, and whooping cough vaccines. Healthcare providers may also use this vaccine to complete the childhood vaccine series for tetanus, diphtheria, and whooping cough in people 7 years or older. Healthcare providers may use this vaccine in place of a Td vaccine every 10 years as a booster shot to people 7 years or older (CDC, 2020a).

Among adolescent recipients of Adacel, injection site pain and low grade fever were observed more frequently than among those who received Td vaccine. Rates of adverse reactions were similar in adults receiving Adacel vaccine or receiving Td vaccine. The durability of the immune response to Adacel is not known.

Boostrix (Tdap) (GlaxoSmithKline) is a combination tetanus toxoid (T), reduced diphtheria toxoid (d) and acellular pertussis vaccine (ap), and has been approved by the FDA as a booster immunization against pertussis in combination with tetanus and diphtheria for individuals 10 years of age and older (GlaxoSmithKline, 2019; Havers et al., 2020). Pertussis is generally less severe in adolescents than in infants, but it is thought that adolescents might transmit the disease to susceptible infants and other family members (FDA, 2005). In the last 20 years, rates of pertussis infection have been increasing in very young infants who have not received all their immunizations and in adolescents and adults (FDA, 2005). Boostrix has the same components as DTaP vaccine for infants and young children, but in reduced quantities. Clinical studies submitted for FDA approval demonstrated that the immune response to the pertussis component of Boostrix in adolescents was adequate compared to the immune response to three doses of DTaP vaccine in infants in a previous study. The immune response to the T and d components of Boostrix was found to be comparable to standard Td vaccine. The durability of the immune response to Boostrix is not known. Since 2005, a single booster dose of Tdap had been recommended for children and adolescents aged 11 - 18 years and adults aged 19 - 64 years to increase protection against tetanus, diphtheria, and pertussis. Booster doses of Td have been recommended every 10 years (decennial vaccination) to ensure continued protection against tetanus and diphtheria. These recommendations were expanded to include a single dose of Tdap for adults aged 65 years of age and older in 2012 (Havers et al, 2020).

Healthcare providers administer a single injection of Boostrix to preteens and teens, as well as adults who need it. Healthcare providers administer to pregnant women during each pregnancy. Healthcare providers also give it as part of a 3-shot series to people 7 years or older who have not previously gotten any tetanus, diphtheria, and whooping cough vaccines. Healthcare providers may also use this vaccine to complete the childhood vaccine series for tetanus, diphtheria, and whooping cough in

people 7 years or older. Healthcare providers may use this vaccine in place of a Td vaccine every 10 years as a booster shot to people 7 years or older (CDC, 2020a).

DTaP Vaccines

As of 2016, two DTaP vaccines were licensed by FDA and made available in the United States: Infanrix (GlaxoSmithKline) and Daptacel (Sanofi Pasteur). Both Infanrix and Daptacel are FDA approved for active vaccination against diphtheria, tetanus, and pertussis as a 5-dose series in infants and children aged 6 weeks through 6 years (Liang et al., 2018).

As of 2016, four combination vaccines that contain the components of DTaP vaccines were licensed by FDA and made available in the United States: DTaP-IPV-HepB (Pediarix, GlaxoSmithKline), DTaP-IPV (Kinrix, GlaxoSmithKline), DTaP-IPV/Hib (Pentacel, Sanofi Pasteur), and DTaP-IPV (Quadracel, Sanofi Pasteur). Combination vaccines with DTaP have been shown to be both safe and immunogenic, and have similar safety profiles and antibody responses compared with DTaP administered by itself (Liang et al., 2018).

TriHIBit (a DTaP/Hib combination) and Tripedia (a DTaP vaccine) were discontinued for business reasons in 2011 (Iannelli, 2016).

Pentacel (Sanofi Pasteur) contains DTaP, IPV, and *Haemophilus influenzae* type b (Hib) conjugate. Pentacel is FDA approved for use as a 4-dose series in children aged 6 weeks through 4 years (prior to 5 years of age). The FDA approval of Pentacel was based on the results of multi-center clinical studies conducted in the United States and Canada that involved more than 5,000 children who received at least one dose of Pentacel. The safety of Pentacel was compared both to separately administered Daptacel, IPOL and ActHIB vaccines and to other single-entity vaccine formulations. Pentacel is approved for administration as a four - dose series at 2, 4 and 6, and 15-18 months of age. The first dose may be given as early as six weeks of age. Four doses of Pentacel constitute a primary immunization course against pertussis. Three doses of Pentacel constitute a primary immunization course against diphtheria, tetanus, *Haemophilis influenzae* type b invasive disease, and poliomyelitis; the fourth dose constitutes a booster vaccination against diphtheria, tetanus, *Haemophilis influenzae* type b invasive disease, and poliomyelitis.

While Pentacel and Daptacel [(DTaP), Sanofi Pasteur Ltd] vaccines contain the same pertussis antigens, manufactured by the same process, Pentacel contains twice the amount of detoxified pertussis toxin (PT) and four times the amount of filamentous hemagglutinin (FHA) as Daptacel. Pentacel may be used to complete the first 4 doses of the 5-dose DTaP series in infants and children who have received 1 or more doses of Daptacel and are also scheduled to receive the other antigens of Pentacel. However, data are not available on the safety and immunogenicity of such mixed sequences of Pentacel and Daptacel for successive doses of the primary DTaP series. Children who have completed a 4-dose series with Pentacel should receive a fifth dose of DTaP vaccine using Daptacel at 4 - 6 years of age (Sanofi Pasteur, 2019).

Kinrix (GlaxoSmithKline) contains DTaP and IPV. Kinrix is licensed by FDA for use as the fifth dose of the DTaP vaccine series and the fourth dose of the IPV series in children aged 4 - 6 years whose previous DTaP vaccine doses were DTaP (Infanrix, GSK) and/or DTaP-HepB-IPV (Pediarix, GSK) for the first 3 doses and DTaP (Infanrix) for the fourth dose (GlaxoSmithKline, 2019). Clinical studies of Kinrix demonstrated that Kinrix offers similar protection to the separately administered DTaP and IPV vaccines, with a comparable safety profile. These results were confirmed in the pivotal Phase III trial of Kinrix, which was a randomized, controlled study conducted in the U.S. in which 3,156 children 4 to 6 years of age were vaccinated with Kinrix. All children studied had previously received 4 doses of DTaP (Infanrix) and 3 doses of IPV (IPOL). All children in the study also received the second dose of U.S.-licensed measles, mumps and rubella (MMR) vaccine (M-M-RII) at the same time.

Pediarix (GlaxoSmithKline) contains DTaP, inactivated poliovirus (IPV), and Hepatitis B (recombinant) (HepB). Pediarix is approved by FDA for use as a 3-dose series in infants born to hepatitis B surface antigen (HBsAg)-negative mothers. Pediarix can be administered as early as age 6 weeks through 6 years. Three doses of Pediarix constitute a primary immunization course for diphtheria, tetanus, pertussis, and poliomyelitis and the complete vaccination course for hepatitis B (GlaxoSmithKline, 2019).

Quadracel (Sanofi Pasteur) contains DTaP and IPV. A single dose of Quadracel is approved for use in children 4 through 6 years of age as a fifth dose in the diphtheria,tetanus, pertussis vaccination (DTaP) series, and as a fourth or fifth dose in the inactivated poliovirus vaccination (IPV) series, in children who have received 4 doses of Pentacel and/or Daptacel vaccine (Sanofi Pasteur, 2019).

Vaxelis (Sanofi Pasteur/Merck) is a hexavalent combination vaccine which contains DTaP, inactivated poliovirus, *Haemophilus b* conjugate and hepatitis B. Vaxelis was FDA approved in 2018 approved for use as a 3-dose series in children from 6 weeks through 4 years of age (prior to the 5th birthday). The 3-dose immunization series consists of a 0.5 mL intramuscular injection, administered at 2, 4, and 6 months of age. A 3-dose series of Vaxelis does not constitute a primary immunization series against pertussis; an additional dose of pertussis-containing vaccine is needed to complete the primary series. Vaxelis may be used to complete the first 3 doses of the 5-dose DTaP series in infants and children who have received 1 or 2 doses of Pentacel or Daptacel and are also scheduled to receive the other antigens in Vaxelis. Data are not available on the safety and immunogenicity of such mixed sequences. Data are not available on the safety and effectiveness of using Vaxelis following 1 or 2 doses of a DTaP vaccine from a different manufacturer. Vaxelis may be administered to infants and children who have received 1 or 2 doses of IPV and are also scheduled to receive the other antigens in Vaxelis. However, data are not available on the

safety and effectiveness of VAXELIS in such infants and children. Vaxelis may be administered to infants and children who have received 1 or 2 doses of *H. influenzae* type b Conjugate Vaccine and are also scheduled to receive the other antigens in Vaxelis. However, data are not available on the safety and effectiveness of Vaxelis in such infants and children (Sanofi Pasteur, 2020).

The effectiveness of Vaxelis is based on the immunogenicity of the individual antigens compared to US licensed vaccines. Serological correlates of protection exist for diphtheria, tetanus, hepatitis B, poliomyelitis, and invasive disease due to *H. influenzae* type b. The effectiveness against pertussis is based upon the pertussis immune responses following 3 doses of Vaxelis compared to 3 doses of Pentacel, as well as the pertussis immune responses following a subsequent dose of Daptacel in the same 2 groups of children. Vaxelis, Pentacel and Daptacel contain the same pertussis antigens, manufactured by the same processes. The safety of Vaxelis has been established in the age group 6 weeks through 15 months (Sanofi Pasteur, 2020).

Vaxelis is to be administered as a 3-dose series at 2, 4, and 6 months of age. The first dose may be given as early as 6 weeks of age. Three doses of Vaxelis constitute a primary immunization course against diphtheria, tetanus, *H. influenzae* type b invasive disease and poliomyelitis. Vaxelis may be used to complete the hepatitis B immunization series. A 3-dose series of Vaxelis does not constitute a primary immunization series against pertussis; an additional dose of pertussis-containing vaccine is needed to complete the primary series (Sanofi Pasteur, 2020).

Children Previously Vaccinated With One or More Doses of Daptacel Vaccine

Pentacel may be used to complete the first 4 doses of the DTaP series in infants and children who have received 1 or more doses of Daptacel and are also scheduled to receive the other antigens of Pentacel. However, the safety and efficacy of Pentacel in such infants have not been evaluated.

Children Previously Vaccinated With One or More Doses of Inactivated Poliovirus Vaccine (IPV)

Pentacel may be used to complete the 4 - dose IPV series in infants and children who have received 1 or more doses of another licensed IPV vaccine and are also scheduled to receive the other antigens of Pentacel. However, the safety and efficacy of Pentacel in such infants have not been evaluated.

Children Previously Vaccinated With One or More Doses of Haemophilus b Conjugate Vaccine

Pentacel may be used to complete the vaccination series in infants and children previously vaccinated with one or more doses of a Haemophilus b Conjugate Vaccine (either separately administered or as part of another combination vaccine), who are also scheduled to receive the other antigens of Pentacel. However, the safety and efficacy of Pentacel in such infants have not been evaluated. If different brands of Haemophilus b Conjugate Vaccines are administered to complete the series, three primary immunizing doses are needed, followed by a booster dose.

Immunization and Pregnancy

ACIP recommends that pregnant women receive 1 dose of Tdap during each pregnancy, irrespective of their history of receiving the vaccine. Tdap should be administered at 27 - 36 weeks' gestation, preferably during the earlier part of this period, although it may be administered at any time during pregnancy (Havers et al., 2020).

Pregnant women who have completed the childhood immunization schedule and were last vaccinated >10 years previously should receive a booster dose of tetanus toxoid-containing vaccine to prevent neonatal tetanus. The risk for neonatal tetanus is minimal if a previously unvaccinated woman has received at least 2 properly spaced doses of a tetanus toxoid-containing vaccine during pregnancy; at least 1 of the doses administered during pregnancy should be Tdap, administered according to published guidance. If >1 dose is needed, either Td or Tdap may be used. The 3-dose primary series should be completed at the recommended intervals (Havers et al., 2020).

The American College of Obstetricians and Gynecologists (ACOG, 2017) make the following recommendations:

- Obstetric care providers should administer the tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine to all pregnant patients during each pregnancy, as early in the 27-36 weeks-of-gestation window as possible.
- Pregnant women should be counseled that the administration of the Tdap vaccine during each pregnancy is safe and important to make sure that each newborn receives the highest possible protection against pertussis at birth.
- If not administered during pregnancy, the Tdap vaccine should be given immediately postpartum if the woman has never received a prior dose of Tdap as an adolescent, adult, or during a previous pregnancy.
- There are certain circumstances in which it is appropriate to administer the Tdap vaccine outside of the 27-36 weeks-of-gestation window. For example, in cases of wound management, a pertussis outbreak, or other extenuating circumstances, the need for protection from infection supersedes the benefit of administering the vaccine during the 27-36 weeks-of-gestation window.

- If a pregnant woman is vaccinated early in her pregnancy (ie, before 27-36 weeks of gestation), she does not need to be vaccinated again during 27-36 weeks of gestation.

Gall (2008) stated that the active immunization of pregnant women during pregnancy to protect them from disease and protect their neonate with passive antibodies is a biologic fact. Fortunately, many infectious diseases occur infrequently due to excellent pediatric vaccine programs. However, most adults and many physicians are unaware of the risks of not administering vaccines especially to pregnant women. Influenza vaccine (trivalent inactivated influenza vaccine) is recommended by ACIP for pregnant women in any trimester of pregnancy and TdaP vaccine is recommended by the ACIP to be given before pregnancy, during pregnancy, or in the immediate post-partum period. Only 2 % of the adult population in the United States are protected against pertussis and it is estimated that only 25 % of pregnant women receive influenza vaccine during the influenza season.

Terranella et al (2013) stated that infants less than 2 months of age are at highest risk of pertussis morbidity and mortality. Until recently, the ACIP recommended protecting young infants by "cocooning" or vaccination of post-partum mothers and other close contacts with tetanus toxoid, reduced Tdap booster vaccine. The ACIP recommends pregnancy vaccination as a preferred and safe alternative to post-partum vaccination. The ACIP cocooning recommendation has not changed. These investigators used a cohort model reflecting U.S. 2009 births and the diphtheria-tetanus-acellular pertussis schedule to simulate a decision and cost-effectiveness analysis of Tdap vaccination during pregnancy compared with post-partum vaccination with or without vaccination of other close contacts (i.e., cocooning). They analyzed infant pertussis cases, hospitalizations, and deaths, as well as direct disease, indirect, and public health costs for infants in the 1st year of life. All costs were updated to 2011 U.S. dollars. Pregnancy vaccination could reduce annual infant pertussis incidence by more than post-partum vaccination, reducing cases by 33 % versus 20 %, hospitalizations by 38 % versus 19 %, and deaths by 49 % versus 16 %. Additional cocooning doses in a father and 1 grandparent could avert an additional 16 % of cases but at higher cost. The cost per quality-adjusted life-year saved for pregnancy vaccination was substantially less than post-partum vaccination ($414,523 versus $1,172,825). The authors concluded that Tdap vaccination during pregnancy could avert more infant cases and deaths at lower cost than post-partum vaccination, even when post-partum vaccination is combined with additional cocooning doses. Pregnancy dose vaccination is the preferred alternative to post-partum vaccination for preventing infant pertussis.

Healy et al (2013) noted that Tdap recommendations assume that pertussis-specific antibodies in women immunized pre-conception, during, or after previous pregnancies persist at sufficient levels to protect newborn infants. These investigators measured pertussis-specific immunoglobulin G (IgG) by IgG-specific enzyme-linked immunosorbent assay (ELISA) in maternal-umbilical cord serum pairs where mothers received Tdap during the prior 2 years. Geometric mean concentrations (GMCs) of pertussis antibodies and cord-maternal GMC ratios were calculated. A total of 105 mothers (mean age of 25.3 years [range of 15.3 to 38.4 years]; mean gestation of 39 weeks [range of 37 to 43 weeks]) immunized with Tdap vaccine a mean of 13.7 months (range of 2.3 to 23.9 months) previously were included; 72 (69 %) had received Tdap post-partum, 31 at a routine healthcare visit and 2 as contacts of another newborn. There was no difference in GMCs for pertussis-specific IgG in maternal delivery or infant cord sera for women immunized before (n = 86) or during (n = 19) early pregnancy. Placental transport of antibodies was 121 % to 186 % from mothers immunized before and during pregnancy, respectively. Estimated GMC of IgG to pertussis toxin was less than 5 ELISA units (EU)/ml at infant age 2 months (start of infant immunization series). More infants of mothers immunized during pregnancy had pertussis toxin levels estimated to be higher than the lower limit of quantitation of the assay (4 EU/ml) through age 2 months (52 % versus 38 %; p = 0.34). The authors concluded that infants of mothers immunized pre-conception or in early pregnancy have insufficient pertussis-specific antibodies to protect against infection. Maternal immunization during the 3rd trimester, immunization of other infant contacts, and re-immunization during subsequent pregnancies may be necessary.

In a retrospective cohort study, Shakib et al (2013) evaluated pregnancy and birth outcomes in infants born to women who did or did not receive Tdap vaccine during pregnancy. Pregnant women 12 to 45 years of age who received Tdap at Intermountain Healthcare facilities and their infants were identified and compared with mother-infant pairs without documented Tdap from May 2005 through August 2009. Primary measures included pregnancy outcomes and infant health outcomes at birth through 12 months. From 162,448 pregnancies these investigators identified 138 women (0.08 %) with documented Tdap administration during pregnancy (cases); 552 pregnant women without documented Tdap were randomly selected as controls. Of 138 immunized women, 63 % received Tdap in the 1st trimester and 37 % after. Tdap was given most commonly as wound prophylaxis. The incidence of spontaneous or elective abortion was no greater in Tdap cases than in controls. There were no significant differences in preterm delivery, gestational age, or birth weight between groups. One or more congenital anomaly was identified in 3.7 % (95 % confidence interval [CI]: 1.2 % to 8.5 %) of case infants and 4.4 % (95 % CI: 2.7 % to 6.5 %) of control infants (p = 0.749). In infants born to women receiving Tdap during pregnancy, 3.6 % (0.8 % to 10.2 %) had International Classification of Diseases, Ninth Revision, Clinical Modification diagnoses consistent with complex chronic conditions within 12 months compared with 10.4 % (95 % CI: 7.2 % to 14.4 %) of infants of controls (p = 0.054). The authors concluded that documented Tdap administration during pregnancy was uncommon and occurred most often in the 1st trimester as prophylaxis following trauma. No increase in adverse outcomes was identified in infants born to women receiving Tdap compared with infants of controls.

In a phase I/II, randomized, double-blind, placebo-controlled, clinical trial, Munoz et al (2014) evaluated the safety and immunogenicity of Tdap immunization during pregnancy and its effect on infant responses to DTaP vaccine. A total of 48 pregnant women aged 18 to 45 years received Tdap (n = 33) or placebo (n = 15) at 30 to 32 weeks' gestation, with cross-over immunization post-partum. Tdap vaccination was carried out at 30 to 32 weeks' gestation or post-partum. Primary outcomes were maternal and infant adverse events, pertussis illness, and infant growth and development until age 13 months. Secondary

outcomes were antibody concentrations in pregnant women before and 4 weeks after Tdap immunization or placebo, at delivery and 2 months' post-partum, and in infants at birth, at 2 months, and after the 3rd and 4th doses of DTaP. No Tdap-associated serious adverse events occurred in women or infants. Injection site reactions after Tdap immunization were reported in 26 (78.8 % [95 % CI: 61.1 % to 91.0 %]) and 12 (80 % [95 % CI: 51.9 % to 95.7 %]) pregnant and post-partum women, respectively ($p > 0.99$). Systemic symptoms were reported in 12 (36.4 % [95 % CI: 20.4 % to 54.9 %]) and 11 (73.3 % [95 % CI: 44.9 % to 92.2 %]) pregnant and post-partum women, respectively ($p = 0.03$). Growth and development were similar in both infant groups. No cases of pertussis occurred. Significantly higher concentrations of pertussis antibodies were measured at delivery in women who received Tdap during pregnancy versus post-partum (e.g., pertussis toxin antibodies: 51.0 EU/ml [95 % CI: 37.1 to 70.1] and 9.1 EU/ml [95 % CI: 4.6 to 17.8], respectively; $p < 0.001$) and in their infants at birth (68.8 EU/ml [95 % CI: 52.1 to 90.8] and 14.0 EU/ml [95 % CI: 7.3 to 26.9], respectively; $p < 0.001$) and at age 2 months (20.6 EU/ml [95 % CI: 14.4 to 29.6] and 5.3 EU/ml [95 % CI: 3.0 to 9.4], respectively; $p < 0.001$). Antibody responses in infants born to women receiving Tdap during pregnancy were not different following the 4th dose of DTaP. The authors concluded that this preliminary assessment did not find an increased risk of adverse events among women who received Tdap vaccine during pregnancy or their infants. For secondary outcomes, maternal immunization with Tdap resulted in high concentrations of pertussis antibodies in infants during the first 2 months of life and did not substantially alter infant responses to DTaP.

Decker and Edwards (2021) noted that pertussis (whooping cough) is a respiratory infection caused by Bordetella pertussis. All ages are susceptible. In the pre-vaccine era, almost all children became infected. Pertussis is especially dangerous in young infants, who account for practically all hospitalizations and deaths; however, clinical disease is burdensome at any age. Widespread use of pertussis vaccines dramatically reduced cases, but concern over adverse reactions led to the replacement of standard whole-cell by acellular pertussis vaccines that contain only a few selected pertussis antigens and are far less reactogenic. Routine administration of acellular pertussis vaccines combined with diphtheria and tetanus toxoids is recommended in infancy with toddler and pre-school boosters, at age 11, and during pregnancy. Boosting in the 2nd half of every pregnancy is critical to protection of the newborn. Waning of vaccine immunity over time has become an increasing concern, and several new pertussis vaccines are being evaluated to address this problem.

Nguyen et al (2022) noted that severe pertussis infection has been reported in infants before receiving routine immunization series. This problem could be solved by vaccinating mothers during pregnancy or children at birth. In a systematic review and meta-analysis, these researchers examined real-world evidence to evaluate the optimal strategy for pertussis vaccination. They searched PubMed, Embase, and the Cochrane Library databases until December 2020; RCTs, cohort studies, case-control studies, and case series were included if they examined the safety, effectiveness, and immunogenicity of acellular pertussis vaccine during pregnancy and at birth. Number of pertussis cases, severe AEs (SAEs), and pertussis antibody concentration in infants before and after they received routine vaccination series were extracted and random-effect model was used to pool the analyses. A total of 29 studies were included. This meta-analysis revealed that pertussis immunization during pregnancy significantly increased the concentrations of 3 pertussis antibodies and reduced the incidence rates of infected infants below 3 months of age (odds ratio [OR], 0.22; 95 % CI: 0.14 to 0.33). Similarly, infants vaccinated at birth had higher levels of pertussis antibody than those who were not. No significant difference in rates of SAEs was observed in all vaccination groups (during pregnancy [RR, 1.18; 95 % CI: 0.76 to 1.82] and at birth [RR, 0.72; 95 % CI: 0.34 to 1.54]). The authors concluded that pertussis vaccination during pregnancy could protect infants against pertussis disease before the routine vaccination. Pertussis immunization at birth would be an alternative for infants whose mothers did not receive pertussis vaccines during pregnancy.

Safety and Effectiveness of Acellular Pertussis Vaccination During Pregnancy

Vygen-Bonnet and colleagues (2020) noted that infants of less than 3 months of age are at highest risk for developing severe complications after pertussis. The majority of pregnant women has low concentrations of pertussis-specific antibodies and therefore newborns are insufficiently protected by maternally transferred antibodies. Acellular pertussis vaccination during pregnancy was recently implemented in various countries. These researchers examined the evidence for safety and effectiveness of pertussis vaccination during pregnancy. They searched Medline, Embase, and ClinicalTrials.gov from January 1, 2010 to January 10, 2019. These investigators examined risk of bias (ROB) using the Cochrane ROB tool and ROBINS-I; and they evaluated the quality of evidence using the GRADE approach. These researchers identified 1,273 articles and included 22 studies (14 for safety; 8 for effectiveness), comprising 1.4 million pregnant women in safety studies and 855,546 mother-infant-pairs in effectiveness studies. No significant differences between vaccinated and unvaccinated women and their infants were observed for safety outcomes with the exception of fever and chorioamnionitis. Compared to no vaccination, three studies showed a significantly increased relative risk (RR) for the presence of the ICD-9 code for chorioamnionitis in electronic patient data after pertussis vaccination. However, no study reported an increased risk for clinical sequelae of chorioamnionitis after vaccination during pregnancy, such as preterm birth or neonatal intensive care unit (ICU) admission. Vaccine effectiveness against pertussis in infants of immunized mothers ranged from 69 to 91 % for pertussis prevention, from 91 to 94 % for prevention of hospitalization and was 95 % for prevention of death due to pertussis. Risk of bias was serious-to-critical for safety outcomes and moderate-to-serious for effectiveness outcomes. GRADE evidence quality was moderate-to-very low, depending on outcome. The authors concluded that although an increased risk for a diagnosis of fever and chorioamnionitis was detected in pregnant women after pertussis vaccination, there was no association with a higher frequency of clinically relevant sequelae. Vaccine effectiveness for prevention of infant pertussis, hospitalization and death was high. These investigators stated that pertussis vaccination during pregnancy had an overall positive benefit-risk ratio. In view of the overall quality of available evidence ongoing surveillance of chorioamnionitis and its potential sequelae is recommended when pertussis vaccination in pregnancy is implemented.

Nasser and associates (2020) stated that pregnant travelers and their offspring are vulnerable to severe outcomes following a wide range of infections. Vaccine-preventable diseases can have a particularly severe course in pregnant women, but little is known about the safety of travel vaccines in pregnant women. These researchers performed a systematic review of all published literature concerning the safety of vaccines frequently given to travelers such as yellow fever, MMR (mumps, measles and rubella), influenza, Tdap (tetanus, diphtheria and pertussis), meningococcus, hepatitis A and B, rabies, polio, typhoid fever, tick-borne encephalitis and Japanese encephalitis vaccines. They included case-series studies, cohort studies and randomized controlled trials (RCTs). For the meta-analysis, these investigators included only RCTs that compared the administration of a vaccine to placebo or to no vaccine. Outcome measures included severe systemic adverse events (AEs), maternal outcomes related to the course of pregnancy, neonatal outcomes and local AEs. They calculated the RR and its 95 % CI as the summary measure. The safety of influenza vaccine was supported by high-quality evidence. For Tdap vaccine, no evidence of any harm was found in the meta-analysis of RCTs. A slight increase in chorioamnionitis rate was reported in 3 out of 12 observational studies. However, this small possible risk was far out-weighed by a much larger benefit in terms of infant morbidity and mortality.

Intra-Nasal Live Attenuated Pertussis Vaccine

Keech et al (2023) noted that Bordetella pertussis epidemics persist as transmission remains unabated despite high acellular pertussis vaccination rates. BPZE1, a live attenuated intra-nasal pertussis vaccine, was designed to prevent B pertussis infection and disease. In a double-blind, multi-center phase-IIb clinical trial, these researchers examined the immunogenicity and safety of BPZE1 compared with Tdap. This trial was carried out at 3 research centers in the U.S.; healthy adults aged 18 to 50 years were randomly assigned (2:2:1:1) via a permuted block randomization schedule to receive BPZE1 vaccination followed by BPZE1 attenuated challenge, BPZE1 vaccination followed by placebo challenge, Tdap followed by BPZE1 attenuated challenge, or Tdap followed by placebo challenge. On day 1, lyophilized BPZE1 was reconstituted with sterile water and given intra-nasally (0.4 ml delivered to each nostril), whereas Tdap was given intra-muscularly. To maintain masking, subjects in the BPZE1 groups received an intra-muscular saline injection, and those in the Tdap groups received intra-nasal lyophilized placebo buffer. The attenuated challenge took place on day 85. The primary immunogenicity endpoint was the proportion of subjects achieving nasal secretory IgA sero-conversion against at least 1 B pertussis antigen on day 29 or day 113. Reactogenicity was assessed up to 7 days after vaccination and challenge, and AEs were recorded for 28 days after vaccination and challenge. Serious AEs were monitored throughout the study. Between June 17 and October 3, 2019, a total of 458 subjects were screened and 280 were randomly assigned to the main cohort: 92 to the BPZE1-BPZE1 group, 92 to the BPZE1-placebo group, 46 to the Tdap-BPZE1 group, and 50 to the Tdap-placebo group. Sero-conversion of at least 1 B pertussis-specific nasal secretory IgA was recorded in 79 (94 % [95 % CI: 87 % to 98 %]) of 84 subjects in the BPZE1-BPZE1 group, 89 (95 % [88 % to 98 %]) of 94 in the BPZE1-placebo group, 38 (90 % [77 % to 97 %]) of 42 in the Tdap-BPZE1 group, and 42 (93 % [82 % to 99 %]) of 45 in the Tdap-placebo group. BPZE1 induced broad and consistent B pertussis-specific mucosal secretory IgA responses, whereas Tdap did not induce consistent mucosal secretory IgA responses. Both vaccines were well-tolerated, with mild reactogenicity and no serious AEs related to study vaccination. The authors concluded that BPZE1 induced nasal mucosal immunity and produced functional serum responses. These researchers stated that BPZE1 has the potential to avert B pertussis infections, which ultimately could result in reduced transmission and diminished epidemic cycles. Moreover, these investigators stated that these findings should be confirmed in large phase-III clinical trials.

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Policy History

- Last Review 09/18/2024

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- Review History
- Definitions

Additional Information

- Clinical Policy Bulletin Notes