HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use KINRIX safely and effectively. See full prescribing information for KINRIX.

KINRIX (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine)
Suspension for Intramuscular Injection
Initial U.S. Approval: 2008

----------INDICATIONS AND USAGE----------

A single dose of KINRIX is indicated for active immunization against diphtheria, tetanus, pertussis, and poliomyelitis as the fifth dose in the diphtheria, tetanus, and acellular pertussis (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. (1)

---------- DOSAGE AND ADMINISTRATION ----------

A single intramuscular injection (0.5 mL). (2.2)

---------- DOSAGE FORMS AND STRENGTHS ----------

Single-dose vials and prefilled syringes containing a 0.5-mL suspension for injection. (3)

----------CONTRAINDICATIONS----------

- Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid-, tetanus toxoid-, pertussis- or poliovirus-containing vaccine, or to any component of KINRIX, including neomycin and polymyxin B. (4.1)
- Encephalopathy within 7 days of administration of a previous pertussis-containing vaccine. (4.2)
- Progressive neurologic disorders. (4.3)

---------- WARNINGS AND PRECAUTIONS----------

- If Guillain-Barré syndrome occurs within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give KINRIX should be based on potential benefits and risks. (5.1)
- The tip caps of the prefilled syringes contain natural rubber latex which may cause allergic reactions. (5.2)
- Syncope (fainting) can occur in association with administration of injectable vaccines, including KINRIX. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope. (5.3)
- If adverse events (i.e., temperature ≥105°F, collapse or shock-like state, persistent, inconsolable crying lasting ≥3 hours, occurring within 48 hours of vaccination; seizures within 3 days of vaccination) have occurred in temporal relation to receipt of a pertussis-containing vaccine, the decision to give KINRIX should be based on potential benefits and risks. (5.4)
- For children at higher risk for seizures, an antipyretic may be administered at the time of vaccination with KINRIX. (5.5)

---------- ADVERSE REACTIONS ----------

- The most frequently reported solicited local reaction (>50%) was injection site pain. Other common solicited local reactions (≥25%) were redness, increase in arm circumference, and swelling. (6.1)
- Common solicited general adverse events (≥15%) were drowsiness, fever (≥99.5°F), and loss of appetite. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact GlaxoSmithKline at 1-888-825-5249 or VAERS at 1-800-822-7967 or www.vaers.hhs.gov.

----------DRUG INTERACTIONS----------

Do not mix KINRIX with any other vaccine in the same syringe or vial. (7.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: xx/xxxx

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FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

A single dose of KINRIX® is indicated for active immunization against diphtheria, tetanus, pertussis, and poliomyelitis as the fifth dose in the diphtheria, tetanus, and acellular pertussis (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® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) and/or PEDIARIX® [Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine] for the first three doses and INFANRIX for the fourth dose.

2 DOSAGE AND ADMINISTRATION

2.1 Preparation for Administration

Shake vigorously to obtain a homogeneous, turbid, white suspension. Do not use if resuspension does not occur with vigorous shaking. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. If either of these conditions exists, the vaccine should not be administered.

For the prefilled syringes, attach a sterile needle and administer intramuscularly.

For the vials, use a sterile needle and sterile syringe to withdraw the 0.5-mL dose and administer intramuscularly. Changing needles between drawing vaccine from a vial and injecting it into a recipient is not necessary unless the needle has been damaged or contaminated. Use a separate sterile needle and syringe for each individual.

Do not administer this product intravenously, intradermally, or subcutaneously.

2.2 Recommended Dose and Schedule

KINRIX is to be administered as a 0.5-mL dose by intramuscular injection. The preferred site of administration is the deltoid muscle of the upper arm.

KINRIX may be used for the fifth dose in the DTaP immunization series and the fourth dose in the IPV immunization series in children 4 through 6 years of age (prior to the seventh birthday) whose previous DTaP vaccine doses have been with INFANRIX and/or PEDIARIX for the first three doses and INFANRIX for the fourth dose *[see Indications and Usage (1)]*.

3 DOSAGE FORMS AND STRENGTHS

KINRIX is a suspension for injection available in 0.5-mL single-dose vials and prefilled TIP-LOK® syringes.

4 CONTRAINDICATIONS

4.1 Hypersensitivity

Severe allergic reaction (e.g., anaphylaxis) after a previous dose of any diphtheria toxoid-, tetanus toxoid-, pertussis- or poliovirus-containing vaccine, or to any component of KINRIX, including neomycin and polymyxin B, is a contraindication to administration of KINRIX *[see Description (11)]*. Because of the uncertainty as to which component of the vaccine might be responsible, no further vaccination with any of these components should be given. Alternatively, such individuals may be referred to an allergist for evaluation if immunization with any of these components is considered.

4.2 Encephalopathy

Encephalopathy (e.g., coma, decreased level of consciousness, prolonged seizures) within 7 days of administration of a previous dose of a pertussis-containing vaccine that is not attributable to another identifiable cause is a contraindication to administration of any pertussis-containing vaccine, including KINRIX.

4.3 Progressive Neurologic Disorder

Progressive neurologic disorder, including infantile spasms, uncontrolled epilepsy, or progressive encephalopathy is a contraindication to administration of any pertussis-containing vaccine, including KINRIX. Pertussis vaccine should not be administered to individuals with such conditions until a treatment regimen has been established and the condition has stabilized.

5 WARNINGS AND PRECAUTIONS

5.1 Guillain-Barré Syndrome

If Guillain-Barré syndrome occurs within 6 weeks of receipt of a prior vaccine containing tetanus toxoid, the decision to give any tetanus toxoid-containing vaccine, including KINRIX, should be based on careful consideration of the potential benefits and possible risks. When a decision is made to withhold tetanus toxoid, other available vaccines should be given, as indicated.

5.2 Latex

The tip caps of the prefilled syringes contain natural rubber latex which may cause allergic reactions.

5.3 Syncope

Syncope (fainting) can occur in association with administration of injectable vaccines, including KINRIX. Syncope can be accompanied by transient neurological signs such as visual disturbance, paresthesia, and tonic-clonic limb movements. Procedures should be in place to avoid falling injury and to restore cerebral perfusion following syncope.

5.4 Adverse Events following Prior Pertussis Vaccination

If any of the following events occur in temporal relation to receipt of a pertussis-containing vaccine, the decision to give any pertussis-containing vaccine, including KINRIX, should be based on careful consideration of the potential benefits and possible risks:

- Temperature of ≥40.5°C (105°F) within 48 hours not due to another identifiable cause;
- Collapse or shock-like state (hypotonic-hyporesponsive episode) within 48 hours;
- Persistent, inconsolable crying lasting ≥3 hours, occurring within 48 hours;
- Seizures with or without fever occurring within 3 days.

When a decision is made to withhold pertussis vaccination, other available vaccines should be given, as indicated.

5.5 Children at Risk for Seizures

For children at higher risk for seizures than the general population, an appropriate antipyretic may be administered at the time of vaccination with a pertussis-containing vaccine, including KINRIX, and for the ensuing 24 hours to reduce the possibility of post-vaccination fever.

5.6 Preventing and Managing Allergic Vaccine Reactions

Prior to administration, the healthcare provider should review the patient's immunization history for possible vaccine sensitivity and previous vaccination-related adverse reactions to allow an assessment of benefits and risks. Epinephrine and other appropriate agents used for the control of immediate allergic reactions must be immediately available should an acute anaphylactic reaction occur.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a vaccine cannot be directly compared with rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice.

A total of 4,013 children were vaccinated with a single dose of KINRIX in 4 clinical trials. Of these, 381 children received a non-US formulation of KINRIX (containing ≤2.5 mg 2-phenoxyethanol per dose as preservative).

The primary study (Study 048), conducted in the United States, was a randomized, controlled clinical trial in which children 4 to 6 years of age were vaccinated with KINRIX (N = 3,156) or control vaccines (INFANRIX and IPOL® vaccine [IPV, Sanofi Pasteur SA]; N = 1,053) as a fifth DTaP vaccine dose following 4 doses of INFANRIX and as a fourth IPV dose following 3 doses of IPOL. Subjects also received the second dose of US-licensed measles, mumps, and rubella (MMR) vaccine (Merck & Co., Inc.) administered concomitantly, at separate sites.

Data on adverse events were collected by parents/guardians using standardized forms for 4

consecutive days following vaccination with KINRIX or control vaccines (i.e., day of vaccination and the next 3 days). The reported frequencies of solicited local reactions and general adverse events in Study 048 are presented in Table 1.

In 3 studies (Studies 046, 047, and 048), children were monitored for unsolicited adverse events, including serious adverse events, that occurred in the 31-day period following vaccination and in 2 studies (Studies 047 and 048), parents/guardians were actively queried about changes in the child's health status, including the occurrence of serious adverse events, through 6 months post-vaccination.

Table 1. Percentage of Children 4 to 6 Years of Age Reporting Solicited Local Reactions or General Adverse Events within 4 Days of Vaccination[a] with KINRIX or Separate Concomitant Administration of INFANRIX and IPV When Coadministered with MMR Vaccine (Study 048) (Total Vaccinated Cohort)

	KINRIX	INFANRIX + IPV
Local[b]	**N = 3,121-3,128**	**N = 1,039-1,043**
Pain, any	57.0[c]	53.3
Pain, Grade 2 or 3[d]	13.7	12.0
Pain, Grade 3[d]	1.6[c]	0.6
Redness, any	36.6	36.6
Redness, ≥50 mm	17.6	20.0
Redness, ≥110 mm	2.9	4.1
Arm circumference increase, any	36.0	37.8
Arm circumference increase, >20 mm	6.9	7.4
Arm circumference increase, >30 mm	2.4	3.2
Swelling, any	26.0	27.0
Swelling, ≥50 mm	10.2	11.5
Swelling, ≥110 mm	1.4	1.8
General	**N = 3,037-3,120**	**N = 993-1,036**
Drowsiness, any	19.1	17.5
Drowsiness, Grade 3[e]	0.8	0.8
Fever, ≥99.5°F	16.0	14.8
Fever, >100.4°F	6.5[c]	4.4
Fever, >102.2°F	1.1	1.1
Fever, >104°F	0.1	0.0
Loss of appetite, any	15.5	16.0
Loss of appetite, Grade 3[f]	0.8	0.6

IPV = Inactivated poliovirus vaccine (Sanofi Pasteur SA); MMR = Measles, mumps, and rubella vaccine (Merck & Co., Inc.).

Total Vaccinated Cohort = All vaccinated subjects for whom safety data were available.

N = Number of children with evaluable data for the events listed.

[a] Within 4 days of vaccination defined as day of vaccination and the next 3 days.

[b] Local reactions at the injection site for KINRIX or INFANRIX.

[c] Statistically higher than comparator group (P <0.05).

[d] Grade 2 defined as painful when the limb was moved; Grade 3 defined as preventing normal daily activities.

[e] Grade 3 defined as preventing normal daily activities.

[f] Grade 3 defined as not eating at all.

In Study 048, KINRIX was non-inferior to INFANRIX with regard to swelling that involved >50% of the injected upper arm length and that was associated with a >30 mm increase in mid-

upper arm circumference within 4 days following vaccination (upper limit of two-sided 95% Confidence Interval for difference in percentage of KINRIX [0.6%, n = 20] minus INFANRIX [1.0%, n = 11] ≤2%).

Serious Adverse Events

Within the 31-day period following study vaccination in 3 studies (Studies 046, 047, and 048), in which all subjects received concomitant MMR vaccine (US-licensed MMR vaccine [Merck & Co., Inc.] in Studies 047 and 048; non—US-licensed MMR vaccine in Study 046), 3 subjects (0.1% [3/3,537]) who received KINRIX reported serious adverse events (dehydration and hypernatremia; cerebrovascular accident; dehydration and gastroenteritis) and 4 subjects (0.3% [4/1,434]) who received INFANRIX and inactivated poliovirus vaccine (Sanofi Pasteur SA) reported serious adverse events (cellulitis, constipation, foreign body trauma, fever without identified etiology).

6.2 Postmarketing Experience

In addition to reports in clinical trials, the following adverse events, for which a causal relationship to components of KINRIX is plausible, have been reported since market introduction. Because these events are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to vaccination.

General Disorders and Administration Site Conditions

Injection site vesicles.

Nervous System Disorders

Syncope.

Skin and Subcutaneous Tissue Disorders

Pruritus.

Additional adverse events reported following postmarketing use of INFANRIX, for which a causal relationship to vaccination is plausible, are: Allergic reactions, including anaphylactoid reactions, anaphylaxis, angioedema, and urticaria; apnea; collapse or shock-like state (hypotonic-hyporesponsive episode); convulsions (with or without fever); lymphadenopathy; and thrombocytopenia.

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration

In US clinical trials, KINRIX was administered concomitantly with the second dose of MMR vaccine (Merck & Co., Inc.); in one of these trials (Study 055), KINRIX was also administered concomitantly with varicella vaccine (Merck & Co., Inc.) *[see Clinical Studies (14.2)]*.

When KINRIX is administered concomitantly with other injectable vaccines, they should be given with separate syringes. KINRIX should not be mixed with any other vaccine in the same syringe or vial.

7.2 Immunosuppressive Therapies

Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune response to KINRIX.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with KINRIX. It is also not known whether KINRIX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity.

8.4 Pediatric Use

Safety and effectiveness of KINRIX in children younger than 4 years of age and children 7 to 16 years of age have not been evaluated. KINRIX is not approved for use in persons in these age groups.

11 DESCRIPTION

KINRIX (Diphtheria and Tetanus Toxoids and Acellular Pertussis Adsorbed and Inactivated Poliovirus Vaccine) is a noninfectious, sterile vaccine for intramuscular administration. Each 0.5-mL dose is formulated to contain 25 Lf of diphtheria toxoid, 10 Lf of tetanus toxoid, 25 mcg of inactivated pertussis toxin (PT), 25 mcg of filamentous hemagglutinin (FHA), 8 mcg of pertactin (69 kiloDalton outer membrane protein), 40 D-antigen Units (DU) of Type 1 poliovirus (Mahoney), 8 DU of Type 2 poliovirus (MEF-1), and 32 DU of Type 3 poliovirus (Saukett). The diphtheria, tetanus, and pertussis components of KINRIX are the same as those in INFANRIX and PEDIARIX and the poliovirus component is the same as that in PEDIARIX.

The diphtheria toxin is produced by growing *Corynebacterium diphtheriae* in Fenton medium containing a bovine extract. Tetanus toxin is produced by growing *Clostridium tetani* in a modified Latham medium derived from bovine casein. The bovine materials used in these extracts are sourced from countries which the United States Department of Agriculture (USDA) has determined neither have nor are at risk of bovine spongiform encephalopathy (BSE). Both toxins are detoxified with formaldehyde, concentrated by ultrafiltration, and purified by precipitation, dialysis, and sterile filtration.

The acellular pertussis antigens (PT, FHA, and pertactin) are isolated from *Bordetella pertussis* culture grown in modified Stainer-Scholte liquid medium. PT and FHA are isolated from the

fermentation broth; pertactin is extracted from the cells by heat treatment and flocculation. The antigens are purified in successive chromatographic and precipitation steps. PT is detoxified using glutaraldehyde and formaldehyde. FHA and pertactin are treated with formaldehyde.

Diphtheria and tetanus toxoids and pertussis antigens (inactivated PT, FHA, and pertactin) are individually adsorbed onto aluminum hydroxide.

The inactivated poliovirus component of KINRIX is an enhanced potency component. Each of the 3 strains of poliovirus is individually grown in VERO cells, a continuous line of monkey kidney cells, cultivated on microcarriers. Calf serum and lactalbumin hydrolysate are used during VERO cell culture and/or virus culture. Calf serum is sourced from countries the USDA has determined neither have nor are at risk of BSE. After clarification, each viral suspension is purified by ultrafiltration, diafiltration, and successive chromatographic steps, and inactivated with formaldehyde. The 3 purified viral strains are then pooled to form a trivalent concentrate.

Diphtheria and tetanus toxoid potency is determined by measuring the amount of neutralizing antitoxin in previously immunized guinea pigs. The potency of the acellular pertussis components (inactivated PT, FHA, and pertactin) is determined by enzyme-linked immunosorbent assay (ELISA) on sera from previously immunized mice. The potency of the inactivated poliovirus component is determined by using the D-antigen ELISA and by a poliovirus-neutralizing cell culture assay on sera from previously immunized rats.

Each 0.5-mL dose contains aluminum hydroxide as adjuvant (not more than 0.6 mg aluminum by assay) and 4.5 mg of sodium chloride. Each dose also contains ≤100 mcg of residual formaldehyde and ≤100 mcg of polysorbate 80 (Tween 80). Neomycin sulfate and polymyxin B are used in the poliovirus vaccine manufacturing process and may be present in the final vaccine at ≤0.05 ng neomycin and ≤0.01 ng polymyxin B per dose.

The tip caps of the prefilled syringes contain natural rubber latex; the plungers are not made with natural rubber latex. The vial stoppers are not made with natural rubber latex.

KINRIX does not contain a preservative.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Diphtheria

Diphtheria is an acute toxin-mediated infectious disease caused by toxigenic strains of *C. diphtheriae*. Protection against disease is due to the development of neutralizing antibodies to the diphtheria toxin. A serum diphtheria antitoxin level of 0.01 IU/mL is the lowest level giving some degree of protection; a level of 0.1 IU/mL is regarded as protective.[1]

Tetanus

Tetanus is an acute toxin-mediated disease caused by a potent exotoxin released by *C. tetani*.

Protection against disease is due to the development of neutralizing antibodies to the tetanus toxin. A serum tetanus antitoxin level of at least 0.01 IU/mL, measured by neutralization assays, is considered the minimum protective level.[2,3] A level of ≥0.1 IU/mL is considered protective.[4]

Pertussis

Pertussis (whooping cough) is a disease of the respiratory tract caused by *B. pertussis*. The role of the different components produced by *B. pertussis* in either the pathogenesis of, or the immunity to, pertussis is not well understood. There is no well established serological correlate of protection for pertussis. The efficacy of the pertussis component of KINRIX was determined in clinical trials of INFANRIX administered as a 3-dose series in infants (see INFANRIX prescribing information).

Poliomyelitis

Poliovirus is an enterovirus that belongs to the picornavirus family. Three serotypes of poliovirus have been identified (Types 1, 2, and 3). Neutralizing antibodies against the 3 poliovirus serotypes are recognized as conferring protection against poliomyelitis disease.[5]

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

KINRIX has not been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

14 CLINICAL STUDIES

14.1 Immunological Evaluation

In a US multicenter study (Study 048), 4,209 children were randomized in a 3:1 ratio to receive either KINRIX or INFANRIX and IPV (Sanofi Pasteur SA) administered concomitantly at separate sites. Subjects also received MMR vaccine (Merck & Co., Inc.) administered concomitantly at a separate site. Subjects were children 4 through 6 years of age who previously received 4 doses of INFANRIX, 3 doses of IPV, and 1 dose of MMR vaccine. Among subjects in both vaccine groups combined, 49.6% were female; 45.6% of subjects were white, 18.8% Hispanic, 13.6% Asian, 7.0% black, and 15.0% were of other racial/ethnic groups.

Levels of antibodies to the diphtheria, tetanus, pertussis (PT, FHA, and pertactin), and poliovirus antigens were measured in sera obtained immediately prior to vaccination and 1 month (range: 31 to 48 days) after vaccination (Table 2). The co-primary immunogenicity endpoints were anti-diphtheria toxoid, anti-tetanus toxoid, anti-PT, anti-FHA, and anti-pertactin booster responses, and anti-poliovirus Type 1, Type 2, and Type 3 geometric mean antibody titers (GMTs) 1 month after vaccination. KINRIX was shown to be non-inferior to INFANRIX and IPV administered separately, in terms of booster responses to DTaP antigens and post-vaccination GMTs for anti-poliovirus antibodies (Table 2).

Table 2. Pre-vaccination Antibody Levels and Post-vaccination[a] Antibody Responses following KINRIX Compared with Separate Concomitant Administration of INFANRIX and IPV in Children 4 to 6 Years of Age When Coadministered with MMR Vaccine (Study 048) (ATP Cohort for Immunogenicity)

	KINRIX N = 787-851	INFANRIX + IPV N = 237-262
Anti-diphtheria Toxoid		
Pre-vaccination % ≥0.1 IU/mL (95% CI)[b]	87.7 (85.3, 89.9)	85.5 (80.6, 89.5)
Post-vaccination % ≥0.1 IU/mL (95% CI)[b]	100 (99.6, 100)	100 (98.6, 100)
% Booster Response (95% CI)[c]	99.5 (98.8, 99.9)[d]	100 (98.6, 100)
Anti-tetanus Toxoid		
Pre-vaccination % ≥0.1 IU/mL (95% CI)[b]	87.8 (85.4, 90.0)	88.2 (83.6, 91.8)
Post-vaccination % ≥0.1 IU/mL (95% CI)[b]	100 (99.6, 100)	100 (98.6, 100)
% Booster Response (95% CI)[c]	96.7 (95.2, 97.8)[d]	93.9 (90.2, 96.5)
Anti-PT		
% Booster Response (95% CI)[e]	92.2 (90.2, 94.0)[d]	92.6 (88.7, 95.5)
Anti-FHA		
% Booster Response (95% CI)[e]	95.4 (93.7, 96.7)[d]	96.2 (93.1, 98.1)
Anti-pertactin		
% Booster Response (95% CI)[e]	97.8 (96.5, 98.6)[d]	96.9 (94.1, 98.7)
Anti-poliovirus 1		
Pre-vaccination % ≥1:8 (95% CI)[b]	88.3 (85.9, 90.4)	85.1 (80.1, 89.2)
Post-vaccination % ≥1:8 (95% CI)[b]	99.9 (99.3, 100)	100 (98.5, 100)
Post-vaccination GMT (95% CI)	2,127 (1,976, 2,290)[f]	1,685 (1,475, 1,925)
Anti-poliovirus 2		
Pre-vaccination % ≥1:8 (95% CI)[b]	91.8 (89.7, 93.6)	87.0 (82.3, 90.8)
Post-vaccination % ≥1:8 (95% CI)[b]	100 (99.6, 100)	100 (98.5, 100)
Post-vaccination GMT (95% CI)	2,265 (2,114, 2,427)[f]	1,818 (1,606, 2,057)
Anti-poliovirus 3		
Pre-vaccination % ≥1:8 (95% CI)[b]	84.7 (82.0, 87.0)	85.0 (80.1, 89.1)
Post-vaccination % ≥1:8 (95% CI)[b]	100 (99.5, 100)	100 (98.5, 100)
Post-vaccination GMT (95% CI)	3,588 (3,345, 3,849)[f]	3,365 (2,961, 3,824)

ATP = According-to-protocol; CI = Confidence Interval; GMT = Geometric mean antibody titer; IPV = Inactivated poliovirus vaccine (Sanofi Pasteur SA); MMR = Measles, mumps, and rubella vaccine (Merck & Co., Inc.).

N = Number of subjects with available results.

[a] One month blood sampling, range 31 to 48 days.

[b] Seroprotection defined as anti-diphtheria toxoid and anti-tetanus toxoid antibody concentrations ≥0.1 IU/mL by ELISA and as anti-poliovirus Type 1, Type 2, and Type 3 antibody titer ≥1:8 by micro-neutralization assay for poliovirus.

[c] Booster response: In subjects with pre-vaccination <0.1 IU/mL, post-vaccination concentration ≥0.4 IU/mL. In subjects with pre-vaccination concentration ≥0.1 IU/mL, an increase of at least 4 times the pre-vaccination concentration.

[d] KINRIX was non-inferior to INFANRIX + IPV based on booster response rates (upper limit of two-sided 95% CI on the difference of INFANRIX + IPV minus KINRIX ≤10%).

[e] Booster response: In subjects with pre-vaccination <5 EL.U./mL, post-vaccination concentration ≥20 EL.U./mL. In subjects with pre-vaccination ≥5 EL.U./mL and <20 EL.U./mL, an increase of at least 4 times the pre-vaccination concentration. In subjects with pre-vaccination ≥20 EL.U./mL, an increase of at least 2 times the pre-vaccination concentration.

[f] KINRIX was non-inferior to INFANRIX + IPV based on post-vaccination anti-poliovirus antibody GMTs adjusted for baseline titer (upper limit of two-sided 95% CI for the GMT ratio [INFANRIX + IPV:KINRIX] ≤1.5).

14.2 Concomitant Vaccine Administration

In a US study (Study 055) that enrolled children 4 to 6 years of age, KINRIX was administered concomitantly at separate sites with MMR vaccine (Merck & Co., Inc.) (N = 237) or with MMR vaccine and varicella vaccine (Merck & Co., Inc.) (N = 239). Immune responses to the antigens contained in KINRIX were measured approximately one month (28 to 48 days) after vaccination. Booster responses to diphtheria, tetanus, and pertussis antigens and GMTs for poliovirus (Type 1, 2, and 3) after the receipt of KINRIX administered concomitantly with MMR vaccine and varicella vaccine were non-inferior to immune responses following concomitant administration of KINRIX administered with MMR vaccine.

15 REFERENCES

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16 HOW SUPPLIED/STORAGE AND HANDLING

KINRIX is available in 0.5-mL single-dose vials and disposable prefilled TIP-LOK syringes (packaged without needles):

NDC 58160-812-01 Vial in Package of 10: NDC 58160-812-11

NDC 58160-812-43 Syringe in Package of 10: NDC 58160-812-52

Store refrigerated between 2° and 8°C (36° and 46°F). Do not freeze. Discard if the vaccine has been frozen.

17 PATIENT COUNSELING INFORMATION

Parents or guardians should be:

- informed of the potential benefits and risks of immunization with KINRIX.
- informed about the potential for adverse reactions that have been temporally associated with administration of KINRIX or other vaccines containing similar components.
- given the Vaccine Information Statements, which are required by the National Childhood Vaccine Injury Act of 1986 to be given prior to immunization. These materials are available free of charge at the Centers for Disease Control and Prevention (CDC) website (www.cdc.gov/vaccines).

Manufactured by **GlaxoSmithKline Biologicals**

Rixensart, Belgium, US License 1617, and

Novartis Vaccines and Diagnostics GmbH

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