



POLICY & PRACTICE

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States Boost Medicaid Rolls

The Department of Health and Human Services has awarded \$206 million to 15 states for enrolling more uninsured children in Medicaid. Last year, the Children's Health Insurance Program Reauthorization bonuses totaled just \$75 million to 10 states. To qualify, states must have adopted specific program features known to encourage Medicaid enrollment and retention and then document increases significantly beyond what would have been expected. States qualifying this year are Alabama, Alaska, Colorado, Illinois, Iowa, Kansas, Louisiana, Maryland, Michigan, New Jersey, New Mexico, Ohio, Oregon, Washington, and Wisconsin.

Less Fluoride Recommended

The Environmental Protection Agency and HHS have joined forces to lower the amount of fluoride in drinking water. Americans don't need as much from that source because they have others — from toothpaste to regular dentists' treatment — than weren't available when public water fluoridation was introduced decades ago. The two agencies announced in the Federal Register that they want to replace the currently recommended range of water fluoridation, 0.7-1.2 mg/L, to a single target of 0.7 mg/L. The action will leave enough fluoride in the water supply to prevent tooth decay but protect children's teeth from dental fluorosis. The announcement said that the HHS expects to finalize the proposed change this spring, based on the EPA's assessment of fluoridation needs.

Combination Vaccines Avoided

One in five pediatricians reported that inadequate reimbursement prevented

them from using at least one of two combination vaccines studied, according to the RAND Corporation. The study looked at infant vaccines — the diphtheria and tetanus toxoids and acellular pertussis, hepatitis B virus and inactivated poliovirus (DTaP-HepB-IPV) vaccine and the DTaP, IPV, and *Haemophilus influenzae* type b (DTaP-

IPV/Hib) vaccine. Although 78% of the 492 pediatricians surveyed said they used one or both of the combination vaccines, more than half said their practice did not receive adequate reimbursement for vaccines in general. More than one-fifth said they didn't use one of the combination vaccines either because of inadequate reimbursement for doses or for administration. Smaller practices were less likely to use the combination vaccines, as were those with fewer publicly insured patients and those in a state with a less generous vaccine-

financing policy, the study said.

Grant Will Fund Residencies

The Josiah Macy Jr. Foundation has awarded \$500,000 to the American Academy of Pediatrics for pediatric residency training initiatives to improve care for underserved children. The two organizations said the grant will support pediatric residency programs that teach community health and advocacy, train future leaders, enhance future pediatricians' involvement in caring for underserved populations, build community partnerships, and use

ROTARIX (Rotavirus Vaccine, Live, Oral)

The following is a brief summary only; see full prescribing information for complete product information.

1 INDICATIONS AND USAGE

ROTARIX® is indicated for the prevention of rotavirus gastroenteritis caused by G1 and non-G1 types (G3, G4, and G9) when administered as a 2-dose series [see *Clinical Studies (14.3)* of full prescribing information]. ROTARIX is approved for use in infants 6 weeks to 24 weeks of age.

4 CONTRAINDICATIONS

4.1 Hypersensitivity: A demonstrated history of hypersensitivity to any component of the vaccine. Infants who develop symptoms suggestive of hypersensitivity after receiving a dose of ROTARIX should not receive further doses of ROTARIX.

4.2 Gastrointestinal Tract Congenital Malformation: History of uncorrected congenital malformation of the gastrointestinal tract (such as Meckel's diverticulum) that would predispose the infant for intussusception. **4.3 Severe Combined Immunodeficiency Disease:** Infants with Severe Combined Immunodeficiency Disease (SCID) should not receive ROTARIX. Postmarketing reports of gastroenteritis, including severe diarrhea and prolonged shedding of vaccine virus, have been reported in infants who were administered live, oral rotavirus vaccines and later identified as having SCID [see *Adverse Reactions (6.2)*].

5 WARNINGS AND PRECAUTIONS

5.1 Gastrointestinal Disorders: Administration of ROTARIX should be delayed in infants suffering from acute diarrhea or vomiting. Safety and effectiveness of ROTARIX in infants with chronic gastrointestinal disorders have not been evaluated.

[See *Contraindications (4.2)*.] **5.2 Altered Immunocompetence:** Safety and effectiveness of ROTARIX in infants with known primary or secondary immunodeficiencies, including infants with human immunodeficiency virus (HIV), infants on immunosuppressive therapy, or infants with malignant neoplasms affecting the bone marrow or lymphatic system have not been evaluated. **5.3 Shedding and Transmission:** Rotavirus shedding in stool occurs after vaccination with peak excretion occurring around day 7 after dose 1. Live rotavirus shedding was evaluated in 2 studies among a subset of infants at day 7 after dose 1. In these studies, the estimated percentages of recipients of ROTARIX who shed live rotavirus were 25.6% (95% Confidence Interval [CI]: 10.2, 41.1) and 26.5% (95% CI: 15.5, 37.5), respectively. Transmission of virus was not evaluated. There is a possibility that the live vaccine virus can be transmitted to non-vaccinated contacts. The potential for transmission of vaccine virus following vaccination should be weighed against the possibility of acquiring and transmitting natural rotavirus. **5.4 Intussusception:** Following administration of a previously licensed oral live rhesus rotavirus-based vaccine, an increased risk of intussusception was observed. The risk of intussusception with ROTARIX was evaluated in a safety study (including 63,225 infants) conducted in Latin America and Finland. No increased risk of intussusception was observed in this clinical trial following administration of ROTARIX when compared with placebo. [See *Adverse Reactions (6.1)*.] In postmarketing experience, cases of intussusception have been reported in temporal association with ROTARIX [see *Adverse Reactions (6.2)*]. **5.5 Post-Exposure Prophylaxis:** Safety and effectiveness of ROTARIX when administered after exposure to rotavirus have not been evaluated.

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 to rates in the clinical trials of another vaccine, and may not reflect the rates observed in practice. As with any vaccine, there is the possibility that broad use of ROTARIX could reveal adverse reactions not observed in clinical trials. Solicited and unsolicited adverse events, serious adverse events and cases of intussusception were collected in 7 clinical studies. Cases of intussusception and serious adverse events were collected in an additional large safety study. These 8

clinical studies evaluated a total of 71,209 infants who received ROTARIX (N = 36,755) or placebo (N = 34,454). The racial distribution for these studies was as follows: Hispanic 73.4%, white 16.2%, black 1.0%, and other 9.4%; 51% were male.

Solicited Adverse Events: In 7 clinical studies, detailed safety information was collected by parents/guardians for 8 consecutive days following vaccination with ROTARIX (i.e., day of vaccination and the next 7 days). A diary card was completed to record fussiness/irritability, cough/runny nose, the infant's temperature, loss of appetite, vomiting, or diarrhea on a daily basis during the first week following each dose of ROTARIX or placebo. Adverse events among recipients of ROTARIX and placebo occurred at similar rates (Table 1).

Table 1. Solicited Adverse Events Within 8 Days Following Doses 1 and 2 of ROTARIX or Placebo (Total Vaccinated Cohort)

	Dose 1		Dose 2	
	ROTARIX N = 3,284	Placebo N = 2,013	ROTARIX N = 3,201	Placebo N = 1,973
	%	%	%	%
Fussiness/irritability ^a	52	52	42	42
Cough/runny nose ^b	28	30	31	33
Fever ^c	25	33	28	34
Loss of appetite ^d	25	25	21	21
Vomiting	13	11	8	8
Diarrhea	4	3	3	3

Total vaccinated cohort = all vaccinated infants for whom safety data were available.

N = number of infants for whom at least one symptom sheet was completed.

^aDefined as crying more than usual.

^bData not collected in 1 of 7 studies; Dose 1: ROTARIX N = 2,583; placebo N = 1,897; Dose 2: ROTARIX N = 2,522; placebo N = 1,863.

^cDefined as temperature $\geq 100.4^{\circ}\text{F}$ ($\geq 38.0^{\circ}\text{C}$) rectally or $\geq 99.5^{\circ}\text{F}$ ($\geq 37.5^{\circ}\text{C}$) orally.

^dDefined as eating less than usual.

Unsolicited Adverse Events: Infants were monitored for unsolicited serious and non-serious adverse events that occurred in the 31-day period following vaccination in 7 clinical studies. The following adverse events occurred at a statistically higher incidence (95% CI of Relative Risk excluding 1) among recipients of ROTARIX (N = 5,082) as compared with placebo recipients (N = 2,902): irritability (ROTARIX 11.4%, placebo 8.7%) and flatulence (ROTARIX 2.2%, placebo 1.3%).

Serious Adverse Events (SAEs): Infants were monitored for serious adverse events that occurred in the 31-day period following vaccination in 8 clinical studies. Serious adverse events occurred in 1.7% of recipients of ROTARIX (N = 36,755) as compared with 1.9% of placebo recipients (N = 34,454). Among placebo recipients, diarrhea (placebo 0.07%, ROTARIX 0.02%), dehydration (placebo 0.06%, ROTARIX 0.02%), and gastroenteritis (placebo 0.3%, ROTARIX 0.2%) occurred at a statistically higher incidence (95% CI of Relative Risk excluding 1) as compared with recipients of ROTARIX.

Deaths: During the entire course of 8 clinical studies, there were 68 (0.19%) deaths following administration of ROTARIX (N = 36,755) and 50 (0.15%) deaths following placebo administration (N = 34,454). The most commonly reported cause of death following vaccination was pneumonia, which was observed in 19 (0.05%) recipients of ROTARIX and 10 (0.03%) placebo recipients (Relative Risk: 1.74, 95% CI: 0.76, 4.23).

Intussusception: In a controlled safety study conducted in Latin America and Finland, the risk of intussusception was evaluated in 63,225 infants (31,673 received ROTARIX and 31,552 received placebo). Infants were monitored by active surveillance including independent, complementary methods (prospective hospital surveillance and parent reporting at scheduled study visits) to identify potential cases of intussusception within 31 days after vaccination and, in a subset of 20,169 infants (10,159 received ROTARIX and 10,010 received placebo), up to one year after

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technology effectively. "It is clear that skills and involvement for pediatricians in community pediatrics focused on improving the health of underserved children are desired and achievable, but more work needs to be done in order to provide effective training," said AAP President Dr. O. Marion Burton.

Food for Kids Found Wanting

Tests showed that 49 out of 58 supposedly healthy foods commonly marketed to children failed to meet at least one "healthy" standard, according to a study from the Prevention

Institute. Food manufacturers increasingly use nutritional claims on the front of food packages to tout the foods as healthier choices. However, almost all the foods contained added sugar, and more than half qualified as high sugar, according to the institute's analysis. In addition, more than half were low in fiber and contained no fruit or vegetable. About one-fourth of the prepared foods contained too much saturated fat, and one-third contained too much sodium, according to the study. Foods evaluated included staples such as Campbell's Tomato Soup,

Skippy Super Chunk Peanut Butter, and Rice Krispies.

FDA Seeks Pediatric Devices

The Food and Drug Administration is inviting grant proposals from nonprofit organizations to facilitate the development, production, and distribution of pediatric medical devices. "There currently exists a great need for medical devices designed specifically with children in mind," the agency said in its announcement. The grants, which will be issued by the agency's Office of Orphan Products Develop-

ment, will go to "consortia whose business model and approach to device development will either result in, or substantially contribute to, market approval of medical devices designed specifically for use in children." However, the program won't support single-device projects, the agency said. Although the grant program is administered by the orphan products development office, it's intended to encompass devices for all conditions, not just rare diseases, the FDA said. Grant applications are due May 2.

-Jane Anderson

the first dose. No increased risk of intussusception following administration of ROTARIX was observed within a 31-day period following any dose, and rates were comparable to the placebo group after a median of 100 days (Table 2). In a subset of 20,169 infants (10,159 received ROTARIX and 10,010 received placebo) followed up to one year after dose 1, there were 4 cases of intussusception with ROTARIX compared with 14 cases of intussusception with placebo [Relative Risk: 0.28 (95% CI: 0.10, 0.81)]. All of the infants who developed intussusception recovered without sequelae.

Table 2. Intussusception and Relative Risk With ROTARIX Compared With Placebo

Confirmed Cases of Intussusception	ROTARIX N = 31,673	Placebo N = 31,552
Within 31 days of diagnosis after any dose	6	7
Relative Risk (95% CI)	0.85 (0.30, 2.42)	
Within 100 days of dose 1^a	9	16
Relative Risk (95% CI)	0.56 (0.25, 1.24)	

CI = Confidence Interval.

^aMedian duration after dose 1 (follow-up visit at 30 to 90 days after dose 2).

Among vaccine recipients, there were no confirmed cases of intussusception within the 0- to 14-day period after the first dose (Table 3), which was the period of highest risk for the previously licensed oral live rhesus rotavirus-based vaccine.

Table 3. Intussusception Cases by Day Range in Relation to Dose

Day Range	Dose 1		Dose 2		Any Dose	
	ROTARIX N =	Placebo N =	ROTARIX N =	Placebo N =	ROTARIX N =	Placebo N =
0-7	0	0	2	0	2	0
8-14	0	0	0	2	0	2
15-21	1	1	2	1	3	2
22-30	0	1	1	2	1	3
Total (0-30)	1	2	5	5	6	7

Kawasaki Disease: Kawasaki disease has been reported in 18 (0.035%) recipients of ROTARIX and 9 (0.021%) placebo recipients from 16 completed or ongoing clinical trials. Of the 27 cases, 5 occurred following ROTARIX in clinical trials that were either not placebo-controlled or 1:1 randomized. In placebo-controlled trials, Kawasaki disease was reported in 17 recipients of ROTARIX and 9 placebo recipients [Relative Risk: 1.71 (95% CI: 0.71, 4.38)]. Three of the 27 cases were reported within 30 days post-vaccination: 2 cases (ROTARIX = 1, placebo = 1) were from placebo-controlled trials [Relative Risk: 1.00 (95% CI: 0.01, 78.35)] and one case following ROTARIX was from a non-placebo-controlled trial. Among recipients of ROTARIX, the time of onset after study dose ranged 3 days to 19 months.

6.2 Postmarketing Experience: The following adverse events have been reported since market introduction of ROTARIX. 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 with ROTARIX. **Gastrointestinal Disorders:** Intussusception (including death), hematochezia, gastroenteritis with vaccine viral shedding in infants with Severe Combined Immunodeficiency Disease (SCID). **Blood and Lymphatic System Disorders:** Idiopathic thrombocytopenic purpura. **Vascular Disorders:** Kawasaki disease. **General Disorders and Administration Site Conditions:** Maladministration.

7 DRUG INTERACTIONS

7.1 Concomitant Vaccine Administration: In clinical trials, ROTARIX was administered concomitantly with US-licensed and non-US-licensed vaccines. In a US coadministration study in 484 infants, there was no evidence of interference in the immune responses to any of the antigens when PEDIARIX® [Diphtheria and Tetanus Toxoids and Acellular

Pertussis Adsorbed, Hepatitis B (Recombinant) and Inactivated Poliovirus Vaccine Combined], a US-licensed 7-valent pneumococcal conjugate vaccine (Wyeth Pharmaceuticals Inc.), and a US-licensed Hib conjugate vaccine (Sanofi Pasteur SA) were coadministered with ROTARIX as compared with separate administration of ROTARIX. **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 ROTARIX. [See Warnings and Precautions (5.2).]

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Pregnancy Category C. Animal reproduction studies have not been conducted with ROTARIX. It is also not known whether ROTARIX can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. **8.4 Pediatric Use:** Safety and effectiveness of ROTARIX in infants younger than 6 weeks or older than 24 weeks of age have not been evaluated. The effectiveness of ROTARIX in pre-term infants has not been established. Safety data are available in pre-term infants (ROTARIX = 134, placebo = 120) with a reported gestational age ≤36 weeks. These pre-term infants were followed for serious adverse events up to 30 to 90 days after dose 2. Serious adverse events were observed in 5.2% of recipients of ROTARIX as compared with 5.0% of placebo recipients. No deaths or cases of intussusception were reported in this population.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility: ROTARIX has not been evaluated for carcinogenic or mutagenic potential, or for impairment of fertility.

17 PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (17.2) of full prescribing information. **17.1 Patient Advice:** Parents or guardians should be informed by the healthcare provider of the potential benefits and risks of immunization with ROTARIX, and of the importance of completing the immunization series. The healthcare provider should inform the parents or guardians about the potential for adverse reactions that have been temporally associated with administration of ROTARIX or other vaccines containing similar components. The parent or guardian accompanying the recipient should be instructed to report any adverse events to their healthcare provider. The parent or guardian should be 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 (CDC) website (www.cdc.gov/vaccines).

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