衛署菌疫輸字第 000825 號
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# 輪達停®

## 口服活性五價輪狀病毒疫苗

**RotaTeq®**

**[Rotavirus Vaccine, Live, Oral, Pentavalent]**

## 說　明

RotaTeq®為一內含5種活性基因重組(reassortant)輪狀病毒的活性口服五價疫苗。這些基因重組株的母株係由人類宿主及牛宿主身上分離而得。其中四種基因重組株各表現一種源自人類輪狀病毒母株的VP7外鞘蛋白(血清型G1、G2、G3或G4)，以及源自牛輪狀病毒母株的VP4吸附蛋白(血清型P7[5])。第五種基因重組株則表現源自人類輪狀病毒母株的VP4吸附蛋白(血清型P1A[8])，以及源自牛輪狀病毒母株的VP7外鞘蛋白(血清型G6) (參見表1)。

表 1

| 基因重組株名稱 | 人類輪狀病毒母株及其外表蛋白組成 | 牛輪狀病毒母株及其外表蛋白組成 | 基因重組株的外表蛋白組成(粗體字為人類輪狀病毒成分) | 最低劑量濃度($10^6$感染單位) |
|---|---|---|---|---|
| G1 | WI79 – G1P1A[8] | WC3 – G6, P7[5] | **G1**P7[5] | 2.2 |
| G2 | SC2 – G2P2A[6] | | **G2**P7[5] | 2.8 |
| G3 | WI78 – G3P1A[8] | | **G3**P7[5] | 2.2 |
| G4 | BrB – G4P2A[6] | | **G4**P7[5] | 2.0 |
| P1A[8] | WI79 – G1P1A[8] | | G6**P1A[8]** | 2.3 |

這些基因重組株是在未添加抗黴菌劑的情況下，利用標準細胞培養技術，於Vero細胞中繁殖而得。

這些基因重組株成分係懸浮於經過緩衝的安定劑溶液中。每劑疫苗均含有蔗糖、檸檬酸鈉、單水合磷酸二氫鈉、氫氧化鈉、聚山梨醇酯80、細胞培養基以及微量的牛胚胎血清。本疫苗不含任何防腐劑或thimerosal。

RotaTeq為一淡黃色並可能略帶粉紅色的澄清液體。

## 臨床藥理學

輪狀病毒是導致嬰幼兒嚴重急性腸胃炎的主因，該等嬰幼兒中有95%以上都是在5歲之前受到感染。[1] 其中最為嚴重的病例都是發生在6至24個月大的嬰幼兒。[2]

據估計，全世界每年有1億3千8百萬的兒童得到輪狀病毒腸胃炎，並造成2千5百萬個門診病例，及2百1十萬個住院病例，更造成352,000至592,000個死亡案例。

台灣地區在2000至2003年間，年齡小於2歲以下幼兒之年人口總數為460,000至570,000位。利用台灣健保局同期資料所做之估算，年齡小於2歲以下之幼兒族群中，每年因急性胃腸炎(acute gastroenteritis， AGE)而看門診之病例為454,992至954,384例，其中較嚴重而需住院者每年約為7,356至11,208例。根據台灣主動監視輪狀病毒的近期資料顯示，急性胃腸炎門診病例中有14%為輪狀病毒感染，住院病例中則約有44%為輪狀病毒感染所致。將主動監視輪狀病毒的近期資料應用到2000-2003年的國家對於急性胃腸炎的估算，則可估計出年齡小於2歲以下之幼兒族群中，因輪狀病毒感染造成之門診病例年發生率為12.4至28.8%，但較嚴重而需住院治療之病例的年發生率則為0.61至0.98%.

在2001至2003 年以及2005年12月至2006年6月兩段期間針對小於5歲的台灣住院病童進行的兩項研究顯示，輪狀病毒是引起嚴重下痢的最常見之病因：43%-45.9%因急性腸胃炎住院病童的糞便檢體呈輪狀病毒陽性反應。在稍後的研究中，13.9%急性腸胃炎門診之病童的糞便檢體呈輪狀病毒抗原陽性反應。在這些研究中證實出有多種G血清型型別流行且不固定，其分佈情形如下：2001-2003 年時為G1 (31%), G2 (10%), G3 (9.3%), G4 (3.7%), G9 (37%) ；以及2005年12月至2006年6月時

則為G1 (41%), G2 (13%), G3 (12%), G5 (0.3%), G9 (33%)。50% 的檢體屬於非-G1血清型(G2, G4, G5 and G9)，而相關的分佈顯然會隨時間而改變。在2005年12月至2006年6月所進行的研究顯示，因輪狀病毒而住院之病童的住院時間平均長度為5.6天(範圍係自2至25天)。如果孩童因輪狀病毒腸胃炎住院而導致父母無法工作的天數平均為4個工作天。[3,4]

**作用機制**

RotaTeq預防輪狀病毒腸胃炎的確切免疫機制，目前並不清楚(參見"臨床研究"中的*免疫生成性*)。 RotaTeq是一種可在小腸中複製並誘發免疫反應的活性病毒疫苗。

**臨床研究**

在跨越3大洲11國所進行的3項安慰劑對照性第3期研究中，共有72,324名嬰兒接受隨機分組。證實RotaTeq對輪狀病毒腸胃炎之預防效果的數據，係來自兩項分別收錄有6,983名美國嬰兒(包括納瓦伙族和白嶺阿帕契族印第安人)和芬蘭嬰兒的研究，該二項研究為：輪狀病毒預防效果及安全性試驗(Rotavirus Efficacy and Safety Trial, REST)與研究007。第三項試驗(研究009)則提供了支持產品一致性的臨床證據，以及更多有助於整體安全性評估的數據。

預防效果研究子群中的種族分佈情形如下：白人(RotaTeq組68%，安慰劑組69%)；西班牙裔美國人(RotaTeq組10%，安慰劑組9%)；黑人(兩組皆為2%)；多重種族(RotaTeq組4%，安慰劑組5%)；亞洲人(兩組皆為<1%)；納伙瓦族美國原住民(RotaTeq組15%，安慰劑組14%)，以及其他種族(兩組皆為<1%)。兩個接種組中的性別分佈比例皆為男性52%及女性48%。

這些研究中的預防效果評估目標包括：1)對任何嚴重度之輪狀病毒腸胃炎的預防效果；2)對依據臨床評分系統評定為重度輪狀病毒腸胃炎的預防效果；以及3)對輪狀病毒腸胃炎所造成之住院率的降低程度。

對健康嬰兒投予一系列三劑的疫苗，第一劑於6至12週齡時投予，之後再以4至10週的間隔投予兩劑。嬰兒接種第三劑時的年齡為32週齡(含)以下。不可投予口服小兒麻痺疫苗；但可與其他小兒疫苗同時投予(參見"劑量與用法"中與"其他疫苗併用"一欄)。所有研究都允許餵哺母乳。

用以確認疫苗預防效果之輪狀病毒腸胃炎病例的定義為受試者必須符合下列兩項臨床標準與實驗室標準：(1)在24小時內解出3次(含)以上的水狀糞便或較正常更為鬆散的糞便，及(或)出現強烈的嘔吐症狀；以及(2)於症狀出現後的14天內，以酵素免疫分析法(Enzyme immunoassay, EIA)在糞便樣本中檢出輪狀病毒抗原。急性輪狀病毒腸胃炎之嚴重度的判定依據，為一種臨床評分系統，其考慮因素包括發燒、嘔吐、腹瀉及行為改變等症狀的強烈程度及持續時間。

基礎預防效果分析包括接種第三劑疫苗至少14天後一直到完成疫苗接種後的第一個輪狀病毒季節期間，所發生的由血清型G1、G2、G3及G4所引起的輪狀病毒腸胃炎病例。

研究人員也針對至少接種一劑疫苗的嬰兒進行分析(意圖治療[Intent- to –treat, ITT]分析)，藉以評估RotaTeq在接種第一劑疫苗後一直到完成疫苗接種後的第一個輪狀病毒季節期間，對血清型G1、G2、G3及G4所引起之輪狀病毒腸胃炎的預防效果。

**輪狀病毒預防效果及安全性試驗**

在完成疫苗接種後的第一個輪狀病毒季節期間，對存在於自然界的血清型G1、G2、G3或G4所引起之任何嚴重度的輪狀病毒腸胃炎，其基礎預防效果為74.0% (95% CI: 66.8, 79.9)，ITT預防效果為60.0% (95% CI: 51.5, 67.1)。在完成疫苗接種後的第一個輪狀病毒季節期間，對存在於自然界的血清型G1、G2、G3或G4所引起之重度輪狀病毒腸胃炎，其基礎預防效果為98.0% (95% CI: 88.3, 100.0)，ITT預防效果為96.4% (95% CI: 86.2, 99.6)。參見表2。

表 2

在REST研究中，RotaTeq在完成疫苗接種後的第一個輪狀病毒季節期間

對任何嚴重度與重度* G1-4輪狀病毒腸胃炎的預防效果

| | 按計畫表分析 | | 意圖治療分析† | |
|---|---|---|---|---|
| | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 |
| 接種疫苗的受試者 | 2,834 | 2,839 | 2,834 | 2,839 |
| 腸胃炎病例 | | | | |
| 任何嚴重度 | 82 | 315 | 150 | 371 |
| 重度病例* | 1 | 51 | 2 | 55 |
| 預防效果估計值(%)及(95%信賴區間) | | | | |
| 任何嚴重度 | 74.0 (66.8, 79.9) | | 60.0 (51.5, 67.1) | |
| 重度病例* | 98.0 (88.3, 100.0) | | 96.4 (86.2, 99.6) | |

* 以發燒、嘔吐、腹瀉及行為改變等症狀之強烈程度及持續時間為評估基礎的臨床評分系統中所定義的重度腸胃炎。

† ITT分析的對象包括預防效果評估世代中所有接種過至少一劑疫苗的受試者。

RotaTeq對重度疾病的預防效果，亦可從REST研究中所收錄之所有受試者的輪狀病毒腸胃炎住院率降低而獲得證實。RotaTeq可使接種完第三劑疫苗後最初2年期間因血清型G1、G2、G3及G4所引起之輪狀病毒腸胃炎而住院治療的病患比率降低95.8% (95% CI: 90.5, 98.2)。降低住院率方面的ITT預防效果為94.7% (95%CI: 89.3, 97.3)，如表3所示。

表 3

在REST研究中，RotaTeq在降低G1-4輪狀病毒相關住院率方面的效果

| | 按計畫表分析 | | 意圖治療分析* | |
|---|---|---|---|---|
| | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 |
| 接種疫苗的受試者 | 34,035 | 34,003 | 34,035 | 34,003 |
| 住院數 | 6 | 144 | 10 | 187 |
| 預防效果估計值(%及95%信賴區間) | 95.8 (90.5, 98.2) | | 94.7 (89.3, 97.3) | |

* ITT分析的世代包括所有接種過至少一劑疫苗的受試者。

**研究007**

在完成疫苗接種後的第一個輪狀病毒季節期間，對存在於自然界之血清型G1、G2、G3或G4所引起的任何嚴重度的輪狀病毒腸胃炎，其基礎預防效果為72.5% (95%CI: 50.6, 85.6) ，以及ITT預防效果為58.4% (95%CI: 33.8, 74.5)。在完成疫苗接種後的第一個輪狀病毒季節期間，對存在於自然界之血清型G1、G2、G3或G4所引起的重度輪狀病毒腸胃炎，其基礎預防效果為100% (95%CI: 13.0, 100.0)，對重度輪狀病毒疾病的ITT預防效果為100% (95%CI: 30.2, 100.0)，如表4所示。

表 4

在研究007中，RotaTeq在完成疫苗接種後的第一個輪狀病毒季節期間對任何嚴重度與重度*
G1-4輪狀病毒腸胃炎的預防效果

| | 按計畫表分析 | | 意圖治療分析† | |
|---|---|---|---|---|
| | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 |
| 接種疫苗的受試者 | 650 | 660 | 650 | 660 |
| 腸胃炎病例 | | | | |
| 任何嚴重度病例 | 15 | 54 | 27 | 64 |
| 重度病例* | 0 | 6 | 0 | 7 |
| 預防效果估計值(%)及(95%信賴區間) | | | | |
| 任何嚴重度 | 72.5 (50.6, 85.6) | | 58.4 (33.8, 74.5) | |
| 重度病例* | 100.0 (13.0, 100.0) | | 100.0 (30.2, 100.0) | |

* 以發燒、嘔吐、腹瀉及行為改變等症狀之強烈程度及持續時間為評估基礎的臨床評分系統中所定義的重度腸胃炎。

† ITT分析的對象包括預防效果研究世代中所有接種過至少一劑疫苗的受試者。

**劑量之間的預防效果**

在劑量之間，RotaTeq 對血清型 G1-G4 所引起之任何嚴重度之輪狀病毒腸胃炎發生率的預防效果沒有統計學上的顯著性。這是以 post hoc 分析方法評估 REST 研究中臨床預防效果評估世代(N=5,673)之數據所得的結論。

於三劑疫苗之每劑間隔期間， RotaTeq 的預防效果以血清型 G1-G4 所引起之輪狀病毒腸胃炎住院與急診率的降低作為測量標準，藉由 post hoc 分析方法分析 REST 研究(N=68,038)之數據以評估 RotaTeq 的預防效果。這些分析的結果如表 5 所示。

表 5

在 REST 研究中，於三劑疫苗之每劑間隔期間，RotaTeq 對輪狀病毒腸胃炎引起之住院與急診的降低

| | RotaTeq n=34,035; 安慰劑 n=34,003 | |
|---|---|---|
| | 接種第一劑 14天後至第二劑 | 接種第二劑 14 天後至第三劑 |
| 血清型 | G1-G4 | G1-G4 |
| 預防效果估計值%及[95% 信賴區間] | 100 [72.2, 100] | 90.9 [62.9, 99.0] |

**早產兒的預防效果**

在 204 名接種疫苗之嬰兒的子研究群(99 名為疫苗組)中，以接種第三劑疫苗至少 14 天後一直到完成疫苗接種後的第一個輪狀病毒季節期間降低血清型 G1-G4 所引起的任何嚴重度之輪狀病毒腸胃炎發生率評估預防效果，預防效果為 70.3 % [95 % CI <0, 94.7]。在 REST 研究 2,070 位接種者(1,007 位為疫苗組)中，以接種第三劑疫苗至少 14 天一直到兩年後降低血清型 G1-G4 所引起的任何嚴重度之輪狀病毒腸胃炎之住院與急診率來評估預防效果，預防效果為 100% [95 % CI 74, 100]。同樣地，以接種第三劑疫苗至少 14 天之一直到兩年後降低任何一種血清型所引起的任何嚴重度之輪狀病毒腸胃炎住院與急診率來評估預防效果，預防效果為 100% [95% CI 82, 100]。

**有效性**

如表 6 所示，三個上市後疫苗有效性試驗的結果顯示與輪狀病毒相關或所有原因的腸胃炎造成的住院、急診及門診大幅且一致性的降低。這些來自美國及法國的疫苗有效性資料也顯示 RotaTeq 針對 G12P[8]特定病毒株的有效性以及兒童直到 7 歲前與輪狀病毒相關之住院和急診的持續保護。

表 6

上市後試驗證實 RotaTeq 預防腸胃炎之有效性

| 試驗設計<br>(地區) | 試驗族群 | 指標 | 有效性<br>% [95%CI] | 輪狀病毒季節 |
|---|---|---|---|---|
| Claims database analysis (美國)* | 33,140 位接種疫苗<br>26,167 位未接種疫苗<br>年齡≥7 個月<br>接種 3 劑疫苗 | 輪狀病毒腸胃炎(RVGE†)造成的住院與急診<br><br>輪狀病毒腸胃炎造成的門診<br>所有原因的腸胃炎造成的住院與急診 | 100% [87,100]<br><br>96% [76,100]<br><br>59% [47,68] | 2007-2008 |
| Cohort study (法國)‡ | 1,895 位接種 3 劑疫苗<br>2,102 位未接種疫苗<br>年齡 <2 歲 | 輪狀病毒腸胃炎造成的住院 | 98% [83,100] | 2007-2008<br>2008-2009 |
| Case-control study (美國)§ | 402 個案例<br>2,559 對照案例¶<br>年齡<8 歲<br>接種 3 劑疫苗 | 輪狀病毒腸胃炎造成的住院與急診<br>***特定病毒株***<br>- G1P[8]<br>- G2P[4]<br>- G3P[8]<br>- G12P[8]<br>***特定年齡***<br>- 1 歲<br>- 2 歲<br>- 3 歲<br>- 4 歲<br>- 5 歲<br>- 6-7 歲 | 80% [74,84]<br><br><br>89% [55,97]<br>87% [65,95]<br>80% [64,89]<br>78% [71,84]<br><br>91% [78,96]<br>82% [69,89]<br>88% [78,93]<br>76% [51,88]<br>60% [16,81]<br>69% [43,84] | 2011-2012<br>2012-2013 |

* Wang FT, et al. Effectiveness of the pentavalent rotavirus vaccine in preventing gastroenteritis in the United States. *Pediatrics.*125 (e208). 2009-1246. 2010.

† RVGE = 輪狀病毒腸胃炎(Rotavirus Gastroenteritis)

‡ Gagneur, A, et al. Impact of rotavirus vaccination on hospitalizations for rotavirus diarrhea: The IVANHOE study. *Vaccine.* (29). 3753-3759. 2011.

§ Payne DC, et al. Long-term consistency in rotavirus vaccine protection: RV5 and RV1 vaccine effectiveness in US children, 2012-2013. *Clin Infect Dis.*1-7. 2015.

¶ 輪狀病毒-陰性急性腸胃炎對照 (RV-negative acute gastroenteritis controls)

**針對跨越數個輪狀病毒季節所做的研究**

在一項單一研究(REST)中，研究人員曾針對RotaTeq在第二個輪狀病毒季節期間的預防效果進行評估。在完成疫苗接種後的兩個輪狀病毒季節期間，對輪狀病毒血清型G1、G2、G3及G4所引起之任何嚴重度的輪狀病毒腸胃炎，其預防效果為71.3% (95%CI: 64.7, 76.9)。對僅發生於完成疫苗接種後之第二個輪狀病毒季節期間的病例，RotaTeq的預防效果為62.6% (95% CI: 44.3, 75.4)。

**輪狀病毒腸胃炎－不考慮血清型**

在REST研究之預防效果子研究群及研究007中所發現的輪狀病毒血清型為G1P1A[8]；G2P1B[4]；G3P1A[8]；G4P1A[8]；以及G9P1A[8]。

REST研究顯示，在不考慮血清型的情況下，RotaTeq對存在於自然界之任何嚴重度的輪狀病毒腸胃炎的預防效果為71.8% (95%CI: 64.5, 77.8)，對重度輪狀病毒疾病的預防效果為98.0%(95%CI: 88.3, 99.9)。就任何嚴重度的輪狀病毒疾病而言，接種第一劑疫苗之後的ITT預防效果為50.9% (95%CI: 41.6, 58.9)，就重度輪狀病毒疾病而言，則為96.4% (95%CI: 86.3, 99.6)。

研究007顯示，在不考慮血清型的情況下，對任何嚴重度之輪狀病毒腸胃炎的基礎預防效果為72.7% (95%CI: 51.9, 85.4)，對重度輪狀病毒疾病的預防效果為100% (95%CI: 12.7, 100)。就任何嚴重度的輪狀病毒疾病而言，接種第一劑疫苗之後的ITT預防效果為48.0% (95%CI: 21.6, 66.1)，就重度輪狀病毒疾病而言則為100% (95%CI: 30.4, 100.0)。

**輪狀病毒腸胃炎－依血清型區分**

在REST研究中5,673名接種之嬰兒(2,834名為疫苗組)，預防效果是藉由接種第三劑疫苗至少14天後一直到完成疫苗接種後的第一個輪狀病毒季節期間降低血清型G1-G4所引起之輪狀病毒腸胃炎發生率作為評估標準。在68,038名接種之嬰兒(34,035名為疫苗組)中，預防效果是藉由接種第三劑疫苗至少14天後降低血清型G1-G4所引起的輪狀病毒腸胃炎住院與急診率作為評估標準。針對血清型的分析結果如下表所示。

表 7

在REST研究中，於完成疫苗接種後的一個完整輪狀病毒季節期間，RotaTeq對輪狀病毒腸胃炎發生率的降低

| (RotaTeq n=2,834) (% [95 % CI]) | | | | | | |
|---|---|---|---|---|---|---|
| | | 對不同輪狀病毒血清型引起的任何嚴重度腸胃炎之預防效果 | | | | |
| 重度病例* (G1-G4) | 任何嚴重度 (G1-G4) | G1 | G2 | G3 | G4 | G9 |
| 98.0% [88.3, 100.0]† | 74.0% [66.8, 79.9]† | 74.9% [67.3, 80.9]† | 63.4% [2.6, 88.2]† | 82.7% [<0, 99.6] | 48.1% [<0, 91.6] | 65.4% [<0, 99.3] |

*在發燒、嘔吐、腹瀉及行為改變等症狀之強烈程度及持續時間為評估基礎的臨床評分系統中積分大於16/24。

† 統計顯著性

表 8

在REST研究中，於接種後兩年期間，RotaTeq對輪狀病毒腸胃炎引起之住院與急診率的降低

| 住院(RotaTeq n=34,035) (% [95 % CI]) | | | | | |
|---|---|---|---|---|---|
| G1-G4 | G1 | G2 | G3 | G4 | G9 |

| | | | | | |
|---|---|---|---|---|---|
| 94.5%<br>[91.2, 96.6]† | 95.1%<br>[91.6, 97.1]† | 87.6%<br>[<0, 98.5] | 93.4%<br>[49.4, 99.1]† | 89.1%<br>[52.0, 97.5]† | 100%<br>[69.6, 100]† |

†統計顯著性

有一項 REST 的延伸研究只在芬蘭執行。芬蘭延伸研究(Finnish Extension Study, FES)納入 REST 研究原先 20,736 名受試者之子研究群。在 FES 研究中，於疫苗接種後追蹤嬰兒長達三年。

在 REST 研究按計畫表分析族群中，有 403 個健康照護接觸(healthcare encounters，疫苗組 20 個， 安慰劑組 383 個)案例與血清型 G1-G4 和 G9 輪狀病毒腸胃炎有關。由 FES 研究所得的資料總共增加 136 個案例，包括疫苗組的 9 個以及安慰劑組的 127 個。整體來說，兩組族群中分別有 31%以及 25%的案例發生於 FES 研究期間。

依據 REST 與 FES 研究所得的合併資料， RotaTeq 對血清型 G1-G4 輪狀病毒腸胃炎引起之住院與急診率的降低為 94.4% (95% CI: 91.6, 96.2)，對血清型 G1, G2, G3, G4 與 G9 輪狀病毒腸胃炎引起之住院與急診率的降低分別為 95.5% (95% CI: 92.8, 97.2)、81.9% (95% CI: 16.1, 98.0)、89.0% (95% CI: 53.3, 98.7)、83.4% (95% CI: 51.2, 95.8)、94.2% (95% CI: 62.2, 99.9)。在第三年期間，疫苗組(n=3,112)沒有因輪狀病毒腸胃炎導致健康照顧需求的案例，而安慰劑組(n=3,126)則有一例(non-typeable)。

**免疫生成性**

RotaTeq所引發之抗體反應和其對輪狀病毒腸胃炎之預防效果間的關聯性，目前尚未確立。在第3期研究的439位RotaTeq接種者中，有92.9%至100%的受試者在完成3劑疫苗接種後，其血中抗輪狀病毒IgA濃度高達3倍(含)以上，而在397位安慰劑接種者中則只有12.3%-20%的受試者達此效果。

## 適應症

預防輪狀病毒所引起的腸胃炎(G1、G2、G3、G4以及含有P1A[8]之G血清型如G9)。

## 用途

RotaTeq是一種對6至32週齡之間的嬰兒陸續投予三劑之口服五價疫苗，第一劑RotaTeq建議於6至12週齡時投予(參見"劑量與用法")。

## 禁忌

已知對此疫苗之任何成分有過敏病史者。

於接種一劑RotaTeq後出現過敏症狀的嬰兒，不應再接種RotaTeq。

有嚴重複合型免疫缺乏症(Individuals with Severe Combined Immunodeficiency Disease, SCID)者。在上市後報告中曾有嚴重複合型免疫缺乏症的嬰兒發生與疫苗病毒相關之腸胃炎案例。

## 注意事項

應預先做好適當的治療準備，包括腎上腺素注射劑(1:1000)，以便在發生過敏性反應時可立即使用。

**免疫功能低弱族群**

對可能有免疫功能低弱問題之嬰兒(如以下所列者)投予RotaTeq的安全性及預防效果，目前並無任何來自臨床試驗的資料可供參考：

- 患有血液惡病質、白血病、任何形式之淋巴瘤、或其他會對骨髓或淋巴系統造成影響之惡性腫瘤的嬰兒。
- 接受免疫抑制治療(包括高劑量的全身性皮質類固醇)的嬰兒。但對正在局部使用皮質類固醇或吸入性類固醇治療的嬰兒，或可投予RotaTeq。
- 有原發性及後天性免疫功能不全問題的嬰兒，包括HIV/AIDS或人類免疫不全病毒感染的其他臨床表徵、細胞性免疫功能不全、以及γ球蛋白過低與γ球蛋白異常狀態。目前並無足夠的臨床試驗資料支持對患有HIV/AIDS之母親所生但HIV狀態不明的嬰兒投予RotaTeq。
- 曾在42天內接受輸血或使用血液製劑(包括免疫球蛋白)的嬰兒。

已有關於疫苗病毒株從疫苗接種者傳播給未接種疫苗之家人或其他接觸者的相關資料[參見"排毒與傳播"]。

**胃腸疾患**

對於具有以下所列之胃腸疾患病史的嬰兒投予RotaTeq的安全性及預防效果，目前並無任何資料可供參考：患有活動性急性胃腸疾病的嬰兒、慢性腹瀉且發育不良的嬰兒、以及有先天性腹部疾患、腹部手術和腸套疊病史的嬰兒。當考慮對這類嬰兒投予RotaTeq時，建議應多加小心。

**腸套疊**

研究人員發現，在投予一種先前核准的活性恆河猴輪狀病毒疫苗後，發生腸套疊的風險升高。[5] REST研究(n=69,625)數據顯示，當與安慰劑相比較，RotaTeq並無增加腸套疊的風險之現象。在全球上市後監測調查中，RotaTeq接種後曾有短暫發生腸套疊的案例被通報。參見"不良反應"中的腸套疊。

**排毒與傳播**

研究人員曾對REST研究中的部份子群受試者於每次接種疫苗的4到6天後，評估排毒情形；亦對於在任何時間送檢之糞便抗原檢測呈輪狀病毒陽性之樣本的受試者，評估排毒情形。接種第1劑後，在360位受檢的疫苗接種者中，有32位出現RotaTeq被排於糞便中的現象 [8.9%, 95% CI (6.2%,12.3%)]；接種第2劑之後，在249位接受檢查的疫苗接種者中，沒有任何人出現這種現象 [0.0%, 95% CI (0.0%,1.5%)]；接種第3劑之後，在385位疫苗接種者中，只有1位出現這種現象 [0.3%, 95% CI (<0.1%, 1.4%)]。第3期研究顯示，排毒現象最早可於接種完一劑疫苗後的1天內出現，也可能遲至15天後才出現。研究人員並未以第三期臨床研究評估過疫苗病毒株的傳播現象。

因此，當考慮是否要對會與下列之免疫功能不全患者親密接觸的嬰兒投予RotaTeq時，建議應多加小心：

- 惡性腫瘤患者或其他免疫功能低弱的患者；或
- 正在接受免疫抑制治療的患者。

RotaTeq是一活性基因重組輪狀病毒的溶液，可能會傳播給接觸疫苗者或疫苗接種者。在上市後觀察中，曾發現疫苗病毒株由疫苗接種者傳播到未接種疫苗之人員。應權衡疫苗病毒株的潛在傳播風險與得到及傳播自然界的輪狀病毒的風險。

**發燒性疾病**

如果發生發燒性疾病，可能必須延後接種RotaTeq，除非醫師認為不接種疫苗會面臨更大的風險。輕度發燒(<38.1°C [100.5°F])本身以及輕度的上呼吸道感染並不妨礙RotaTeq的接種。

**不完整的療程**

臨床研究並不是為了評估一劑或兩劑RotaTeq提供的預防程度而設計。大型臨床研究的post hoc數據分析顯示在三劑接種療程中之第一劑後14天起，RotaTeq即可預防輪狀病毒腸胃炎所引起的住院與急診。

**疫苗有效性的限制**

和其他疫苗一樣，接種RotaTeq並不一定能對所有的接種者都產生完整的保護效果。

**接觸後的預防**

目前並無任何於接觸輪狀病毒之後再接種RotaTeq的臨床資料。

**父母/監護人須知**

應向父母及(或)監護人說明疫苗相關效益及風險並鼓勵父母及(或)監護人在門診時盡量提問。

建議在幫嬰兒更換尿片後須洗手。

**藥物交互作用**

免疫抑制療法，包括放射療法、抗代謝藥物、烷化劑、細胞毒性藥物及皮質類固醇(使用劑量高於生理劑量)，可能會降低身體對疫苗的免疫反應。

關於RotaTeq和其他疫苗之合併使用，請參見"劑量與用法"中的*與其他疫苗併用*。

**致癌性、致突變性、生育力損害**

目前尚未評估過RotaTeq之致癌性或致突變性，及其損害生育能力的可能性。

**懷孕婦女**

RotaTeq是一小兒疫苗，不適用於成人。目前沒有以婦女或動物為對象之適當、對照良好的研究。

**授乳婦女**

因為RotaTeq是一小兒疫苗，不適用於成人，目前沒有疫苗於授乳期間使用的安全性資訊。

**小兒使用**

對6週齡以下或32週齡以上之嬰兒的安全性及預防效果尚未確立。

目前已有臨床研究的資料支持根據出生後的週齡對早產兒使用RotaTeq (參見"不良反應"中的*對早產兒的安全性*)。

目前已有臨床研究的資料支持對患有胃食道逆流疾病但病情已獲控制的嬰兒使用RotaTeq。

## 不良反應

有3項安慰劑對照性臨床試驗曾對71,725名嬰兒進行評估，其中包括36,165名接種RotaTeq的嬰兒，以及35,560名接種安慰劑的嬰兒。研究人員會在投予每劑疫苗後的第7、14及第42天，和嬰兒的父母/監護人聯繫，以確認有無腸套疊或任何其他的嚴重不良事件。種族分佈情形如下：白人(兩組皆為69%)；西班牙裔美國人(兩組皆為14%)；黑人(兩組皆為8%)；多重種族(兩組皆為5%)；亞洲人(兩組皆為2%)；美國原住民(RotaTeq組2%，安慰劑組1%)，以及其他種族(兩組皆為<1%)。這兩個接種組中的性別分佈比例皆為男性51%及女性49%。

由於臨床試驗是在可能並非是臨床實務中的典型條件下進行，因此，以下所列的不良反應發生率，可能無法反應臨床實務中的不良反應發生率。

**嚴重不良事件**

針對RotaTeq所進行的第3期研究顯示，在接種一劑疫苗後的42天內，RotaTeq組的嚴重不良事件發生率為2.4%，而安慰劑組則為2.6%。RotaTeq組與安慰劑組中最常見於報告的嚴重不良事件為：

| | |
|---|---|
| 支氣管炎 | (RotaTeq組0.6%，安慰劑組0.7%) |
| 腸胃炎 | (RotaTeq組0.2%，安慰劑組0.3%) |
| 肺炎 | (RotaTeq組0.2%，安慰劑組0.2%) |
| 發燒 | (RotaTeq組0.1%，安慰劑組0.1%) |
| 尿道感染 | (RotaTeq組0.1%，安慰劑組0.1%) |

**死亡**

在臨床研究期間共報告有52個死亡病例。其中有25個死亡病例為RotaTeq接種者，有27個死亡病例為安慰劑接種者。報告最多的死亡原因為嬰兒猝死症候群，在RotaTeq接種者中有8例，在安慰劑接種者中有9例。

**腸套疊**

在REST研究中，研究人員對34,837位疫苗接種者和34,788位安慰劑接種者，於每次接種後的第7、14及第42天，進行主動監視，以確認可能的腸套疊病例，之後並每隔6週監視一次，如此持續監視1年(自接種第一劑後算起)。

就基礎的安全性結果評估而言，接種任何劑次後42天內所發生的腸套疊病例，有6例在接種者中，有5例在安慰劑接種者中(參見表9)。這些數據顯示，和安慰劑相比較，RotaTeq並不會升高發生腸套疊的風險。

表 9

在REST研究期間，RotaTeq接種者與安慰劑接種者中的腸套疊確定病例數

| | RotaTeq (n=34,837) | 安慰劑(n=34,788) |
|---|---|---|
| 接種任何劑次後42天內的腸套疊確定病例數 | 6 | 5 |
| 相對風險(95%CI)† | 1.6 (0.4, 6.4) | |
| 接種第一劑後365天內的腸套疊確定病例數 | 13 | 15 |
| 相對風險(95%CI) | 0.9 (0.4, 1.9) | |

† 相對風險及95%信賴區間的評估基礎為REST研究中所採用的分組逐次設計中止標準。

本疫苗接種者在接種第一劑後的42天內並未出現任何腸套疊確定病例，但這段期間對恆河猴輪狀病毒疫苗而言，卻是風險最高的時期(參見表10)。

表 10

在REST研究中，在接種各劑次後於不同時間範圍內所發生的腸套疊病例數

| | 第1劑 | | 第2劑 | | 第3劑 | | 任何劑次 | |
|---|---|---|---|---|---|---|---|---|
| 時間範圍(天) | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 |
| 1-7 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |
| 1-14 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 1-21 | 0 | 0 | 3 | 0 | 0 | 1 | 3 | 1 |
| 1-42 | 0 | 1 | 4 | 1 | 2 | 3 | 6 | 5 |

除了一名9個月大的男嬰之外，所有發生腸套疊的兒童後來都恢復正常，並且未留下任何後遺症；該名男嬰係於接種第3劑的98天後發生腸套疊，因手術後的敗血症而死亡。在參與第1期及第2期研究(有716名安慰劑接種者)的2,470名RotaTeq接種者中，只有一名7個月大的男嬰發生腸套疊。

**血便**

接受疫苗或安慰劑任何劑次後的 42 天內，疫苗接種者中被通報為不良經驗的血便病例發生率為 0.6% (39/6,130)，在安慰劑接種者中的發生率亦為 0.6% (34/5,560)；接受疫苗或安慰劑任何劑次後的 42 天內，疫苗接種者中被通報為嚴重不良經驗的血便病例發生率<0.1% (4/36,150)，在安慰劑接種者的發生率也<0.1% (7/35,536)。

**癲癇**

在針對RotaTeq所進行的第3期試驗中所通報的所有癲癇發作病例(依疫苗接種組別和接種後的間隔時間列表)如表11所示。

表 11

在針對RotaTeq所進行的第3期試驗中，接種任何劑次後於不同時間範圍內所通報的癲癇發作病例

| 時間範圍(天) | 1-7 | 1-14 | 1-42 |
|---|---|---|---|
| RotaTeq | 10 | 15 | 33 |
| 安慰劑 | 5 | 8 | 24 |

被通報為嚴重不良經驗的癲癇病例，在疫苗接種者中的發生率為<0.1% (27/36,150)，在安慰劑接種者中的發生率亦為<0.1% (18/35,536)(不具顯著性)。共有10個發燒性癲癇發作病例被通報為嚴重不良經驗，其中5例為疫苗接種者，另5例則見於安慰劑接種者。

**川崎氏症**

當進行phase III臨床試驗時，接受疫苗或安慰劑後的42天內報告有川崎氏症的比率在疫苗接受者中為<0.1(5/36,150)及在安慰劑接受者中為<0.1(1/35,536)(不具統計意義)。

**最為常見的不良事件**

***收集而得的不良事件***

研究人員曾針對11,711名嬰兒(其中6,138名為RotaTeq接種者)收集詳細的安全性資訊，這些嬰兒包括REST研究中的部份子群受試者以及研究007與009中的所有受試者(詳細的安全性評估世代)。在每次接種後的第一週期間，這些嬰兒的父母/監護人必須每天在疫苗接種報告卡上記錄嬰兒的體溫以及腹瀉和嘔吐等任何狀況發生。這些不良事件及易怒反應的發生頻率如表12所列。

表 12

投予第1、2及第3劑後的第一週內所收集到的不良經驗(詳細的安全性評估世代)

| 不良經驗 | 第1劑 | | 第2劑 | | 第3劑 | |
|---|---|---|---|---|---|---|
| | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 |
| | n=5,616 | n=5,077 | n=5,215 | n=4,725 | n=4,865 | n=4,382 |
| 體溫升高* | 17.1% | 16.2% | 20.0% | 19.4% | 18.2% | 17.6% |
| | n=6,130 | N=5,560 | n=5,703 | n=5,173 | n=5,496 | n=4,989 |
| 嘔吐 | 6.7% | 5.4% | 5.0% | 4.4% | 3.6% | 3.2% |
| 腹瀉 | 10.4% | 9.1% | 8.6% | 6.4% | 6.1% | 5.4% |
| 易怒 | 7.1% | 7.1% | 6.0% | 6.5% | 4.3% | 4.5% |

*肛溫≥38.1°C [100.5°F]，肛溫相當於耳溫或口溫加1°F，或腋溫加2°F。

***其他不良事件***

研究人員也要求這11,711名嬰兒的父母/監護人於接種每劑疫苗後的42天期間在疫苗接種報告卡上記錄其他出現的事件。

疫苗接種者(N=6,138)與安慰劑接種者(N=5,573)中的發燒發生率大致相當(分別為42.6%與42.8%)。在RotaTeq接種者中，接種任何劑次後42天內之發生率，就統計學而言，係高於安慰劑接種者(即雙尾分析p值<0.05)的不良事件如表13所示。

表 13

在RotaTeq接種者中，接種任何劑次後42天內之發生率就統計學而言係高於安慰劑接種者的不良事件

| 不良事件 | RotaTeq N=6,138 | 安慰劑 N=5,573 |
|---|---|---|
| | n (%) | n (%) |
| 腹瀉 | 1,479 (24.1%) | 1,186(21.3%) |
| 嘔吐 | 929 (15.2%) | 758 (13.6%) |
| 中耳炎 | 887 (14.5%) | 724 (13.0%) |
| 鼻咽炎 | 422 (6.9%) | 325 (5.8%) |
| 支氣管痙攣 | 66 (1.1%) | 40 (0.7%) |

在所有研究中都可投予其他已獲核准之疫苗。三項安慰劑對照性第三期研究均有評估RotaTeq併用預先指定的核准疫苗之安全性，這些疫苗包括B型流行性感冒嗜血桿菌接合疫苗(Haemophilus Infuenzae type b conjugate vaccine, Hib)、B型肝炎疫苗、白喉類毒素、破傷風類毒素及非細胞性百日咳(diphtheria and tetanus toxoids and acellular pertussis, DTaP)疫苗、去活化小兒麻痺疫苗(inactivated poliovirus vaccine, IPV)、肺炎球菌接合疫苗以及六合一疫苗。在後續的對照性研究中，對於RotaTeq併用口服小兒麻痺疫苗(oral poliovirus vaccine, OPV)、腦膜炎雙球菌C型接合疫苗或六合一疫苗的安全性及免疫生成性均有評估。在所有研究中，併用這些疫苗具良好耐受性; 不良經驗被觀察到的頻率大致與對照組相似。

**對早產兒的安全性**

在REST研究中，研究人員曾對2,070名早產兒(妊娠週數為25至36週，中位數為34週)依其出生後的週數投予RotaTeq或安慰劑。研究人員並追蹤所有早產兒以了解嚴重不良經驗的發生情形；並監視包含308名嬰兒之子群的各種不良經驗。在整個研究期間有4個死亡病例，其中2例為疫苗接種者(1名死於嬰兒猝死症候群，1名死於汽車意外)，另2例為安慰劑接種者(1名死於嬰兒猝死症候群，1名死因不明)。並無任何腸套疊的報告病例。疫苗接種者中的嚴重不良經驗發生率為5.5%，安慰劑接種者則為5.8%。最為常見的嚴重不良經驗為支氣管炎，其在疫苗接種者中的發生率為1.4%，在安慰劑接種者中則為2.0%。在每次接種後的第一週期間，這些嬰兒的父母/監護人必須每天在疫苗接種報告卡上記錄嬰兒的體溫以及腹瀉和嘔吐等任何不良狀況。這些不良經驗及易怒反應在每次接種後第一週內之發生頻率如表14所列。

表 14

在早產兒中，投予第1、2及第3劑後第一週內所收集到的不良經驗

| | 第1劑 | | 第2劑 | | 第3劑 | |
|---|---|---|---|---|---|---|
| 不良事件 | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 | RotaTeq | 安慰劑 |
| | N=127 | N=133 | N=124 | N=121 | N=115 | N=108 |
| 體溫升高* | 18.1% | 17.3% | 25.0% | 28.1% | 14.8% | 20.4% |
| | N=154 | N=154 | N=137 | N=137 | N=135 | N=129 |
| 嘔吐 | 5.8% | 7.8% | 2.9% | 2.2% | 4.4% | 4.7% |
| 腹瀉 | 6.5% | 5.8% | 7.3% | 7.3% | 3.7% | 3.9% |
| 易怒 | 3.9% | 5.2% | 2.9% | 4.4% | 8.1% | 5.4% |

*肛溫≥38.1°C [100.5°F ]，肛溫相當於耳溫或口溫加1°F，或腋溫加2°F。

**上市後報告**

於RotaTeq核准後的使用時間，曾有下列不良經驗的自發性報告。因為這些經驗係由人數不明的族群主動報告而來，因此無法可靠地估計出其頻率，或與疫苗使用建立出一個因果關係。

**免疫系統異常:** 過敏性反應

**皮膚或皮下組織異常:** 蕁麻疹、血管性水腫

**胃腸道異常:** 嚴重複合型免疫缺乏症(SCID)的嬰兒有發生腸胃炎並排出疫苗病毒的現象、腸套疊、血便

**上市後觀察性安全監視研究**

利用大型醫療費用索償資料庫所執行的一項前瞻性上市後觀察性研究中，針對85,150名接種至少一劑RotaTeq的嬰兒，評估接種任何一劑疫苗後30天因腸套疊或川崎氏症導致急診或住院的風險。對病歷進行審查以確認診斷。此外，搜尋所有急診

與住院自動化紀錄資料庫以監測一般安全性。這項研究包含一個獨立外部的安全監視委員會。

在接種後0-30天的追蹤期中，腸套疊或川崎氏症發生率與預期的背景發生率之間沒有統計顯著差異。此外，在接種後0-30天的追蹤期中，比較接種RotaTeq者(N=85,150)的17,433 person-years of follow-up與接種白喉類毒素、破傷風類毒素及非細胞性百日咳(DTaP)疫苗但沒有接種RotaTeq者(N=62,617)的12,339 person-years of follow-up，這些不良反應並沒有統計上顯著的增加。在接種RotaTeq的嬰兒中有6個確定的腸套疊案例，而接種白喉類毒素、破傷風類毒素及非細胞性百日咳(DTaP)疫苗的併行控制組中則有5個案例(relative risk = 0.8, 95% CI: 0.22-3.52)。在接種RotaTeq的嬰兒中有1個病歷確定的川崎氏症案例，而接種白喉類毒素、破傷風類毒素及非細胞性百日咳(DTaP)疫苗的併行控制組中有1個案例(relative risk = 0.7, 95% CI: 0.01-55.56)。在一般安全性分析中，安全監視委員會沒有發現任何特定之安全性疑慮。(參見"注意事項")

**通報不良事件**

行政院衛生署已建立一套全國藥物不良反應通報系統，以接受接種任何疫苗後所發生之所有可疑不良事件的通報，可透過http://adr.doh.gov.tw進行線上通報。若需進一步的資訊，可撥打本公司免付費電話0800 038 538。

## 過量

曾有使用高於建議劑量 RotaTeq 的案例。一般而言，使用過量的案例其不良反應相似於接種建議劑量時會發生的不良反應。

## 劑量與用法

**僅供口服使用。切勿注射投予。**

RotaTeq的接種系列共包含三劑現成可用的口服液劑，第一劑開始於6至12週齡時投予，然後再以4至10週的間隔時間投予後續的劑次。第3劑不可於32週齡之後投予(參見"臨床研究")。

在接種RotaTeq之前或之後，對嬰兒的飲食攝取(包括母乳)均無任何限制。

切勿將RotaTeq疫苗和任何其他疫苗或溶液混合使用。切勿泡製或稀釋(參見"使用指示")。

每劑疫苗都以一個不含乳膠成分(latex)之塑膠製的可擠壓投藥軟管供應，該軟管頂端並附有一個可轉下的帽蓋，可直接口服。此投藥軟管另包裝在一個包裝袋中(參見"使用指示")。

***與其他疫苗併用***

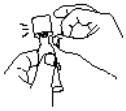
RotaTeq可以和白喉類毒素、破傷風類毒素及非細胞性百日咳(diphtheria and tetanus toxoids and acellular pertussis, DTaP)疫苗、去活化或口服小兒麻痺疫苗(inactivated or oral poliovirus vaccine, IPV or OPV)、B型流行性感冒嗜血桿菌接合疫苗(Haemophilus Infuenzae type b conjugate vaccine, Hib)、B型肝炎疫苗、肺炎球菌接合疫苗以及六合一疫苗同時給予。

併用RotaTeq與口服小兒麻痺病毒疫苗(OPV) 不會影響對於小兒麻痺病毒抗原之免疫反應。雖然併用OPV 可能會輕微降低對輪狀病毒疫苗的一些免疫反應，但目前沒有證據顯示對嚴重輪狀病毒胃腸炎之臨床保護力受到影響。於投予RotaTeq兩週後投予OPV不影響RotaTeq之免疫反應。

**使用指示**

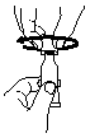
疫苗投予步驟：

撕開包裝袋，取出投藥軟管。

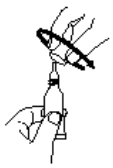


垂直拿住軟管，輕彈帽蓋，藉此清空管尖中的液體。

以2個簡單的步驟打開投藥軟管：



1. 依***順時鐘***方向轉緊帽蓋以戳破軟管尖端。



2. 再依***逆時鐘***方向轉下帽蓋。

投予方式為向著嬰兒的臉頰內側，將液劑緩緩擠入嬰兒口中，直到投藥軟管擠空為止。(可能會殘留一滴在管尖)

若因任何緣故造成投予劑量不完整時(例如嬰兒將疫苗吐出或嘔出)，並不建議另外補充一劑，因為目前尚未在臨床試驗中研究過這種投藥方式。嬰兒應繼續接種建議系列中的其餘劑次。
請依當地法規將空軟管與帽蓋拋棄於經過核准的生物廢棄物容器中。

**包裝規格**

RotaTeq 2毫升裝口服用液劑，為一淡黃色並可能略帶粉紅色的澄清液體。其包裝規格如下：

每盒裝有1支個別包裝的單劑軟管。

每盒裝有10支個別包裝的單劑軟管。

**貯存**

貯存與運送均應冷藏在2-8°C (36-46°F)的溫度下。RotaTeq於離開冷藏狀態後應儘快投予。
避光貯存。
RotaTeq應依當地法規拋棄於經過核准的生物廢棄物容器中。
本品必須於有效日期前使用。

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# 輪達停®口服活性五價輪狀病毒疫苗
# RotaTeq [Rotavirus Vaccine, Live, Oral, Pentavalent]
# 病患須知

## RotaTeq 是什麼？

RotaTeq (活性口服五價輪狀病毒疫苗)是一種病毒疫苗，本疫苗可以幫助預防您的孩子發生輪狀病毒感染所引起的腸胃炎(腹瀉及嘔吐)。

RotaTeq 產生功效的方式是幫助身體對最為常見的輪狀病毒類型(或「病毒株」)產生自然的防禦反應。

RotaTeq 的產品規格為：口服液劑。

**產品許可證持有廠商：**

美商默沙東藥廠股份有限公司台灣分公司

**產品製造廠商：**

Merck Sharp & Dohme Corp.

## 醫師為什麼會處方 RotaTeq？

醫師建議使用 RotaTeq 或為您的孩子投予 RotaTeq 是為了幫助您的孩子預防輪狀病毒感染，這是一種發生於腸胃道的病毒感染，並且是造成腸胃炎(胃腸發炎，會導致腹瀉及嘔吐)的主要導因。

輪狀病毒腸胃炎可能會導致發燒、嘔吐及腹瀉。這些症狀可能導致脫水，甚至因為嚴重脫水而死亡。

輪狀病毒乃是全世界之嬰兒及幼童發生嚴重脫水性腹瀉的主要導因。在此疫苗問世之前，每年有 2 千 5 百萬個就醫診次可歸因於這種病毒。它也是造成全球每年 2 百 10 萬個住院病例及 352,000 至 592,000 個死亡病例的元兇。幾乎所有兒童在 5 歲之前都會感染輪狀病毒，即使在衛生標準很高的地方也是如此。

## 在接種 RotaTeq 之前，我應該要注意哪些事項？

### *哪些人不可接種 RotaTeq？*

如果您的孩子有下列情形，則不可接種此疫苗：

- 在接種一劑疫苗之後出現過敏反應。
- 對本疫苗的任何成分過敏。詳細的成分內容參見"RotaTeq 的成分是什麼?"。
- 患有嚴重複合型免疫不全症(SCID).

## 在我的孩子接種 RotaTeq 疫苗之前，我應該告訴醫師哪些訊息？

您的孩子在接種此疫苗之前，如有以下的情形，請先告訴醫師：

- 患有任何併有發燒症狀的疾病。但並不須因輕度的發燒或上呼吸道感染(感冒)本身而延後接種疫苗。
- 有腹瀉或嘔吐的現象。
- 體重一直沒有增加。
- 成長速度不如預期。
- 患有血液疾病。
- 患有任何類型的癌症。
- 免疫功能因某種疾病〔包括人類免疫不全病毒(HIV)感染症或後天免疫缺乏症候群(AIDS)〕而低弱。
- 正在接受可能會減弱免疫功能的治療或藥物(例如高劑量的全身性皮質類固醇)或曾在 42 天內接受輸血或使用血液製劑(包括免疫球蛋白)。
- 有先天性的胃腸道問題，或曾發生腸阻塞、腸套疊或腹部手術。
- 經常與免疫功能低弱的家庭成員發生親密接觸。例如患有癌症的家人，或正在使用可能會減弱其免疫功能之藥物的家人。

和其它疫苗一樣，RotaTeq 並不一定能對所有的接種者都產生完整的保護效果。有些兒童可能已經感染病毒但尚未出現染病的徵兆。在這類情況下，疫苗可能無法防止疾病發生。

RotaTeq 只能幫助預防輪狀病毒所引起的腹瀉及嘔吐。本疫苗並不能預防任何其它因素所引起的腹瀉及嘔吐。

建議在換尿片之後一定要洗手，這樣可以防止疫苗病毒擴散。

### *懷孕與餵哺母乳期間的使用*

RotaTeq 是嬰幼兒使用的疫苗，不建議用於大於 8 個月以上的兒童與成人，包括孕婦與授乳的婦女。目前並無任何在懷孕或授乳期間使用本疫苗的人類研究資料。

### *我的孩子可以同時接種 RotaTeq 並使用其它藥物或疫苗嗎？*

您的孩子可以同時接種 RotaTeq 和其它兒童疫苗，包括白喉類毒素、破傷風類毒素及非細胞性百日咳疫苗、去活化或口服小兒麻痺疫苗、B 型流行性感冒嗜血桿菌接合疫苗、B 型肝炎疫苗、肺炎球菌接合疫苗及六合一疫苗，但不可將其和任何其它疫苗或溶液混合使用。

### *疫苗接種者在接種 RotaTeq 之後可以開車或操作機械嗎？*

RotaTeq 並非供成人使用的疫苗。

### *RotaTeq 的成分是什麼?*

RotaTeq 為一內含 5 種活性基因重組輪狀病毒的活性口服五價疫苗。這些基因重組株的母株係由人類宿主及牛宿主身上分離而得。每劑疫苗均含有蔗糖、檸檬酸鈉、單水合磷酸二氫鈉、氫氧化鈉、聚山梨醇酯 80、細胞培養基以及微量的牛胚胎血清。本疫苗不含任何防腐劑或硫柳汞(thimerosal)。

如果您的孩子曾對上述成分產生過敏反應，一定要告訴醫師。

## RotaTeq 的接種時程為何？

本疫苗為口服使用，其接種時程共包含 3 劑。第一劑於 6 至 12 週大時投予。之後的二劑，建議的間隔為四至十週，第 3 劑不可於 32 週齡之後投予。

## 如果漏掉一劑該怎麼辦？

您的孩子共須接種 3 劑疫苗。請務必遵循健康照護人員關於您的孩子應於何時回診接種後續劑量之疫苗的指示。請按照預約的時間回診。如果您忘記或無法在排定的時間回診，請洽詢您的健康照護人員。

## RotaTeq 可能會產生哪些不良作用？

和所有的疫苗一樣，RotaTeq也可能會產生副作用。

使用RotaTeq時最常見的副作用包括腹瀉、嘔吐、發燒、流鼻水與喉嚨痛、喘鳴或咳嗽、以及耳朵感染。

其它的通報副作用包括過敏反應，可能會相當嚴重(全身性過敏反應)；過敏性腫脹；蕁麻疹；以及腸套疊(一段腸管折疊陷入另一段腸管的腸阻塞型式)，其症狀與徵兆包括嚴重腹痛、持續嘔吐、糞便帶血、腹部腫脹、以及發燒。

這些並未涵蓋RotaTeq的所有可能副作用。您可以向您的醫師或健康照護人員索取較為詳盡的副作用清單。

如果您發現任何本說明書未提及的副作用，請告知您的醫師或藥師。如果症狀持續不退或出現惡化的現象，請就醫診治。

## 如何才能獲得更多關於 RotaTeq (及其適應症)的資訊？

本說明書只是扼要提供某些和本疫苗有關的資訊。如果您對 RotaTeq 有任何問題或顧慮，請和您的健康照護人員討論。您的醫師或藥師可以提供您另一份針對健康照護專業人員撰寫的說明書[您也可以拜訪台灣默沙東網站(http://www.msd.com.tw/Pages/home.aspx)，然後從中取得這份說明書]。

## 這份說明書最近一次修訂是什麼時候？

本說明書最近一次修訂的時間是 105 年 8 月。

WPC-V260-OS-082016
V260-TWN-2016-014276

# RotaTeq®

[Rotavirus Vaccine, Live, Oral, Pentavalent]

## DESCRIPTION

RotaTeq is a live, oral pentavalent vaccine that contains 5 live reassortant rotaviruses. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Four reassortant rotaviruses express one of the outer capsid VP7 proteins (serotypes G1, G2, G3, or G4) from the human rotavirus parent strain and the VP4 attachment protein (serotype P7[5]) from the bovine rotavirus parent strain. The fifth reassortant virus expresses the VP4 attachment protein (serotype P1A[8]), from the human rotavirus parent strain and the outer capsid VP7 protein (serotype G6) from the bovine rotavirus parent strain (see Table 1).

Table 1

| Name of Reassortant | Human Rotavirus Parent Strains and Outer Surface Protein Compositions | Bovine Rotavirus Parent Strain and Outer Surface Protein Composition | Reassortant Outer Surface Protein Composition (Human Rotavirus Component in Bold) | Minimum Dose Levels ($10^6$ infectious units) |
|---|---|---|---|---|
| G1 | WI79 – G1P1A[8] | WC3 - G6, P7[5] | **G1**P7[5] | 2.2 |
| G2 | SC2 – G2P2A[6] | | **G2**P7[5] | 2.8 |
| G3 | WI78 – G3P1A[8] | | **G3**P7[5] | 2.2 |
| G4 | BrB – G4P2A[6] | | **G4**P7[5] | 2.0 |
| P1A[8] | WI79 – G1P1A[8] | | G6**P1A[8]** | 2.3 |

The reassortants are propagated in Vero cells using standard cell culture techniques in the absence of antifungal agents.

The reassortants are suspended in a buffered stabilizer solution. Each vaccine dose contains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, and trace amounts of fetal bovine serum. There are no preservatives or thimerosal present.

RotaTeq is a pale yellow clear liquid that may have a pink tint.

## CLINICAL PHARMACOLOGY

Rotavirus is a leading cause of severe acute gastroenteritis in infants and young children[1], with over 95% of these children infected by the time they are 5 years old. The most severe cases occur among infants and young children between 6 months and 24 months of age[2].

Worldwide it is estimated that 138 million children develop rotavirus gastroenteritis each year which results in 25 million clinic visits, 2.1 million hospitalizations and 352,000 to 592,000 deaths.

In Taiwan, during the period from 2000 to 2003, the total population of children under 2 years of age ranged from 460,000 to 570,000. Using data from the Taiwan Bureau of National Health Insurance for the same period, it is estimated that there were 454,992 to 954,384 annual outpatient visits attributable to acute gastroenteritis (AGE) among the population of children < 2 years of age and 7,356 to 11,208 hospitalizations attributable to severe acute gastroenteritis. Data from a recent active rotavirus surveillance in Taiwan suggests that approximately 14% of outpatient cases and 44% inpatient cases of AGE were attributable to rotavirus infection. By applying recent active rotavirus surveillance data to the 2000-2003 national estimates of acute gastroenteritis, it is estimated that the annual incidence rate of outpatient visits in children < 2 years of age due to rotavirus infection ranged from 12.4 to 28.8% and that the incidence of severe rotavirus-related hospitalizations ranged from 0.61 to 0.98%.

In 2 studies conducted from 2001 to 2003 and December 2005-June 2006 among hospitalized children < 5 years old in Taiwan, rotavirus was the most common cause of severe diarrhea: 43%-45.9% of stool samples from children hospitalized for acute gastroenteritis were positive for rotavirus. In the latter study, 13.9% of stools samples from children with acute gastroenteritis at outpatient clinics were positive for rotavirus antigen. The rotavirus G-types identified in these studies was diverse and dynamic; the distribution was G1 (31%), G2 (10%), G3 (9.3%), G4 (3.7%), G9 (37%) in 2001-2003 and G1 (41%), G2 (13%), G3 (12%), G5 (0.3%), G9 (33%) in December 2005-June 2006. Non-G1 serotypes (G2, G4, G5 and G9) represented approximately 50% of all samples and, moreover, the relevant distribution appears to change over time. In the study conducted December 2005-June 2006, the mean length of hospital stay for children with rotavirus gastroenteritis was 5.6 days (range 2 - 25 days). Parents who missed work lost an average of 4 days of work if their children were hospitalized with rotavirus gastroenteritis[3, 4].

### Mechanism of Action

The exact immunologic mechanism by which RotaTeq protects against rotavirus gastroenteritis is unknown (see CLINICAL STUDIES, *Immunogenicity*). RotaTeq is a live viral vaccine that replicates in the small intestine and induces immunity.

## CLINICAL STUDIES

Overall, 72,324 infants were randomized in 3 placebo-controlled, phase 3 studies conducted in 11 countries on 3 continents. The data demonstrating the efficacy of RotaTeq in preventing rotavirus gastroenteritis come from 6,983 of these infants from the US (including Navajo and White Mountain Apache Nations) and Finland who were enrolled in 2 of these studies: the Rotavirus Efficacy and Safety Trial (REST) and Study 007. The third trial, Study 009, provided clinical evidence supporting the consistency of manufacture and contributed data to the overall safety evaluation.

The racial distribution of the efficacy subset was as follows: White (RotaTeq 68%, placebo 69%); Hispanic-American (RotaTeq 10%, placebo 9%); Black (2% in both groups); Multiracial (RotaTeq 4%, placebo 5%); Asian (<1% in both groups); Native American (RotaTeq 15%, placebo 14%), and Other (<1% in both groups). The gender distribution was 52% male and 48% female in both vaccination groups.

The efficacy evaluations in these studies included: 1) Prevention of any grade of severity of rotavirus gastroenteritis; 2) Prevention of severe rotavirus gastroenteritis, as defined by a clinical scoring system; and 3) Reduction in hospitalizations due to rotavirus gastroenteritis.

The vaccine was given as a three-dose series to healthy infants with the first dose administered between 6 and 12 weeks of age and followed by two additional doses administered at 4- to 10-week intervals. The age of infants receiving the third dose was 32 weeks of age or less. Oral polio vaccine administration was not permitted; however, other childhood vaccines could be concomitantly administered (Please refer to the DOSAGE AND ADMINISTRATION, *Use with Other Vaccines* ). Breast-feeding was permitted in all studies.

The case definition for rotavirus gastroenteritis used to determine vaccine efficacy required that a subject meet both of the following clinical and laboratory criteria: (1) greater than or equal to 3 watery or looser-than-normal stools within a 24-hour period and/or forceful vomiting; and (2) rotavirus antigen detection by enzyme immunoassay (EIA) in a stool specimen taken within 14 days of onset of symptoms. The severity of rotavirus acute gastroenteritis was determined by a clinical scoring system that took into account the intensity and duration of symptoms of fever, vomiting, diarrhea, and behavioral changes.

The primary efficacy analyses included cases of rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4 that occurred at least 14 days after the third dose through the first rotavirus season post vaccination.

Analyses were also done to evaluate the efficacy of RotaTeq against rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4 at any time following the first dose through the first rotavirus season postvaccination among infants who received at least one vaccination (Intent-to-treat, ITT).

### Rotavirus Efficacy and Safety Trial

Primary efficacy against any grade of severity of rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 74.0% (95% CI: 66.8, 79.9) and the ITT efficacy was 60.0% (95% CI: 51.5, 67.1). Primary efficacy against severe rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 98.0% (95% CI: 88.3, 100.0), and ITT efficacy was 96.4%, (95% CI: 86.2, 99.6). See Table 2.

Table 2
Efficacy of RotaTeq against any grade of severity of and severe* G1-4 rotavirus gastroenteritis through the first rotavirus season postvaccination in REST

| | Per Protocol | | Intent-to-Treat† | |
|---|---|---|---|---|
| | RotaTeq | Placebo | RotaTeq | Placebo |
| Subjects vaccinated | 2,834 | 2,839 | 2,834 | 2,839 |
| Gastroenteritis cases | | | | |
| Any grade of severity | 82 | 315 | 150 | 371 |
| Severe* | 1 | 51 | 2 | 55 |
| Efficacy estimate % and (95% confidence interval) | | | | |
| Any grade of severity | 74.0 (66.8, 79.9) | | 60.0 (51.5, 67.1) | |
| Severe* | 98.0 (88.3, 100.0) | | 96.4 (86.2, 99.6) | |

*Severe gastroenteritis defined by a clinical scoring system based on the intensity and duration of symptoms of fever, vomiting, diarrhea, and behavioral changes
†ITT analysis includes all subjects in the efficacy cohort who received at least one dose of vaccine.

The efficacy of RotaTeq against severe disease was also demonstrated by a reduction in hospitalizations for rotavirus gastroenteritis among all subjects enrolled in REST. RotaTeq reduced hospitalizations for rotavirus gastroenteritis caused by serotypes G1, G2, G3, and G4 through the first two years after the third dose by 95.8% (95% CI: 90.5, 98.2). The ITT efficacy in reducing hospitalizations was 94.7% (95% CI: 89.3, 97.3) as shown in Table 3.

Table 3
Efficacy of RotaTeq in reducing G1-4 rotavirus-related hospitalizations in REST

| | Per Protocol | | Intent-to-Treat* | |
|---|---|---|---|---|
| | RotaTeq | Placebo | RotaTeq | Placebo |
| Subjects vaccinated | 34,035 | 34,003 | 34,035 | 34,003 |
| Number of hospitalizations | 6 | 144 | 10 | 187 |
| Efficacy estimate % and (95% ) | 95.8 (90.5, 98.2) | | 94.7 (89.3, 97.3) | |

*ITT analysis includes all subjects who received at least one dose of vaccine.

### Study 007

Primary efficacy against any grade of severity of rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 72.5% (95% CI: 50.6, 85.6) and the ITT efficacy was 58.4% (95% CI: 33.8, 74.5). Primary efficacy against severe rotavirus gastroenteritis caused by naturally occurring serotypes G1, G2, G3, or G4 through the first rotavirus season after vaccination was 100% (95% CI: 13.0, 100.0) and ITT efficacy against severe rotavirus disease was 100%, (95% CI: 30.2, 100.0) as shown in Table 4.

Table 4
Efficacy of RotaTeq against any grade of severity of and severe* G1-4 rotavirus gastroenteritis through the first rotavirus season postvaccination in Study 007

| | Per Protocol | | Intent-to-Treat† | |
|---|---|---|---|---|
| | RotaTeq | Placebo | RotaTeq | Placebo |
| Subjects vaccinated | 650 | 660 | 650 | 660 |
| Gastroenteritis cases | | | | |
| Any grade of severity | 15 | 54 | 27 | 64 |
| Severe* | 0 | 6 | 0 | 7 |
| Efficacy estimate % and (95% confidence interval) | | | | |
| Any grade of severity | 72.5 (50.6, 85.6) | | 58.4 (33.8, 74.5) | |
| Severe* | 100.0 (13.0, 100.0) | | 100.0 (30.2, 100.0) | |

*Severe gastroenteritis defined by a clinical scoring system based on the intensity and duration of symptoms of fever, vomiting, diarrhea, and behavioral change
†ITT analysis includes all subjects in the efficacy cohort who received at least one dose of vaccine.

**Efficacy between Doses**

The protective efficacy of RotaTeq against the incidence of rotavirus gastroenteritis of any severity caused by serotypes G1-G4 in the intervals between doses was not statistically significant. This was evaluated in a post hoc analysis of data from the clinical efficacy cohort of REST (n=5,673 infants).

The protective efficacy of RotaTeq as measured by a reduction in the rate of hospitalizations and emergency department visits for rotavirus gastroenteritis caused by serotypes G1-G4 in the intervals between doses during administration of the 3-dose vaccination series was evaluated in post hoc analyses of data from REST (n=68,038 infants). The results of these analyses are presented in Table 5.

Table 5
Reduction in hospitalizations and emergency department visits for rotavirus gastroenteritis in the intervals between doses during administration of the 3-dose vaccination series in REST

| | RotaTeq n=34,035 infants; Placebo n=34,003 infants | |
|---|---|---|
| | From ≥14 days after dose 1 until dose 2 | From 14 ≥days after dose 2 until dose 3 |
| Serotype | G1-G4 | G1-G4 |
| Efficacy estimate % and [95% confidence interval] | 100 [72.2, 100] | 90.9 [62.9, 99.0] |

**Efficacy in Pre-term Infants**

In a subset of 204 vaccinated infants (99 in the vaccine group), protective efficacy, as measured by a reduction in the incidence of rotavirus gastroenteritis of any severity caused by vaccine serotypes (G1-G4) that occurred at least 14 days after the third dose of vaccine through the first full rotavirus season after vaccination, was 70.3 % [95 % CI <0, 94.7]. In 2,070 vaccinated infants (1,007 in the vaccine group) in REST, protective efficacy, as measured by a reduction in the rate of hospitalizations and emergency department visits for rotavirus gastroenteritis caused by G1-G4 from 14 days for up to 2 years after the third dose, was 100% [95 % CI 74, 100]. Likewise, the protective efficacy, as measured by a reduction in the rate of hospitalizations and emergency department visits for rotavirus gastroenteritis caused by any serotype from 14 days for up to 2 years after the third dose, was 100% [95% CI 82, 100].

**Effectiveness**

The results of the three post-licensure vaccine effectiveness studies presented in Table 6 demonstrated high and consistent reduction in rotavirus-related or all-cause gastroenteritis hospitalizations, emergency department visits and office visits. These vaccine effectiveness data from the US and France also showed that RotaTeq provided strain specific effectiveness against G12P[8] and sustained protection against rotavirus-related hospitalizations and emergency department visits in children up to the 7th year of life.

**Table 6**
Post-Marketing Studies Demonstrating the Effectiveness of RotaTeq to Prevent Gastroenteritis

| Study design (Region) | Study population | Endpoints | Effectiveness % [95%CI] | RV seasons |
|---|---|---|---|---|
| Claims database analysis (US)* | 33,140 vaccinated<br>26,167 unvaccinated<br>Aged ≥7 months<br>Received 3 doses | Hospitalization and Emergency Department (ED) visits due to RVGE†<br>Outpatient visits due to RVGE<br>Hospitalization and ED visits due to all-cause gastroenteritis | 100% [87,100]<br>96% [76,100]<br>59% [47,68] | 2007-2008 |
| Cohort study (France)‡ | 1,895 vaccinated with 3 doses<br>2,102 unvaccinated<br>Aged <2 years | Hospitalization due to RVGE | 98% [83,100] | 2007-2008<br>2008-2009 |
| Case-control study (US)§ | 402 cases<br>2,559 controls¶<br>Aged <8 years<br>Received 3 doses | Hospitalization and ED visits due to RVGE<br>***Strain-specific***<br>- G1P[8]<br>- G2P[4]<br>- G3P[8]<br>- G12P[8]<br>***Age-specific***<br>- 1st year of life<br>- 2nd year of life<br>- 3rd year of life<br>- 4th year of life<br>- 5th year of life<br>- 6th-7th year of life | 80% [74,84]<br><br>89% [55,97]<br>87% [65,95]<br>80% [64,89]<br>78% [71,84]<br><br>91% [78,96]<br>82% [69,89]<br>88% [78,93]<br>76% [51,88]<br>60% [16,81]<br>69% [43,84] | 2011-2012<br>2012-2013 |

*Wang FT, et al. Effectiveness of the pentavalent rotavirus vaccine in preventing gastroenteritis in the United States. *Pediatrics.*125 (e208). 2009-1246. 2010.
†RVGE = Rotavirus Gastroenteritis
‡Gagneur, A, et al. Impact of rotavirus vaccination on hospitalizations for rotavirus diarrhea: The IVANHOE study. *Vaccine.* (29). 3753-3759. 2011.
§Payne DC, et al. Long-term consistency in rotavirus vaccine protection: RV5 and RV1 vaccine effectiveness in US children, 2012-2013. *Clin Infect Dis.*1-7. 2015.
¶RV-negative acute gastroenteritis controls

**Multiple Rotavirus Seasons**

The efficacy of RotaTeq through a second rotavirus season was evaluated in a single study (REST). Efficacy against any grade of severity of rotavirus gastroenteritis caused by rotavirus serotypes G1, G2, G3, and G4 through the two rotavirus seasons after vaccination was 71.3% (95% CI: 64.7, 76.9). The efficacy of RotaTeq in preventing cases occurring only during the second rotavirus season postvaccination was 62.6% (95% CI: 44.3, 75.4).

**Rotavirus Gastroenteritis Regardless of Serotype**

The rotavirus serotypes identified in the efficacy subset of REST and Study 007 were G1P1A[8]; G2P1B[4]; G3P1A[8]; G4P1A[8]; and G9P1A[8].

In REST, the efficacy of RotaTeq against any grade of severity of naturally occurring rotavirus gastroenteritis regardless of serotype was 71.8% (95% CI: 64.5, 77.8) and efficacy against severe rotavirus disease was 98.0% (95% CI: 88.3, 99.9). The ITT efficacy starting at dose 1 was 50.9% (95% CI: 41.6, 58.9) for any grade of severity of rotavirus disease and was 96.4% (95% CI: 86.3, 99.6) for severe rotavirus disease.

In Study 007, the primary efficacy of RotaTeq against any grade of severity of rotavirus gastroenteritis regardless of serotype was 72.7% (95% CI: 51.9, 85.4) and efficacy against severe rotavirus disease was 100% (95% CI: 12.7, 100). The ITT efficacy starting at dose 1 was 48.0% (95% CI: 21.6, 66.1) for any grade of severity of rotavirus disease and was 100% (95% CI: 30.4, 100.0) for severe rotavirus disease.

**Rotavirus Gastroenteritis by Serotype**

In REST among 5,673 vaccinated infants (2,834 in the vaccine group), protective efficacy was measured as a reduction in the incidence of rotavirus gastroenteritis caused by vaccine G serotypes (G1-G4) that occurred at least 14 days after the third dose of vaccine through the first full rotavirus season after vaccination. In 68,038 vaccinated infants (34,035 in the vaccine group), protective efficacy was measured as a reduction in the rate of hospitalizations and emergency department visits for rotavirus gastroenteritis from 14 days after the third dose. The results of these analyses by serotype are presented in the following tables.

Table 7
Reduction in incidence of rotavirus gastroenteritis through one full season post-vaccination in REST

| (RotaTeq n=2,834) (% [95 % CI]) | | | | | | |
|---|---|---|---|---|---|---|
| | | Efficacy against any severity by rotavirus serotype | | | | |
| Severe* disease (G1-G4) | Any severity (G1-G4) | G1 | G2 | G3 | G4 | G9 |
| 98.0% [88.3,100.0]† | 74.0% [66.8,79.9]† | 74.9% [67.3,80.9]† | 63.4% [26,88.2]† | 82.7% [<0,99.6] | 48.1% [<0,91.6] | 65.4% [<0,99.3] |

* Severe defined as a score >16/24 using a validated clinical scoring system based on the intensity and duration of symptoms (fever, vomiting, diarrhoea and behavioural changes)
† Statistically significant

Table 8
Reduction in hospitalizations and emergency department visits for RV gastroenteritis for up to 2 years post-vaccination in REST

| hospitalization(RotaTeq n=34,035) (% [95 % CI]) | | | | | |
|---|---|---|---|---|---|
| G1-G4 | G1 | G2 | G3 | G4 | G9 |
| 94.5% [91.2,96.6]† | 95.1% [91.6,97.1]† | 87.6% [<0,98.5] | 93.4% [49.4,99.1]† | 89.1% [52.0,97.5]† | 100% [69.6,100]† |

† Statistically significant

There was an extension of REST conducted in Finland only. This Finnish Extension Study (FES) included a subset of 20,736 subjects that had been enrolled previously in REST. The infants were followed for up to 3 years post-vaccination in the FES.

In REST there were 403 healthcare encounters (20 in the vaccine group and 383 in the placebo group) associated with G1-G4 and G9 rotavirus gastroenteritis in the per protocol population. The additional data from the FES increased the number by 136 encounters in total, including 9 in the vaccine group and 127 in the placebo

group. Overall, 31% and 25% of the encounters in the respective groups occurred during the FES.

Based upon combined data from REST and the FES, the reduction in the rate of hospitalisations and emergency department visits for RV gastroenteritis was 94.4% (95% CI: 91.6, 96.2) for serotypes G1-G4**,** 95.5% (95% CI: 92.8, 97.2) for serotype G1, 81.9% (95% CI: 16.1, 98.0) for serotype G2, 89.0% (95% CI: 53.3, 98.7) for serotype G3, 83.4% (95% CI: 51.2, 95.8) for serotype G4, and 94.2% (95% CI: 62.2, 99.9) for serotype G9. During year 3, there were no health care contacts for RV gastroenteritis in the vaccine group (n=3,112) and one (non-typeable) in the placebo group (n=3,126).

**Immunogenicity**

A relationship between antibody responses to RotaTeq and protection against rotavirus gastroenteritis has not been established. In phase 3 studies, 92.9% to 100% of 439 recipients of RotaTeq achieved a 3-fold or more rise in serum anti-rotavirus IgA after a three-dose regimen when compared to 12.3%-20.0% of 397 placebo recipients.

## INDICATIONS

RotaTeq is an oral pentavalent vaccine indicated for the prevention of rotavirus gastroenteritis in infants and children caused by the serotypes G1, G2, G3, G4, and G-serotypes that contain P1A[8] (e.g., G9).

## USAGE

RotaTeq is an oral pentavalent vaccine administered as a 3-dose series to infants between the ages of 6 to 32 weeks. The first dose of RotaTeq should be administered between 6 and 12 weeks of age (see DOSAGE AND ADMINISTRATION).

## CONTRAINDICATIONS

A demonstrated history of hypersensitivity to any component of the vaccine.

Infants who develop symptoms suggestive of hypersensitivity after receiving a dose of RotaTeq should not receive further doses of RotaTeq.

Individuals with Severe Combined Immunodeficiency Disease (SCID). Cases of gastroenteritis associated with vaccine virus have been reported post-marketing in infants with SCID.

## PRECAUTIONS

Adequate treatment provisions, including epinephrine injection (1:1000), should be available for immediate use should an anaphylactic reaction occur.

**Immunocompromised Populations**

No safety or efficacy data are available from clinical trials regarding the administration of RotaTeq to infants who are potentially immunocompromised including:

- Infants with blood dyscrasias, leukemia, lymphomas of any type, or other malignant neoplasms affecting the bone marrow or lymphatic system.
- Infants on immunosuppressive therapy (including high-dose systemic corticosteroids). RotaTeq may be administered to infants who are being treated with topical corticosteroids or inhaled steroids.
    - Infants with primary and acquired immunodeficiency states, including HIV/AIDS or other clinical manifestations of infection with human immunodeficiency viruses; cellular immune deficiencies; and hypogammaglobulinemic and dysgammaglobulinemic states. There are insufficient data from the clinical trials to support administration of RotaTeq to infants with indeterminate HIV status who are born to mothers with HIV/AIDS.
    - Infants who have received a blood transfusion or blood products, including immunoglobulins within 42 days.

Data are available regarding vaccine virus transmission from vaccine recipient to non-vaccinated household or other contacts [see Shedding and Transmission].

**Gastrointestinal Illness**

No safety or efficacy data are available for administration of RotaTeq to infants with a history of gastrointestinal disorders including infants with active acute gastrointestinal illness, infants with chronic diarrhea and failure to thrive, and infants with a history of congenital abdominal disorders, abdominal surgery, and intussusception. Caution is advised when considering administration of RotaTeq to these infants.

**Intussusception**

Following administration of a previously licensed live rhesus rotavirus-based vaccine, an increased risk of intussusception was observed.1 In the Rotavirus Efficacy and Safety Trial [REST] (n=69,625), the data did not show an increased risk of intussusception for RotaTeq when compared to placebo. In worldwide post-marketing surveillance, cases of intussusception have been reported in temporal association with RotaTeq. [See Adverse Reactions.]

**Shedding and Transmission**

Shedding was evaluated among a subset of subjects in REST 4 to 6 days after each dose and among all subjects who submitted a stool antigen rotavirus positive sample at any time. RotaTeq was shed in the stools of 32 of 360 [8.9%, 95% CI (6.2%, 12.3%)] vaccine recipients tested after dose 1; 0 of 249 [0.0%, 95% CI (0.0%, 1.5%)] vaccine recipients tested after dose 2; and in 1 of 385 [0.3%, 95% CI (<0.1%, 1.4%)] vaccine recipients after dose 3. In phase 3 studies, shedding was observed as early as 1 day and as late as 15 days after a dose. Transmission was not evaluated in phase 3 studies.

Caution is advised when considering whether to administer RotaTeq to individuals with immunodeficient close contacts such as:

Individuals with malignancies or who are otherwise immunocompromised; or

Individuals receiving immunosuppressive therapy.

RotaTeq is a solution of live reassortant rotaviruses and can potentially be transmitted to persons who have contact with the vaccine or vaccinee. Transmission of vaccine virus strains from vaccinees to non-vaccinated contacts has been observed post-marketing. The potential risk of transmission of vaccine virus should be weighed against the risk of acquiring and transmitting natural rotavirus.

**Febrile Illness**

Febrile illness may be reason for delaying use of RotaTeq except when, in the opinion of the physician, withholding the vaccine entails a greater risk. Low-grade fever (<100.5°F [38.1°C]) itself and mild upper respiratory infection do not preclude vaccination with RotaTeq.

**Incomplete Regimen**

The clinical studies were not designed to assess the level of protection provided by only one or two doses of RotaTeq. Post hoc analyses of data from a large clinical study suggest that RotaTeq provides protection against hospitalizations and emergency department visits for rotavirus gastroenteritis during administration of the 3-dose vaccination series starting from 14 days post dose 1.

**Limitations of Vaccine Effectiveness**

RotaTeq may not protect all vaccine recipients against rotavirus.

**Post-Exposure Prophylaxis**

No clinical data are available for RotaTeq when administered after exposure to rotavirus.

**Information for Parents/Guardians**

Parents and/or guardians should be informed of the benefits and risks associated with the vaccine and encouraged to ask any question they may have during the visit.

Hand washing after diaper changing is recommended.

**Drug Interactions**

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

For administration of RotaTeq with other vaccines, see DOSAGE AND ADMINISTRATION, *Use with Other Vaccines*.

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

RotaTeq has not been evaluated for its carcinogenic or mutagenic potential or its potential to impair fertility.

**Pregnancy**

RotaTeq is a pediatric vaccine and is not indicated for use in adults. There have been no adequate, well-controlled studies in women or animals.

**Nursing Mothers**

As RotaTeq is a pediatric vaccine and is not indicated for use in adults, information on the safety of the vaccine when used during lactation is not available.

**Pediatric Use**

Safety and efficacy have not been established in infants less than 6 weeks of age or greater than 32 weeks of age.

Data are available from clinical studies to support the use of RotaTeq in pre-term infants according to their age in weeks since birth (see ADVERSE REACTIONS, Safety in Pre-Term Infants).

Data are available from clinical studies to support the use of RotaTeq in infants with controlled gastroesophageal reflux disease.

## ADVERSE REACTIONS

71,725 infants were evaluated in 3 placebo-controlled clinical trials including 36,165 infants in the group that received RotaTeq and 35,560 infants in the group that received placebo. Parents/guardians were contacted on days 7, 14, and 42 after each dose regarding intussusception and any other serious adverse events. The racial distribution was as follows: White (69% in both groups); Hispanic-American (14% in both groups); Black (8% in both groups); Multiracial (5% in both groups); Asian (2% in both groups); Native American (RotaTeq 2%, placebo 1%), and Other (<1% in both groups). The gender distribution was 51% male and 49% female in both vaccination groups.

Because clinical trials are conducted under conditions that may not be typical of those observed in clinical practice, the adverse reaction rates presented below may not be reflective of those observed in clinical practice.

**Serious Adverse Events**

Serious adverse events occurred in 2.4% of recipients of RotaTeq when compared to 2.6% of placebo recipients within the 42-day period of a dose in the phase 3 clinical studies of RotaTeq. The most frequently reported serious adverse events for RotaTeq compared to placebo were:

| | |
|---|---|
| bronchiolitis | (0.6% RotaTeq vs. 0.7% Placebo), |
| gastroenteritis | (0.2% RotaTeq vs. 0.3% Placebo), |
| pneumonia | (0.2% RotaTeq vs. 0.2% Placebo), |
| fever | (0.1% RotaTeq vs. 0.1% Placebo), and |
| urinary tract infection | (0.1% RotaTeq vs. 0.1% Placebo). |

**Deaths**

Across the clinical studies, 52 deaths were reported. There were 25 deaths in the RotaTeq recipients compared to 27 deaths in the placebo recipients. The most commonly reported cause of death was sudden infant death syndrome, which was observed in 8 recipients of RotaTeq and 9 placebo recipients.

**Intussusception**

In REST, 34,837 vaccine recipients and 34,788 placebo recipients were monitored by active surveillance to identify potential cases of intussusception at 7, 14, and 42 days after each dose, and every 6 weeks thereafter for 1 year after the first dose.

For the primary safety outcome, cases of intussuception occurring within 42 days of any dose, there were 6 cases among RotaTeq recipients and 5 cases among placebo recipients (see Table 9). The data did not suggest an increased risk of intussusception relative to placebo.

Table 9
Confirmed Cases of Intussusception in Recipients of RotaTeq as Compared with Placebo Recipients during REST

| | RotaTeq (n=34,837) | Placebo (n=34,788) |
|---|---|---|
| Confirmed intussusception cases within 42 days after each dose | 6 | 5 |
| Relative Risk (95% CI)[†] | 1.6 (0.4, 6.4) | |
| Confirmed intussusception cases within 365 days after dose one | 13 | 15 |
| Relative Risk (95% CI) | 0.9 (0.4, 1.9) | |

[†] Relative Risk and 95% Confidence Interval based upon group sequential design stopping criteria employed in REST

Among vaccine recipients, there were no confirmed cases of intussusception within the 42-day period after the first dose, which was the period of highest risk for the rhesus rotavirus-based product (see Table 10).

Table 10
Intussusception cases by day range in relation to dose in REST

| | Dose 1 | | Dose 2 | | Dose 3 | | Any Dose | |
|---|---|---|---|---|---|---|---|---|
| Day Range | RotaTeq | Placebo | RotaTeq | Placebo | RotaTeq | Placebo | RotaTeq | Placebo |
| 1-7 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 |
| 1-14 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 |
| 1-21 | 0 | 0 | 3 | 0 | 0 | 1 | 3 | 1 |
| 1-42 | 0 | 1 | 4 | 1 | 2 | 3 | 6 | 5 |

All of the children who developed intussusception recovered without sequelae with the exception of a 9-month-old male who developed intussusception 98 days after dose 3 and died of post-operative sepsis. There was a single case of intussusception among 2,470 recipients of RotaTeq in a 7-month-old male in the phase 1 and 2 studies (716 placebo recipients).

**Hematochezia**

Hematochezia reported as an adverse experience occurred in 0.6% (39/6,130) of vaccine and 0.6% (34/5,560) of placebo recipients within 42 days of any dose. Hematochezia reported as a serious adverse experience occurred in <0.1% (4/36,150) of vaccine and <0.1% (7/35,536) of placebo recipients within 42 days of any dose.

**Seizures**

All seizures reported in the phase 3 trials of RotaTeq (by vaccination group and interval after dose) are shown in Table 11.

Table 11
Seizures reported by day range in relation to any dose in the phase 3 trials of RotaTeq

| Day range | 1-7 | 1-14 | 1-42 |
|---|---|---|---|
| RotaTeq | 10 | 15 | 33 |
| Placebo | 5 | 8 | 24 |

Seizures reported as serious adverse experiences occurred in <0.1% (27/36,150) of vaccine and <0.1% (18/35,536) of placebo recipients (not significant). Ten febrile seizures were reported as serious adverse experiences, 5 were observed in vaccine recipients and 5 in placebo recipients.

**Kawasaki Disease**

Kawasaki's disease was reported in the phase III clinical trials in <0.1% (5/36,150) of vaccine recipients and <0.1% (1/35,536) of placebo recipients within 42 days of any dose (not statistically significant).

**Most Common Adverse Events**

**Solicited Adverse Events**

Detailed safety information was collected from 11,711 infants (6,138 recipients of RotaTeq) which included a subset of subjects in REST and all subjects from Studies 007 and 009 (Detailed Safety Cohort). A Vaccination Report Card was used by parents/guardians to record the child's temperature and any episodes of diarrhea and vomiting on a daily basis during the first week following each vaccination. Table 12 summarizes the frequencies of these adverse events and irritability.

Table 12
Solicited adverse experiences within the first week after doses 1, 2 and 3 (Detailed Safety Cohort)

| Adverse experience | Dose 1 | | Dose 2 | | Dose 3 | |
|---|---|---|---|---|---|---|
| | RotaTeq | Placebo | RotaTeq | Placebo | RotaTeq | Placebo |
| Elevated temperature* | N=5,616 | N=5,077 | N=5,215 | N=4,725 | N=4,865 | N=4,382 |
| | 17.1% | 16.2% | 20.0% | 19.4% | 18.2% | 17.6% |
| Vomiting | N=6,130 | N=5,560 | N=5,703 | N=5,173 | N=5,496 | N=4,989 |
| | 6.7% | 5.4% | 5.0% | 4.4% | 3.6% | 3.2% |
| Diarrhea | 10.4% | 9.1% | 8.6% | 6.4% | 6.1% | 5.4% |
| Irritability | 7.1% | 7.1% | 6.0% | 6.5% | 4.3% | 4.5% |

* Temperature ≥100.5°F [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

**Other Adverse Events**

Parents/guardians of the 11,711 infants were also asked to report the presence of other events on the Vaccination Report Card for 42 days after each dose.

Fever was observed at similar rates in vaccine (N=6,138) and placebo (N=5,573) recipients (42.6% vs. 42.8%). Adverse events that occurred at a statistically higher incidence (i.e., 2-sided p-value <0.05) within the 42 days of any dose among recipients of RotaTeq as compared with placebo recipients are shown in Table 13.

Table 13
Adverse events that occurred at a statistically higher incidence within 42 days of any dose among recipients of RotaTeq as compared with placebo recipients

| Adverse event | RotaTeq N=6,138 n (%) | Placebo N=5,573 n (%) |
|---|---|---|
| Diarrhea | 1,479 (24.1%) | 1,186 (21.3%) |
| Vomiting | 929 (15.2%) | 758 (13.6%) |
| Otitis media | 887 (14.5%) | 724 (13.0%) |
| Nasopharyngitis | 422 (6.9%) | 325 (5.8%) |
| Bronchospasm | 66 (1.1%) | 40 (0.7%) |

Administration of other licensed vaccines was permitted in all studies. The safety of RotaTeq when administered concomitantly with pre-specified licensed vaccines including Haemophilus influenzae type b and hepatitis B vaccine, diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, inactivated poliovirus vaccine (IPV), pneumococcal conjugate vaccine, and hexavalent vaccines was evaluated in all 3 phase III, placebo-controlled studies. In subsequent controlled studies, the safety and immunogenicity of RotaTeq when administered concomitantly with oral poliovirus vaccine, meningococcal group C conjugate vaccine, or hexavalent vaccine were evaluated. In all these studies, concomitant use with these vaccines was well tolerated; the frequency of adverse experiences observed was generally similar to that seen in the control group.

**Safety in Pre-Term Infants**

RotaTeq or placebo was administered to 2,070 pre-term infants (25 to 36 weeks gestational age, median 34 weeks) according to their age in weeks since birth in REST. All pre-term infants were followed for serious adverse experiences; a subset of 308 infants was monitored for all adverse experiences. There were 4 deaths throughout the study, 2 among vaccine recipients (1 SIDS and 1 motor vehicle accident) and 2 among placebo recipients (1 SIDS and 1 unknown cause). No cases of intussusception were reported. Serious adverse experiences occurred in 5.5% of vaccine and 5.8% of placebo recipients. The most common serious adverse experience was bronchiolitis, which occurred in 1.4% of vaccine and 2.0% of placebo recipients. Parents/guardians were asked to record the child's temperature and any episodes of vomiting and diarrhea daily for the first week following vaccination. The frequencies of these adverse experiences and irritability within the week after dose 1 are summarized in Table 14.

Table 14
Solicited adverse experiences within the first week of doses 1, 2, and 3 among pre-term infants

| Adverse event | Dose 1 | | Dose 2 | | Dose 3 | |
|---|---|---|---|---|---|---|
| | RotaTeq | Placebo | RotaTeq | Placebo | RotaTeq | Placebo |
| Elevated temperature* | N=127 | N=133 | N=124 | N=121 | N=115 | N=108 |
| | 18.1% | 17.3% | 25.0% | 28.1% | 14.8% | 20.4% |
| Vomiting | N=154 | N=154 | N=137 | N=137 | N=135 | N=129 |
| | 5.8% | 7.8% | 2.9% | 2.2% | 4.4% | 4.7% |
| Diarrhea | 6.5% | 5.8% | 7.3% | 7.3% | 3.7% | 3.9% |
| Irritability | 3.9% | 5.2% | 2.9% | 4.4% | 8.1% | 5.4% |

* Temperature ≥ 100.5°F [38.1°C] rectal equivalent obtained by adding 1 degree F to otic and oral temperatures and 2 degrees F to axillary temperatures

**Post-marketing Reports**

The following adverse experiences have been spontaneously reported during post-approval use of RotaTeq. Because these experiences were reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or to establish a causal relation ship to vaccine exposure.

***Immune system disorders*:** anaphylactic reaction.

***Skin and subcutaneous tissue disorders:*** Urticaria, angioedema.

***Gastrointestinal disorders***: gastroenteritis with vaccine viral shedding in infants with Severe Combined Immunodeficiency Disease (SCID), intussusception, hematochezia.

*Post-Marketing Observational Safety Surveillance Study*

In a prospective post-marketing observational study conducted using a large medical claims database, the risks of intussusception or Kawasaki disease resulting in emergency department visits or hospitalizations during the 30 days following any dose of vaccine were analyzed among 85,150 infants receiving one or more doses of RotaTeq. Medical charts were reviewed to confirm these diagnoses. In addition, general safety was monitored by electronic search of the automated records database for all emergency department visits and hospitalizations. The study included an independent, external Safety Monitoring Committee.

During the 0-30 day follow-up period after vaccination, there were no statistically significant differences in the rates of intussusception or Kawasaki disease compared with the expected background rates. In addition, there was no statistically significant increased risk of these adverse events during the 0-30 day follow-up period when comparing the 17,433 person-years of follow-up among infants receiving RotaTeq (n=85,150) with the 12,339 person-years of follow-up among a concurrent control group of infants who received DTaP, but not RotaTeq (n=62,617). There were 6 confirmed cases of intussusception among infants vaccinated with RotaTeq compared with 5 among the concurrent controls vaccinated with DTaP (relative risk = 0.8, 95% CI: 0.22-3.52). There was one chart-confirmed case of Kawasaki disease identified among infants vaccinated with RotaTeq and one chart-confirmed case of Kawasaki disease among concurrent DTaP controls (relative risk = 0.7, 95% CI: 0.01-55.56). In the general safety analyses, the Safety Monitoring Committee did not identify any specific safety concerns. (See PRECAUTIONS.)

**Reporting Adverse Events**

Department of Health has established a National Reporting System of Adverse Drug Reactions to accept all reports of suspected adverse events after the administration of any vaccine by reporting on line to http://adr.doh.gov.tw. For further information, please call the toll-free number at 0800 038 538.

OVERDOSAGE

There have been reports of administration of higher than recommended doses of RotaTeq. In general, the adverse event profile reported with overdose was comparable to that observed with recommended doses of RotaTeq.

**DOSAGE AND ADMINISTRATION**

**FOR ORAL USE ONLY. NOT FOR INJECTION**.

The vaccination series consists of three ready-to-use liquid doses of RotaTeq administered orally starting at 6 to 12 weeks of age, with the subsequent doses administered at 4- to 10-week intervals. The third dose should not be given after 32 weeks of age (see CLINICAL STUDIES).

There are no restrictions on the infant's consumption of food or liquid, including breast milk, either before or after vaccination with RotaTeq.

Do not mix the RotaTeq vaccine with any other vaccines or solutions. Do not reconstitute or dilute (see INSTRUCTIONS FOR USE).

Each dose is supplied in a container consisting of a squeezable plastic, latex-free dosing tube with a twist-off cap, allowing for direct oral administration. The dosing tube is contained in a pouch (see *INSTRUCTIONS FOR USE*).

**Use with Other Vaccines**

RotaTeq can be administered with diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, inactivated or oral poliovirus vaccine (IPV or OPV), *Haemophilus influenzae* type b conjugate vaccine, hepatitis B vaccine, pneumococcal conjugate vaccine, and hexavalent vaccines.

Concomitant administration of RotaTeq and oral poliovirus vaccine (OPV) does not affect the immune response to the poliovirus antigens. Although concomitant administration of OPV may reduce some immune responses to rotavirus vaccine,

there is evidence that a high level of efficacy against severe rotavirus gastroenteritis is maintained. The immune responses to RotaTeq are unaffected when OPV is administered two weeks after RotaTeq.

**INSTRUCTIONS FOR USE**

To administer the vaccine:

Tear open the pouch and remove the dosing tube.

Clear the fluid from the dispensing tip by holding tube vertically and tapping cap.

Open the dosing tube in 2 easy motions:

1. Puncture the dispensing tip by screwing cap ***clockwise*** until it becomes tight.

2. Remove cap by turning it ***counterclockwise***.

Administer dose by gently squeezing liquid into infant's mouth toward the inner cheek until dosing tube is empty. (A residual drop may remain in the tip of the tube.)

If for any reason an incomplete dose is administered (e.g., infant spits or regurgitates the vaccine), a replacement dose is not recommended, since such dosing was not studied in the clinical trials. The infant should continue to receive any remaining doses in the recommended series.

Discard the empty tube and cap in approved biological waste containers according to local regulations.

**HOW SUPPLIED**

RotaTeq, 2 mL, a solution for oral use, is a pale yellow clear liquid that may have a pink tint. It is supplied as follows:

package of 1 individually pouched single-dose tube

package of 10 individually pouched single-dose tubes.

**Storage**

Store and transport refrigerated at 2-8°C (36-46°F). RotaTeq should be administered as soon as possible after being removed from refrigeration.

Protect from light. RotaTeq should be discarded in approved biological waste containers according to local regulations.

The product must be used before the expiration date.

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Manufacturer: Merck Sharp & Dohme Corp.

Address: 770 Sumneytown Pike, West Point, PA 19486, U.S.A.

# Patient Product Information (WPPI)

## Information for the Patient about RotaTeq
## (Rotavirus Vaccine, Live, Oral, Pentavalent, MSD)

## What is RotaTeq?

RotaTeq (Rotavirus Vaccine, Live, Oral, Pentavalent) is a viral vaccine that helps protect your child against gastroenteritis (diarrhea and vomiting) caused by rotavirus infection.

RotaTeq works by helping the body develop natural defenses against the most common types or "strains" of rotavirus.

RotaTeq is available: as oral solution

## Product License Holder:

Merck Sharp & Dohme Corp. Taiwan Branch

## Product Manufacturer:

Merck Sharp & Dohme Corp.

## Why has the doctor prescribed RotaTeq?

The doctor has recommended or administered RotaTeq to help protect your child against rotavirus infection, a viral infection of the digestive tract and a major cause of gastroenteritis (inflammation of the stomach and intestines which causes diarrhea and vomiting).

Rotavirus gastroenteritis may cause fever, vomiting, and diarrhea. These symptoms can lead to dehydration and even to death.

It is the chief cause of severe dehydrating diarrhea among infants and young children around the world. Before the vaccine was used, the virus was the cause for about 25 million physician visits per year. It also accounted for 2.1 million hospital admissions, and 352,000 to 592,000 deaths per year worldwide.

Nearly all children are infected with rotavirus by the time they are 5 years old. This is true even where standards of hygiene are high.

[Rotavirus Vaccine, Live, Oral, Pentavalent, MSD]

## What should I know before vaccination with RotaTeq?

***Who should not be vaccinated with RotaTeq?***

Your child should not get the vaccine if:

- He or she has an allergic reaction after getting a dose of the vaccine.

He or she is allergic to any of the ingredients of the vaccine. A list of ingredients can be found in ***Information about the ingredients in RotaTeq***.

- He or she has Severe Combined Immunodeficiency Disease (SCID).

## What should the doctor be told before my child gets the RotaTeq vaccine?

Before your child gets the vaccine, you should tell your doctor if your child:

- Has any illness with fever. A mild fever or upper respiratory infection (cold) by itself is not a reason to delay taking the vaccination.
- Has diarrhea or is vomiting.
- Has not been gaining weight.
- Is not growing as expected.
- Has a blood disorder.
- Has any type of cancer.
- Has an immune system that is weakened because of a disease〔(this includes human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS)〕.
- Gets treatment or takes medicines that may weaken the immune system (such as high-dose systemic corticosteroids) or has received a blood transfusion or blood products, including immunoglobulins within the past 42 days.
- Was born with gastrointestinal problems, or has had an intestinal blockage, intussusception or abdominal surgery.
- Has regular close contact with a member of the family or household who has a weakened immune system. For example, a person in the house with cancer or one who is taking medicines that may weaken their immune system.

As with other vaccines, RotaTeq may not fully protect all those who get it. Some children may already have the virus but not yet show signs of being sick. In those cases, the vaccine may not be able to prevent the illness.

RotaTeq helps protect against diarrhea and vomiting only if they are caused by rotavirus. It does not protect against them if they are caused by anything else.

Hand washing is recommended after diaper changes to help prevent the spread of vaccine virus.

***Use in pregnancy and breast feeding.***

RotaTeq is a pediatric vaccine not intended for children older than 8 months of age or adults, including pregnant or lactating women. There are no data available on the use during pregnancy or lactation in humans.

***Can my child be vaccinated with RotaTeq and other medicines or vaccines at the same time?***

Your child may get RotaTeq at the same time as other pediatric vaccines, such as diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, inactivated or oral poliovirus vaccine (IPV or

OPV), Haemophilus influenzae type b conjugate vaccine, hepatitis B vaccine, pneumococcal conjugate vaccine, and hexavalent vaccines, but it should not be mixed with any other vaccines or solutions.

***Can the vaccine recipient drive or operate machinery following vaccination with RotaTeq?***

RotaTeq is not intended for adults.

***Information about the ingredients in RotaTeq.***

RotaTeq is a live, oral pentavalent vaccine that contains 5 live reassortant rotaviruses. The rotavirus parent strains of the reassortants were isolated from human and bovine hosts. Each vaccine dosecontains sucrose, sodium citrate, sodium phosphate monobasic monohydrate, sodium hydroxide, polysorbate 80, cell culture media, and trace amounts of fetal bovine serum. There are no preservatives or thimerosal present.

Tell the doctor if your child has ever had an allergic reaction to these ingredients.

## What is the vaccination schedule for RotaTeq?

The vaccine is given by mouth. Your child will receive 3 doses of the vaccine. The first dose is given when your child is 6 to 12 weeks of age. The next two doses are given 4 to 10 weeks apart. The third dose should not be given to your child when your child is older than 32 weeks of age.

## What should I do if I miss a dose?

Your child needs 3 doses of the vaccine. It is important that you follow the instructions of your health care provider regarding your child's return visits for the follow-up doses. Please keep those appointments. If you forget or are not able to go back to your health care provider at the planned time, ask your health care provider for advice.

## What undesirable effects may RotaTeq have?

Like all medicines, RotaTeq can have side effects.

The most common side effects reported with the use of RotaTeq were diarrhea, vomiting, fever, runny nose and sore throat, wheezing or coughing, and ear infection.

Other reported side effects include allergic reactions, which may be severe (anaphylaxis); allergic swelling; hives; and intussusception (a form of blockage of the bowel in which one segment of bowel becomes enfolded within another segment), the symptoms and signs of which may include severe stomach pain, persistent vomiting, blood in stools, a swollen belly and fever.

These are NOT all the possible side effects of RotaTeq. You can ask your doctor or health care provider for a more complete list.

If you noticed any side effects not mentioned in this leaflet, please inform your doctor or pharmacist. If the condition persists or worsens, seek medical attention.

## How to learn more about RotaTeq (and the condition for which it is prescribed):

[Rotavirus Vaccine, Live, Oral, Pentavalent, MSD]

This leaflet gives just a summary of certain information about the vaccine. If you have any questions or concerns about RotaTeq, talk to your health care provider. Your doctor or pharmacist can give you an added leaflet that is written for health professionals [or you can visit (http://www.msd.com.tw/Pages/home.aspx) and find the leaflet there].

## When was this package leaflet last revised?

This package leaflet was last revised in 2016 August.