Pneumococcal Conjugate Vaccines (PCV)
WHO recommendations & general information

Every year, 2.58 million episodes of severe pneumonia caused by *Streptococcus pneumoniae* occur globally in children aged under five years, accounting for 18% of all episodes of severe pneumonia and 33% of all pneumonia-related deaths. Most of this burden is disproportionately borne by low- and middle-income countries. Children with HIV are eight times more likely to develop invasive pneumococcal disease than are their HIV-negative peers.

In 2007, WHO recommended pneumococcal conjugate vaccine (PCV) for inclusion in national immunisation programmes. PCV is considered safe for administration in all target groups, including immunocompromised individuals. Vaccine efficacy against invasive pneumococcal disease caused by serotypes contained in PCV vaccine was found to be 71% when following the schedule in Option 2 (see table below). WHO’s recommendation was updated in 2012 to include and focus on the available 10-valent and 13-valent conjugate vaccines.

In 2012, 88 countries had introduced PCV into their routine immunisation schedules, including 23 countries with Gavi support. As of October 2013 that number increased to 32 Gavi-eligible countries, with a further 19 approved for introduction with Gavi support beyond 2013.

If the primary series is interrupted, resume without repeating the previous dose.

### Recommended schedules

<table>
<thead>
<tr>
<th>Recommended schedules</th>
<th>Age at 1&lt;sup&gt;st&lt;/sup&gt; dose</th>
<th>Doses in primary series (interval between doses)</th>
<th>Booster</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Option 1</strong></td>
<td>6 weeks (minimum)</td>
<td>3 doses with DTP (4 weeks between doses 1, 2 and 3)</td>
<td>No booster with 3-dose schedule except for HIV+ and preterm neonates in their 2&lt;sup&gt;nd&lt;/sup&gt; year if 3 primary doses were completed within the 1st year</td>
</tr>
<tr>
<td><strong>Option 2</strong></td>
<td>6 weeks (minimum)</td>
<td>2 doses before 6 months (8 weeks)</td>
<td>Booster dose at 9–15 months</td>
</tr>
<tr>
<td><strong>Delayed start</strong></td>
<td>If &lt;1 year: 2- or 3-dose schedule</td>
<td>8-week interval between doses for both groups</td>
<td>Booster at 9–15 months if following 2-dose schedule. Second booster if HIV+ or preterm neonate</td>
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<tr>
<td></td>
<td>If aged 1–2 years or 2–5 years + high risk: 2 doses</td>
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</tbody>
</table>
### Products & manufacturers

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>WHO PQ date</th>
<th>Form and presentation</th>
<th>Lowest known price (UNICEF, US$)</th>
<th>Vaccine vial monitor (VVM) type and cold chain volume (per dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevnar 7</td>
<td>Wyeth-Pfizer</td>
<td>Dec 2009</td>
<td>Liquid, single-dose vial*</td>
<td>N/A</td>
<td>VVM 30, Box, 5 vials = 21 cm³</td>
</tr>
<tr>
<td>PCV7* vaccine</td>
<td></td>
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<td></td>
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<tr>
<td>Prevnar 13</td>
<td>Wyeth-Pfizer</td>
<td>Aug 2010</td>
<td>Liquid, single-dose vial**</td>
<td>3.30264</td>
<td>VVM 30, Box, 50 vials = 12 cm³, Box, 25 vials = 15.7 cm³</td>
</tr>
<tr>
<td>PCV13 vaccine</td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Synflorix</td>
<td>GSK</td>
<td>Single-dose vial: Oct 2009, 2-dose vial: Mar 2010</td>
<td>Liquid, available in 1-or 2-dose preservative-free vial†</td>
<td>3.40–3.50264</td>
<td>VVM 30, Carton, single 1-dose vial = 58 cm³, Carton, single 2-dose vial = 4.8 cm³</td>
</tr>
<tr>
<td>PCV10 vaccine</td>
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</tbody>
</table>

### PIPELINE PRODUCTS

- No new PCV vaccines are expected to achieve WHO prequalification or meet the Gavi Advance Market Commitment Target Product Profile (TPP) before 2018.263
- PATH has two products in the pipeline. One is a protein plus conjugate vaccine developed in partnership with GSK, the Medical Research Council Unit in The Gambia and the London School of Hygiene & Tropical Medicine, about to enter Phase III trials after evaluation of data from Phase II. The second is a PCV10 vaccine focused on serotypes prevalent in developing countries, under development by Serum Institute of India.213,266,267
- Merck has a pneumoconjugate vaccine candidate provisionally named V114 in Phase II.134,268
- Sanofi Pasteur is reportedly collaborating with Korean company SK Chemicals to develop, produce and market a pneumococcal conjugate vaccine soon.269

### CHALLENGES

- Supply of the WHO prequalified products has been constrained in developing countries, particularly as scale-up of introductions in Gavi-eligible countries continues.263,270
- For the two-dose presentation of GSK’s preservative-free PCV10 vaccine, specific pre-introduction measures are required, including training. Post-introduction evaluations are also required.258,265

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* Being replaced by PCV13 or PCV10.
** Also available in prefilled syringe but not WHO prequalified.
† Two-dose presentation requires specific training and management.268
The PCV vaccine market is a duopoly of manufacturers Pfizer and GSK. Together with the HPV and rotavirus vaccines, PCV vaccines are some of the newest and most expensive vaccines, and present affordability challenges that prevent access.

**PRICE EVOLUTION: UNICEF AND PAHO**

(See Annex A for more information on prices used in this section)

- PCV vaccine is significantly more expensive than the traditional vaccines. According to volumes and prices published on the UNICEF Supply Division (SD) website, purchases of PCV accounted in value for 39.2% of all UNICEF SD vaccine purchases but only for 3% in terms of volume.

- Prices of PCV for PAHO have declined, but remain high, at US$14.12 and US$15.68 for PCV10 and PCV13, respectively [Graph 18, overleaf], at more than four times the Gavi tail price [see box below] offered to UNICEF.

**THE PNEUMOCOCCAL ADVANCE MARKET COMMITMENT (AMC) FOR GAVI**

The pneumococcal Advance Market Commitment (AMC) is a mechanism to incentivise companies to scale-up manufacturing capacity to meet the needs of Gavi-eligible countries. The AMC sets a maximum price of US$3.50 (‘tail price’) per dose for Gavi and Gavi-eligible countries through the UNICEF supply channel only. Manufacturers commit to not exceed this price for ten years, and in exchange they receive a part of the committed AMC subsidy (US$1.5 billion) in proportion to their contribution to the target demand (target demand at 200 million doses per year). Critiques of the AMC have been discussed earlier in this report.

- All Gavi-graduated and graduating countries that have not yet introduced a PCV vaccine are eligible to apply to introduce the vaccine under the AMC, which means that these countries can purchase the vaccine at the tail price, but have to finance it themselves. Some other conditions apply.271

- As of July 2013, 73% of the Gavi AMC subsidy had been awarded to Pfizer and GSK (corresponding to US$1,095 million).

- As of 2016, the annual supply of PCV to Gavi/UNICEF is projected to be 146 million doses, representing 73% of the 200 million doses per year targeted by the AMC.263

- In 2013, Pfizer reduced its tail price to US$3.40 per dose, with a subsequent decrease to US$3.30 per dose starting in 2014. Special conditions of the Pfizer price decrease include that the AMC donor funding for Pfizer contracts will be fully disbursed by 2015 at the latest, and that Gavi provides a financial guarantee for the tail price component of a total of 80% of the doses contracted in 2013–2015.272 GSK also reduced its tail price to US$3.40 per dose for the 2014–2024 contract.
**PRICES IN COUNTRIES**

The high price of PCV has hindered access in middle-income countries. While many Gavi-eligible countries have already introduced the vaccine, many middle-income countries have not [see Graph 3, page 14]. Cost effectiveness and especially the price of the vaccine have been cited by several countries as major barriers to introduction.41 A study by Nakamura et al. in 2011 estimated that the vaccine could be cost effective in most low- to middle-income countries at US$10 per dose or lower.273 But in 2014 Brazil was the only country outside of Gavi-eligible countries to have access to the vaccine at this price.

Brazil is an example of a country using technology transfer agreements to produce PCV domestically. The country entered a partnership with GSK in 2009 to vaccinate 13 million children (39 million doses) per year for at least eight years, until the country is ready to manufacture PCV on its own.274 The price per dose* was EUR11.50/US$16.03 in the first years, then decreasing to EUR5.00/US$6.97.170,275 However, the terms of the technology transfer arrangements are not publicly available and could limit the opportunity for Brazil to benefit from real competition when emerging manufacturers enter the market with cheaper products. The strategy could therefore not be advantageous for Brazil in the long term, for instance when Serum Institute of India enters the market with a PCV candidate in 2016/2017 at the expected lower price of US$2 per dose.84

As Pfizer’s PCV vaccine, Prevnar 13 (PCV13), has an advantage over GSK’s Synflorix (PCV10) because of its additional serotypes (PCV10 vs PCV13), GSK remains competitive by setting the price below that of Pfizer. The price difference is grounds for many middle-income countries to opt for the introduction of Synflorix over that of Prevnar 13.

Companies claim that they use differential pricing strategies like tiered pricing to maximise access, in effect maximising their revenues in middle- and low-income countries. In practice, prices in middle-income countries are extremely high and sometimes comparable to prices in high-income countries. Graphs 19 and 20, opposite, show that despite claims of differential pricing, the price of Pfizer’s PCV13 remains high in many countries, and Graph 5 on page 26 of this report shows that the price countries pay for PCV13 is not entirely dependent on their wealth – despite relative wealth often being used by companies as a proxy to set prices for different markets.

* Using OANDA average 2009 exchange rate euros to US dollars at 1.3937.
Graph 19: Prices for GSK's Pneumococcal Conjugate Vaccine (PCV10) in several countries, by income group and price type, 2013/2014*

Graph 20: Prices for Pfizer's Pneumococcal Conjugate Vaccine (PCV13) in several countries, by income group and price type, 2013/2014*

Sources:
PAHO Revolving Fund, UNICEF Supply Division, country price analysis.
*Annex A, Section C