## **Evidence based prevention of pneumococcal disease**

### Ros Hollingsworth PhD

*Therapeutic Team Leader, Anti-infectives & Vaccines Medical Department* 



### Prevenar\*\* (PCV7)

- Licensed in USA in 2000 and throughout Europe in 2001
  - Over 160 million doses distributed to date
- Introduced into UK's infant immunisation schedule in September 2006
- Product license indicates a primary course of 4 doses: three doses in infancy and a fourth dose in the second year of life
- PCV7 has been introduced in different countries using a variety of schedules
  - History
  - Evidence

\* Trade Mark



CMO Letter, Important changes to the childhood immunisation schedule. 12<sup>th</sup> July 2006 PL/CMO/2006/1, PL/CNO/2006/1, PL/CPHO/2006/1

### Prevenar – National Immunisation Programmes

Country	NIP	Start
	Schedule	Date
Australia	3+0	Jan-05
Belgium	2+1	Jan-07
Canada <sup>1</sup>	-	Jan-05
Denmark	2+1	Oct-07
France	3+1	Mar-03
Germany	3+1	Jul-06
<b>Greece</b> <sup>2</sup>	3+1	Jan-06
Italy <sup>3</sup>	2+1	Dec-06
Kuwait	3+1	Oct-06
Luxembourg	3+1	Feb-03
Mexico <sup>4</sup>	2+1	Jul-06
Netherlands	3+1	Jun-06
Norway	2+1	Jul-06
Qatar	3+1	Feb-04
Switzerland	2+1	Jul-06
United Kingdom	2+1	Sep-06
United States	3+1	Jul-00

- 1. Quebec and British Columbia schedules = 2+1 (34% of national birth cohort)
- 2. Government reimbursement rate = 75% for all children
- 3. 15 of 20 regions have adopted reimbursement programmes covering >75% of national birth cohort

4. Initial programme targeted to birth cohorts within low income regions and at-risk children (13% of national birth cohort)



### Rates of IPD, Children < 5 Years of Age U.S. CDC Active Bacterial Core Surveillance





## Rates of IPD, Adults ≥50 Years of Age U.S. CDC Active Bacterial Core Surveillance



Vaccines

Lexau et al JAMA 2005 294 2043-2051

### Estimated Number of Cases of Vaccine Serotype IPD Prevented by Direct and Indirect effects of PCV7





CDC MMWR 2005 54 893-797

### Alternative dosage schedules – US data: ABC surveillance system matched case-control study

Schedule	Effectiveness	95% CI
1 dose ≤ 7 months	73%	43 to 87%
2 doses ≤ 7 months	96%	88 to 99%
3 doses ≤ 7 months	95%	88 to 98%
2 doses ≤ 7 months, 1 dose 12-16 months	98%	75% to 100%
1 dose 12-23 months	93%	68 to 98%
2 doses 12-23 months	96%	81 to 99%
1 dose ≥ 24 months	94%	49 to 99%

•782 cases of IPD identified in children aged 3-59 months: 2512 controls identified
•Vaccine effectiveness estimated using equation; 1- (adjusted matched odds ratio) x 100



Whitney et al Lancet 2006;368:1495-1505

## UK National Vaccine Evaluation Consortium (NVEC)

- U.K. infants were given either 2 or 3 doses (at 2 and 4 or 2/3/4 months of age) of a 9-valent pneumococcal conjugate vaccine (PCV9) followed by boosting at 12 months of age
- In a separate study, toddlers (12 months of age) received 1 or 2 doses (2 months apart) of PCV9 followed by pneumococcal polysaccharide vaccine at 18 months of age



Goldblatt et al Pediatr Infect Dis J 2006 25: 312–319



**Conclusions:** 

• The 2-dose infant priming schedule of PCV9 is comparable to the 3-dose schedule

U.K. Schedule = 2+1

1 dose in toddlers may suffice for catch-up



Goldblatt et al Pediatr Infect Dis J 2006 25: 312–319

## **2006 Changes to Infant Immunisation Schedule: What vaccinations do infants now receive?**

Childs Age	Schedule			
2 months	DTP-Hib-IPV	PCV7		
3 months	DTP-Hib-IPV	Meningitis C		
4 months	DTP-Hib-IPV	PCV7	Meningitis C	
12 months	HiB/Meningitis C			
13 months	MMR	PCV7		

• Plus 'Catch up' for PCV7 to 2 years of age



Department of Health Feb 8th 2006

# What next for pneumococcal disease in the UK?

### Impact of vaccination

- All syndromes burden, mortality, morbidity
- Emerging serotypes
- Quantify direct and indirect effects

### •2+1 schedule

Catch up to 2 years of age



Unique Reference: ZPRE957, Date of Preparation: 31<sup>st</sup> October 2007

### **Evidence based prevention of pneumococcal disease**

### The Pneumococcal Surveillance Programme and Vaccine Policy



### Rates of Non-Vaccine Serotype IPD U.S. CDC Active Bacterial Core Surveillance



Whitney et al NEJM 2003 348 1737-1746 Lexau et al JAMA 2005 294 2043-2051



## Certain populations at greater risk from replacement disease?

#### HIV positive adults

- 1998 to 2003: IPD among adults infected with HIV decreased from 1127 to 919 cases per 100,000 adults with AIDS
- Decline in vaccine serotype IPD from 659 to 249 cases per 100,000 adults with AIDS
- Increase in non-vaccine serotypes from 298 to 430 cases per 100,000 adults with AIDS

#### Alaskan Natives

- Alaskan Native children are known to be particularly vulnerable to pneumococcal disease (pre-PCV7: 403.2 cases per 100,000, 2-3x higher than other US children of the same age)
- Decline in IPD from 403.2 cases per 100,000 in 1995-2000 to 134.3 cases per 100,000 in 2001-2003
- ▶ By 2006, that rate had increased once again to 244.6 cases per 100,000
- Non-Alaskan Native population <2 years of age: the decrease in IPD incidence was maintained without subsequent increase
- The recent increase in IPD in this small, high-risk population was caused by non-vaccine serotypes
  - mostly 3, 6A, 7F and 19A.

Flannery Bet al. Ann Intern Med. 2006;144:1-9 Singleton RJ et al. JAMA 2007; 297(16): 1784-1792



#### Prevenar\*▼

Pneumococcal saccharide conjugated vaccine, adsorbed

Presentation: Each 0.5ml dose of Prevenar contains 2 micrograms of each of the following saccharide serotypes: 4, 9V, 14, 18C, 19F, 23F and 4 micrograms of saccharide serotype 6B. Each saccharide is conjugated to the CRM<sub>197</sub> carrier protein and adsorbed on aluminium phosphate.

Indications: Immunisation against disease (including sepsis, meningitis, pneumonia, bacteraemia and acute otitis media) caused by *Streptococcus pneumoniae* serotypes 4, 6B, 9V, 14, 18C, 19F and 23F in infants and children from 2 months up to 5 years of age.

Dosage and Administration: The immunisation schedules for Prevenar should be based on official recommendations.

For intramuscular injection.

Infants 2-6 months: Three doses with at least a 1 month interval between doses. A fourth dose is recommended in the second year of life.

Infants 7-11 months: Two doses with at least a 1 month interval between doses. A third dose is recommended in the second year of life.

Children 12-23 months: Two doses with at least a 2 month interval between doses.

Children 24 months-5 years: one single dose.

Contra-indications: Hypersensitivity to any component of the vaccine or to diphtheria toxoid.

Warnings and Precautions: Do not administer intravenously. Appropriate treatment must be available in case of anaphylaxis. Impaired immune responsiveness may affect antibody levels. Prevenar does not replace 23-valent polysaccharide vaccine in at risk children ≥ 24 months of age. Children ≥ 24 months of age at high risk, previously immunised with Prevenar should receive 23-valent pneumococcal polysaccharide vaccine whenever recommended. Prophylactic antipyretics recommended when vaccinating children with history of seizure disorders, or when vaccinating simultaneously with whole cell pertussis vaccines. Delay vaccination in acute moderate or severe febrile illness. The immunogenicity of Prevenar has been demonstrated in infants with sickle cell disease. Safety and immunogenicity data are not yet available for children in other specific high-risk groups for invasive pneumococcal disease.

Side Effects: Very common: Decreased appetite, vomiting, diarrhoea, injection site reactions (e.g. erythema, induration/swelling, pain/tenderness), fever equal to or over 38 °C, irritability, drowsiness, restless sleep. Common: Injection site swelling/induration and erythema larger than 2.4cm, tenderness interfering with movement, fever over 39 °C. Uncommon: rash/urticaria. Rare: Seizures including febrile seizures, hypotonic hyporesponsive episode, injection site hypersensitivity reactions (e.g. dermatitis, pruritus, urticaria), hypersensitivity reactions including face oedema, angioneurotic oedema, dyspnoea, bronchospasm, anaphylactic/anaphylactoid reaction including shock. Very rare: Lymphadenopathy localised to the region of the injection site, erythema multiforme.

Legal Category: POM

Package Quantities: Pack of 1 single-dose pre-filled syringe (with separate needle) or pack of 10 single-dose pre-filled syringes

Cost: Single-dose pre-filled syringe (with separate needle) pack of 1: £34.50. Single-dose pre-filled syringe pack of 10: £345.00

Marketing Authorisation Numbers: Single-dose pre-filled syringe (with separate needle) pack of 1: EU/1/00/167/006, single-dose pre-filled syringe pack of 10: EU/1/001/167/004 Marketing Authorisation Holder: Wyeth-Lederle Vaccines S.A., Rue du Bosquet 15.

B-1348 Louvain-la-Neuve, Belgium

For full prescribing information and details of other side effects see Summary of Product Characteristics

Full prescribing information is available on request from:

Wyeth Pharmaceuticals, Huntercombe Lane South, Taplow, Maidenhead, Berkshire, UK, SL6 0PH. Telephone: 0845 367 0098

Date of Prescribing Information: 02Apr07

Code no. ZAPI056/0507 Doc ID: 43993

\*Trade mark

