



Public Health
England

Protecting and improving the nation's health

Use of Infanrix-IPV+Hib in the infant schedule

Information for healthcare professionals

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About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. It does this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. PHE is an operationally autonomous executive agency of the Department of Health.

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Use of Infanrix-IPV+Hib in the infant schedule

Over the summer of 2014, Infanrix-IPV+Hib was introduced alongside Pediacel as an alternative infant vaccine for the primary immunisation programme. The following questions and answers are intended to provide healthcare professionals with more information about this vaccine.

Infanrix-IPV+Hib indication

Infanrix-IPV+Hib is a combination vaccine that protects infants against five diseases: diphtheria, tetanus, whooping cough, polio and *Haemophilus influenzae* type b.

When Infanrix-IPV+Hib was introduced into the infant schedule

From June 2014, both Infanrix-IPV+Hib and Pediacel vaccines were made available to order online via the ImmForm website (www.immform.dh.gov.uk) and are distributed by Movianto UK for use in the primary schedule.

Why it was introduced into the infant schedule

Following a tender, which included careful evaluation of protection offered by the available vaccines, Infanrix-IPV+Hib was secured at a competitive price. By providing a market to multiple vaccine suppliers, there is also improved security of vaccine supply for the infant immunisation programme.

Other countries where Infanrix-IPV+Hib is used

Infanrix-IPV+Hib vaccine or similar vaccines including hepatitis B are used in 52 other countries across the world including France, Germany, Norway, Ireland and Poland. The vaccine was first licensed for use in Europe in 1997 so hundreds of millions of doses have been given. It was used for pre-school children in the UK for the Hib Catch-up campaign between 2007 and 2009.

Differences between Infanrix-IPV+Hib and Pediacel

Both vaccines protect against the same five diseases (tetanus, diphtheria, whooping cough, polio and Hib). The main differences are that the Infanrix-IPV+Hib vaccine contains three pertussis components, while Pediacel has five components but with slightly lower antigen content. Infanrix-IPV+Hib requires reconstitution before being administered, Pediacel is presented in a pre-filled syringe.

Efficacy

Pediacel is a five component pertussis vaccine and Infanrix-IPV+Hib is a three component pertussis vaccine. Both offer good protection against whooping cough

When the UK primary immunisation programme changed from whole cell to acellular pertussis vaccines in 2004, a five component vaccine (Pediacel), which contains pertussis toxoid (PT),

filamentous haemagglutinin (FHA), fimbrial agglutinogens (FIM) 2 and 3, and pertactin (PRN) was chosen. This vaccine had been shown to offer equal or better protection against clinically typical pertussis disease as the whole-cell pertussis vaccine previously used in the UK¹. Although a three-component vaccine (Infanrix-Hib) containing PT, FHA and PRN was available for primary immunisation, this was not used because of limited data on efficacy at the time. Subsequent analysis suggested that the cohorts who had Infanrix-Hib, which was used in the UK in 1999-2001 because of a shortage of whole cell vaccine, were as well protected up to the age of the pre-school booster as those cohorts who had been eligible for whole cell or 5aP vaccines in infancy².

In 2008, the JCVI advised that a change to a three-component pertussis vaccine for primary immunisation was unlikely to have a discernible effect on pertussis epidemiology, particularly as 3-component vaccines are already given as a pre-school booster. In 2010, the World Health Organisation reviewed all the global data on pertussis control in countries using acellular vaccines³. They concluded that acellular pertussis vaccines with three or more components have higher protective efficacy than vaccines with fewer components but did not find consistent evidence of a difference between 3 and 5 components.

Hib antibody levels after use of DTaP-IPV+Hib combination vaccine

The effectiveness of the Hib component (when combined with DTaP, DTaP-IPV or DTaP-HBV-IPV) has been looked at in post-licensure surveillance studies and the vaccine has been shown to provide good protection. Other countries using Infanrix-IPV+Hib for the primary schedule with a toddler Hib booster have not reported any problems with Hib disease control.

The booster vaccination (the combined Hib/MenC vaccine - Menitorix) given at 12 months of age provides long-term protection against Hib and MenC disease.

Efficacy of the other components

Results from several randomised controlled trials show that nearly all infants given the 3-dose primary vaccination course of Infanrix-IPV+Hib given at two, three and four months of age develop protective levels of antibodies against diphtheria (99%), tetanus (100%) and polio (96 - 100%).

Administration

Presentation of Infanrix-IPV+Hib

The Hib (*Haemophilus influenzae* type b) vaccine is supplied as a lyophilized (freeze-dried) white powder in a glass vial.

The diphtheria, tetanus, acellular pertussis and inactivated poliomyelitis vaccine is supplied as a cloudy white suspension in a pre-filled (0.5 ml) syringe.

The vaccine is supplied in single dose packs containing the syringe, vial and two needles –one for reconstitution and one for vaccine administration.

¹ Miller E (1999) Overview of recent clinical trials of acellular pertussis vaccines. *Biologicals* **27**: 79–86.

² Campbell H, Amirthalingam G, Andrews N *et al.* (2012) Accelerating control of pertussis in England and Wales. *Emerg Infect Dis* **18**(1): 38-47.

³ World Health Organization (2010) Pertussis vaccines: WHO position paper. *Weekly Epidemiological Record* No 40 **85**: 385-400.

Steps involved in preparing Infanrix-IPV+Hib include:

1. Shake the pre-filled syringe containing the DTaP-IPV suspension.
2. Attach a needle to the pre-filled syringe of DTaP-IPV and inject the entire contents of the syringe into the Hib vial.
3. With the needle still inserted, shake the Hib vial vigorously until the powder has completely dissolved.
4. Withdraw the entire mixture back into the syringe.
5. Replace the needle with an appropriate size needle for injection and administer the vaccine.
6. If the vaccine is not administered immediately, shake the solution vigorously again before injection.

Actions to take if the immuniser administers Infanrix-IPV OR forgets to reconstitute the Hib component of the vaccine and only gives the Infanrix-IPV component of Infanrix-IPV-Hib in the pre-filled syringe

If the error occurs at two months, give Menitorix vaccine at the same visit (or as soon as possible after error realised) and then give MenC as per the schedule at three months (at least one month after the Menitorix dose).

If the error occurs at three months and MenC vaccine has **not** yet been given at visit, give Menitorix. The infant will still need a MenC vaccine at four months because Menitorix contains a lower MenC antigen dose compared with the single antigen MenC vaccines.

If the error occurs at three months and MenC vaccine has **already** been given at visit before the error is realised, give a dose of Menitorix in addition to the vaccines already given. The child requires early protection against Hib and the additional MenC antigen in the Menitorix vaccine will not be harmful.

If the error occurs at four months, give Menitorix at the same visit (or as soon as possible after error realised).

If the error is picked up retrospectively (or, for example, identified from a look back exercise), the following action should be taken:

- **children aged >4 months to <12 months who have two recorded doses of Hib** - give the 12-month Menitorix dose on time
- **children aged >4 months to <12 months who have only one or no recorded doses of Hib** - give Menitorix at the time that the error is identified and give the 12-month Menitorix dose on time (with an interval of at least 1 month between the doses)
- **children aged >12 months** – children over the age of 12 months and less than 10 years old require only one dose Hib (ie one dose of Menitorix). Therefore, if they have received their 12-month booster, then no additional action needs to be taken

Although PHE is aware of some children who may have received **Infanrix-IPV+Hib** as a pre-school booster instead of the recommended Infanrix-IPV, this is not a clinical safety issue. From a supply viewpoint, however, efforts should be made to use the correct vaccine.

All vaccine errors should be reported to the local Screening and Immunisation Team. It is important to establish if the error was a one-off occurrence or a systematic error that might require a look back exercise.

Interchanging Pediacel and Infanrix-IPV+Hib vaccines

Studies suggest that a mixed primary course of Infanrix IPV Hib and Pediacel produce adequate responses to all antigens and therefore vaccination should never be delayed because the vaccine used for previous doses is unavailable or not known. Where possible and if local stock allows, it is preferable that the same DTaP-containing vaccine be used for all three doses of the primary course.

Contents of Infanrix-IPV+Hib besides the vaccine antigens

Infanrix-IPV+Hib contains:

- aluminium hydroxide
- lactose
- medium 199 (as stabilizer containing amino acids, mineral salts, vitamins and other substances)
- sodium chloride
- water for injections

There may also be traces of neomycin, polymyxin and polysorbate 80.

The vaccine does not contain gelatin or thiomersal

Contraindications to Infanrix-IPV+Hib

As with Pediacel, the vaccine should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of a tetanus, diphtheria, pertussis, polio, or Hib-containing vaccine, or
- a confirmed anaphylactic reaction to any of the components of the vaccine

The same contraindications and precautions that apply to Pediacel (as listed in the tetanus, diphtheria, polio, pertussis and Hib Green Book chapters) apply to Infanrix-IPV+Hib.

Minimum age for the first dose of Infanrix-IPV+Hib and minimum intervals between doses

The infant immunisation schedule remains unchanged at two, three and four months of age.

The minimum age for a first dose is six weeks of age.

The minimum intervals between subsequent doses of Infanrix-IPV+Hib are the same as those for Pediacel (four weeks).

Administration of Infanrix-IPV+Hib with other vaccines

Infanrix-IPV+Hib can be administered at the same time or at any time before or after any other vaccine. As recommended for other vaccines, it should be administered at a separate injection site, by separate needle and syringe.

Adverse events

Adverse events after immunisation with Pediacel and Infanrix-IPV+Hib compared

Clinical trial data from more than 3500 subjects given the vaccine show that Infanrix-IPV+Hib is generally well tolerated. Any adverse events experienced are the same as those experienced following administration of Pediacel vaccine (redness, swelling and tenderness at the injection site, fever, irritability, loss of appetite, diarrhoea and vomiting)

Post-immunisation care recommendations

The recommendations following administration of Infanrix-IPV+Hib vaccine are the same as those after the administration of Pediacel

Useful references

Public Health England. Immunisation against infectious disease (The Green Book) Diphtheria, Tetanus, Pertussis, Polio and Hib chapters. Available at:
<https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book>

Infanrix-IPV+Hib Summary of Product Characteristics. October 2013. Available at:
<http://www.medicines.org.uk/emc/medicine/28678/SPC/INFANRIX-IPV%2BHib+powder+and+suspension+for+suspension+for+injection/>