The hexavalent DTaP/IPV/Hib/HepB combination vaccine

Information for healthcare practitioners about the introduction of the hexavalent vaccine into the routine infant immunisation programme
Aim of resource

To provide information to healthcare practitioners about the introduction of a hexavalent DTaP/IPV/Hib/HepB vaccine in order that:

• immunisers are knowledgeable and confident in administering and discussing this vaccine with parents/carers

• high uptake of the routine infant immunisation schedule is sustained as the hexavalent vaccine replaces the pentavalent vaccine

To improve uptake of childhood immunisations via:

• increasing understanding about best methods of communication with parents

• preparing healthcare practitioners to be able to respond to parents’ Frequently Asked Questions
Why is a hepatitis B containing vaccine being offered to all infants?

• In 1992, the World Health Assembly recommended every country should have a universal hepatitis B immunisation programme

• As of 2008, 177 countries had incorporated hepatitis B vaccine in their national infant immunisation programmes

• However, as the UK is a low prevalence and low incidence country for hepatitis B, introducing a universal hepatitis B programme using a monovalent hepatitis B vaccine would not have been cost-effective

• Recently, infant combination hepatitis B vaccines (which also protect against diphtheria, tetanus, polio, pertussis and Hib) have become available in the UK

• In 2014, the Joint Committee of Vaccination and Immunisation (JCVI) re-evaluated the benefits and cost-effectiveness of a universal hepatitis B infant immunisation programme in the UK

• They subsequently recommended the use of the hexavalent DTaP/IPV/Hib/HepB combination vaccine for all infants
What is hepatitis B?

- Hepatitis B is a viral infection that attacks the liver and can cause both acute and chronic disease.
- Acute HBV infection occasionally leads to sudden and severe liver damage which can be fatal.
- Chronic HBV infection can result in progressive liver disease.
- This can lead to cirrhosis (development of scar tissue) and an increased risk of developing liver cancer.
How is hepatitis B virus (HBV) transmitted?

- HBV is highly transmissible through the exchange of infected blood and bodily fluids
- It can survive outside the body for at least 7 days
- Transmission mostly occurs:
  - through vaginal or anal intercourse
  - as a result of blood-to-blood contact through percutaneous exposure (e.g. sharing of needles and other equipment by people who inject drugs or through ‘needlestick’ injuries)
  - through perinatal transmission from mother to child
- Transmission has also followed bites from infected persons although this is rare
- Transfusion-associated infection now also rare in UK as blood donors and donations are screened
Clinical presentation

• Many new infections are subclinical showing no signs of infection. Often infections are only detected through other blood tests.

• If symptomatic, symptoms of acute infection start insidiously and may present as flu like illness with or without mild fever or symptoms may be non-specific

• Anorexia, nausea, vomiting and aching in the right upper abdomen may be present

• Followed by malaise, decreased appetite, joint pain and jaundice with progressive darkening of urine and lightening of the faeces

• Symptoms may last several weeks to months
Treatment and prevention

• No specific treatment is available for acute hepatitis B

• Children less than 6 years of age who become infected with hepatitis B virus are the most likely to develop chronic infection

• Chronic hepatitis B infection can be treated with oral antivirals which can slow the progression of cirrhosis, reduce incidence of liver cancer and improve long term survival

• **Hepatitis B vaccination is the most effective prevention**

• A completed course of vaccine induces protective antibody levels in more than 95% of infants, children and young adults

• Protection lasts at least 20 to 30 years

• The vaccine has an excellent record of safety and effectiveness
UK hepatitis B epidemiology

- UK is a very low-prevalence country for HepB:
  0.3 - 0.4% UK population infected

- Prevalence of HepB infection varies across the country
  e.g. prevalence rates in antenatal women vary from 0.05 to 0.08% in some rural areas but rise to 1% or more in certain inner city areas

- Higher prevalence in those born in high-endemicity countries, many of whom will have acquired infection at birth or in early childhood

- Incidence of acute infection is low but is higher among those with certain behavioural or occupational risk factors

- England and Wales sees around 500-600 laboratory-confirmed cases of HepB every year
Globally, hepatitis B is one of the most common infectious diseases. WHO estimates around 250 million people worldwide are chronically infected with hepatitis B.
The Infanrix hexa® vaccine programme
The recommended vaccine

- Brand name: Infanrix hexa®
- Multi-component **inactivated** vaccine marketed by GlaxoSmithKline
- Licensed for use from six weeks of age
- Routinely recommended for infants as part of the primary immunisation schedule at 8, 12 and 16 weeks
- Infanrix hexa® can also be used for catch-up immunisation for children up to their 10th birthday where these children have missed out on doses of primary immunisations
Who is eligible to receive Infanrix hexa® vaccine?

• All babies born on or after 1st August 2017 will become eligible for the vaccine eight weeks after their birth

• Infanrix hexa® vaccine is expected to be made available to order online through the ImmForm website (www.immform.dh.gov.uk) from 1st September 2017

• Movianto UK will distribute Infanrix hexa® for use in the routine childhood primary immunisation schedule

• Infants born before 1st August 2017 should complete the course with pentavalent vaccine (Pediacel® or Infanrix-IPV+Hib®)

• Infanrix hexa® should only be given to babies born before 1st August if there is no locally held vaccine stock and no further Pediacel® or Infanrix-IPV+Hib® can be ordered through ImmForm or if pentavalent vaccine is not readily available

• Stocks of pentavalent vaccine (Pediacel® or Infanrix-IPV+Hib®) may be used for pre-school booster to use up national vaccine stocks.
Is Infanrix hexa® a new vaccine?

- Infanrix hexa® is not a new vaccine
- First licensed for use in Europe in October 2000
- Licensed for use in 97 other countries including Canada, Australia and New Zealand
- Approximately 150 million doses have been given to infants in Europe and across the world
- Infanrix hexa® protects against the same five diseases (tetanus, diphtheria, whooping cough, polio and Hib) as the ‘5 in 1’ vaccines Infanrix®-IPV+Hib and Pediacel®
- The main difference is that Infanrix hexa® also offers protection against hepatitis B
Is Infanrix hexa® vaccine safe and effective?

• The safety profile of Infanrix hexa® is excellent
• Any adverse events experienced are mild to moderate
  • Same as those experienced following administration of the Pediacel®
    and Infanrix®-IPV+Hib vaccines
  • Include redness, swelling and tenderness at the injection site, fever,
    irritability, loss of appetite, diarrhoea and vomiting
• Multiple studies have shown Infanrix hexa® to be safe and highly
  immunogenic for all its component toxoids/antigens

Dhillon S. DTPa-HBV-IPV/Hib vaccine (Infanrix hexa™) A Review of its Use as a Primary and Booster Vaccination. Drugs 2010: 70(8): 1021-1058 Available at: https://www.ncbi.nlm.nih.gov/pubmed/20481658
Vaccine scheduling

- The infant immunisation schedule remains unchanged at eight, twelve and sixteen weeks of age.

- First dose of Infanrix hexa® can be given from six weeks (if required in exceptional circumstances only e.g. travel to an endemic country) but not before. In these cases rotavirus, Td/IPV and MenB should be given at the same time. Vaccines given early need to be given via PSD.

- The minimum interval between doses of Infanrix hexa® is four weeks.

- Infanrix hexa® can be administered at the same time as, or at any time before or after, any other vaccine.

- If primary course is interrupted, resume but don’t repeat, allowing an interval of four weeks between the remaining doses.

- As with the pentavalent vaccines, Infanrix hexa® should be given to premature infants at the appropriate chronological age, according to the schedule.

- Booster doses of hepatitis B will not usually be required for children vaccinated according to the routine childhood schedule.
Contraindications

There are very few individuals who cannot receive the Infanrix hexa® vaccine

Infanrix hexa® should not be administered to those who have had:

1. A confirmed anaphylactic reaction to a previous dose of the vaccine OR
2. A confirmed anaphylactic reaction to any component of the vaccine (this includes formaldehyde, neomycin and polymyxin)

Where there is doubt, instead of withholding immunisation, appropriate advice should be sought from a member of the local Screening and Immunisation or Health Protection team

Precautions are the same as with the pentavalent vaccines. For further information refer to Green Book or SPC documents.
Systemic and local reactions following a previous immunisation

Children who have had a systemic or local reaction following a previous immunisation with DTaP/IPV/Hib/HepB or DTaP/IPV/Hib including:

- fever, irrespective of its severity
- hypotonic-hyporesponse episodes (HHE)
- persistent crying or screaming for more than three hours, or
- severe local reaction, irrespective of extent

can continue to receive subsequent doses of DTaP/IPV/Hib/HepB vaccine
After reconstitution, 1 dose (0.5 ml) contains:

- Diphtheria toxoid
- Tetanus toxoid
- *Bordetella pertussis* antigens
  - Pertussis toxoid (PT)
  - Filamentous Haemagglutinin (FHA)
  - Pertactin (PRN)
- Hepatitis B surface antigen (HBs)
- Poliovirus (inactivated) (IPV)
  - type 1 (Mahoney strain)
  - type 2 (MEF-1 strain)
  - type 3 (Saukett strain)
- *Haemophilus influenzae* type b polysaccharide (polyribosylribitol phosphate, PRP)
  - conjugated to tetanus toxoid as carrier protein

Adjuvants:
- Aluminium hydroxide, hydrated (Al(OH)3)
- Aluminium phosphate (AlPO4)

Excipients:
- Lactose anhydrous
- Sodium chloride (NaCl)
- Medium 199 containing principally amino acids, mineral salts, vitamins
- Water for injections

The vaccine may contain traces of formaldehyde, neomycin and polymyxin which are used during the manufacturing process.

Infanrix hexa® does not contain any porcine gelatine or thiomersal
How is Infanrix hexa® vaccine presented?

- The DTaP/IPV/HepB component is presented as a cloudy white suspension in a pre-filled glass syringe. Upon storage, a clear liquid and a white deposit may be observed.

- The lyophilised (freeze dried) Hib vaccine is presented as a white powder in a glass vial.

- The vaccine is supplied in single dose packs containing the syringe, vial and two needles:
  - Green needle for reconstitution
  - Blue needle for vaccine administration
What are the steps involved in preparing Infanrix hexa®?

1. Shake the pre-filled syringe containing the DTaP/IPV/HepB suspension to obtain a consistent, cloudy, white suspension

2. Attach the green needle supplied to the pre-filled syringe of DTaP/IPV/HepB and inject the entire contents of the syringe into the vial containing the Hib vaccine

3. Shake the vial vigorously until the powder has completely dissolved

4. Withdraw the entire mixture back into the syringe

5. Inspect the vaccine suspension for any foreign particulate matter and/or abnormal physical appearance. If either is observed, discard the vaccine

6. Replace the green needle with the blue needle supplied and administer the vaccine intramuscularly

*DO NOT FORGET TO RECONSITUTE THE HIB COMPONENT*
Storage and administration

- Infanrix hexa® should be stored between +2°C to +8°C
- It must be stored in its original packaging to:
  - protect it from light
  - ensure the component parts are kept together
  - retain the batch number and expiry date for the entire product which is printed on the outer vaccine carton
- Infanrix hexa® should be administered intramuscularly
- Infants with a bleeding disorder should receive the vaccine by deep subcutaneous injection to reduce the risk of bleeding
- Preferred site of injection for infants under one year of age is the anterolateral aspect of the thigh
- It can be given in the same thigh as the PCV vaccine at the 8 and 16 week immunisation appointments (minimum of 2.5cm apart)
Post-immunisation care recommendations

- The recommendations following administration of Infanrix hexa® vaccine are the same as with the administration of Pediacel® and Infanrix®-IPV+Hib vaccines.

- When PCV is given alongside infant DTaP-containing combination vaccines, the rate of fever is higher than when either vaccine is administered alone.

- In the current UK schedule, infants receive these vaccines alongside MenB vaccination at 8 and 16 weeks of age.

- The routine recommendation to offer prophylactic paracetamol with the infant doses of MenB is expected to also reduce the rate of fever attributed to co-administration of PCV.

- Please see MenB vaccine and paracetamol information and “What to expect after vaccinations” leaflet on the PHE Immunisation webpage for more information.
Administration of Infanrix hexa®

Infanrix hexa® should only be supplied and administered:

- Against a prescription written manually or electronically by a registered medical practitioner or other authorised prescriber
- Against a Patient Specific Direction
- Against a Patient Group Direction

The NHS England PGD is available here:

https://www.england.nhs.uk/south/info-professional/pgd/south-west/downloads/
Possible adverse reactions

Most commonly reported (seen in more than 1 in 10 doses of the vaccine)

- Loss of appetite, fever (>38°C), abnormal crying, irritability and restlessness
- Local swelling, pain and redness at the injection site

Hypersensitivity reactions, such as angioedema, urticaria and anaphylaxis can occur but are rare, as can convulsions (with or without fever) and hypotonic-hyporesponsive episodes (also rare)

Suspected adverse reactions should be reported to the MHRA using the Yellow Card reporting scheme at: https://yellowcard.mhra.gov.uk/
Neonatal selective immunisation programme for babies at risk of hepatitis B
Implications for babies at high risk of hepatitis B infection

- Babies born to mothers chronically infected with HBV or who have had acute hepatitis B during pregnancy are at risk of becoming infected with HBV.

- Objective of the selective neonatal hepatitis B immunisation programme is to provide post exposure immunisation to infants born to HBV infected mothers to prevent mother to child transmission at or around the time of birth.

- With the introduction of hepatitis B vaccine into the routine schedule:
  - The maternal hepatitis B screening programme will continue as it remains essential to identify unborn babies at risk of infection.
  - The neonatal selective immunisation programme will continue so that high risk infants receive a dose of HepB vaccine at birth followed by a dose at four weeks of age.
Why is the selective neonatal immunisation programme continuing if all infants will receive hepatitis B vaccine?

- HBV infection can be transmitted from infected mothers to their babies at or around the time of birth
- Babies acquiring infection at this time have a high risk of becoming chronically infected with the virus
- The post exposure vaccine is over 90% effective in preventing these infants from developing HBV infection
- Timely vaccination at birth and at one month of age is critical to preventing infant infection
- The dose that is given to all babies at eight weeks of age (as part of the universal programme) would be too late to prevent infection in those high risk babies who are exposed at or around birth
- It is particularly important that these babies have a blood test for HepB at 12 months. More information on blood testing available at: https://www.gov.uk/guidance/hepatitis-b-dried-blood-spot-dbs-testing-for-infants
# Hepatitis B vaccine schedule for routine and at risk infant immunisation programmes

<table>
<thead>
<tr>
<th>Age</th>
<th>Routine childhood</th>
<th>Babies born to hepatitis B infected mothers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>X*</td>
<td>✔ Monovalent HepB (Engerix B or HBvaxPRO Paediatric) (with HBIG if indicated)</td>
</tr>
<tr>
<td>4 weeks</td>
<td>X</td>
<td>✔ Monovalent HepB (Engerix B or HBvaxPRO Paediatric)</td>
</tr>
<tr>
<td>8 weeks</td>
<td>✔ DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
<td>✔ DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
</tr>
<tr>
<td>12 weeks</td>
<td>✔ DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
<td>✔ DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
</tr>
<tr>
<td>16 weeks</td>
<td>✔ DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
<td>✔ DTaP/IPV/Hib/HepB (Infanrix hexa)</td>
</tr>
<tr>
<td>1 year</td>
<td>X</td>
<td>✔ Monovalent HepB (Engerix B or HBvaxPRO Paediatric) Test for HBsAg</td>
</tr>
</tbody>
</table>

*Babies born to hepB negative mothers but going home to a household with another hepatitis B infected person may be at immediate risk of hepatitis B infection so should be given a monovalent dose of hepatitis B vaccine before discharge from hospital
What if a high risk baby is late for or misses their first or second dose of Hep B?

Receiving Hep B vaccines as soon as possible after a delay is of critical importance in preventing maternally-acquired Hep B

IN THIS INSTANCE YOU CANNOT RELY ON CHIS SCHEDULING AND MAY NEED TO START THE HEXAVALENT SCHEDULE EARLY

- PLEASE SEE GUIDANCE:


AND/OR CONTACT:

england.southwestscrimms@nhs.net

Tel: 0113 8255084
Sources of information
Healthcare practitioner questions

Further information and commonly asked questions about the inclusion of hepatitis B containing vaccine in the routine and selective infant immunisation schedule are available in the following documents:

• **The hexavalent DTaP/IPV/Hib/HepB combination vaccine:**
  Information for healthcare practitioners about the inclusion of hepatitis B vaccine in the routine infant immunisation programme

• **The hexavalent DTaP/IPV/Hib/HepB combination vaccine**
  Information for healthcare practitioners about the neonatal selective immunisation programme for babies at risk of hepatitis B

Available on PHE Immunisation webpage
https://www.gov.uk/government/collections/immunisation
Further sources of information


• Infanrix hexa® Summary of Product Characteristics. Available at: https://www.medicines.org.uk/emc/medicine/33313

• The NHS England PGD is available here: https://www.england.nhs.uk/south/info-professional/pgd/south-west/downloads
What do parents want to know?

Communication and information
FAQs
2017 Cochrane review of routine vaccinations

• Parents wanted more information than they were getting
• Parents wanted balanced information about benefits and risks of vaccination

Parents view health workers (HWs) as important source of info and have specific expectations of their interactions with them

• Parents find it difficult to know which vaccination info sources to trust and find it difficult to find info they believe to be unbiased and balanced

2017 Cochrane review – what works?

- Tailored information for different audiences (e.g. vaccine hesitant parents)
- Information given to parents before the appointment
- HCWs should make it clear they have the child’s best interest as their focus, as opposed to performance targets
- HCWs should be helpful, caring and willing to have open, non-judgemental discussions with parents about their questions and concerns
- Parents offered opportunities for discussion
- Information provided to address media headlines/rumours about vaccinations
- Provide parents with information they perceive as impartial, balanced and unbiased.
- Information provided in multiple settings outside the health centre
- Information should be communicated in a clear, simple way in a variety of formats

Health visitor immunisation & screening training

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The "vaccine overload" myth

The baby’s immune system copes very well with thousands and thousands of bacteria and viruses

As soon as babies are born they come into contact with a huge number of different bacteria and viruses every day

The vaccines that a baby has in the first year of life are a tiny number compared to the thousands of wild bacteria and viruses it will meet at the same time

Full video at NHS Choices:
http://www.nhs.uk/video/Pages/vaccines-and-your-childs-immune-system.aspx
“I’m concerned about the ingredients in the vaccine”

- All the information about what ingredients are in the vaccines are in the Patient Information Leaflets (PIL) which are found online. Nothing is hidden.

- Vaccines need additives to make them safe and the three main ingredients are:
  - Adjuvants or enhancers – to make the vaccine more effective
  - Stabilisers – to stop the vaccine deteriorating when exposed changes such as heat or light
  - Preservatives – to increase the vaccines shelf life

- More information can be found on NHS choices [http://www.nhs.uk/Conditions/vaccinations/Pages/vaccine-ingredients.aspx](http://www.nhs.uk/Conditions/vaccinations/Pages/vaccine-ingredients.aspx)

- All the vaccines in the UK schedule are thoroughly tested for safety.

“Can I delay some or all the vaccinations?”

• Babies are vaccinated when they are at highest risk of getting sick or dying if they are exposed to the disease. Any time a vaccine is delayed you leave your baby vulnerable to disease.

• If parents are very uncomfortable they can split the vaccines into two appointments, but this is not recommended.
Support

- The national immunisation leaflets contain lots of detail and are great resources;
- Check you have copies readily available;
- If a parent decides to delay vaccination use the leaflet to alert them to signs and symptoms of the diseases they haven’t vaccinated against.

NHS Choices has a short animation explaining how vaccines do not overload a child’s immunisation system: http://www.nhs.uk/video/Pages/vaccines-and-your-childs-immune-system.aspx
Questions?

Contact the Screening & Immunisations team on: england.southwestscrimms@nhs.net