UK Health Security Agency

The hexavalent DTaP/IPV/Hib/HepB combination vaccine

Information for healthcare practitioners

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Contents

Background

From autumn 2017, a hexavalent (6 in 1) vaccine called Infanrix hexa®, replaced the previously used pentavalent (5 in 1) infant vaccines Infanrix®-IPV+Hib and Pediacel®. All babies born on or after 1 August 2017 became eligible for this hexavalent vaccine, which includes hepatitis B (HepB) in addition to the other antigens/toxoids previously included in the pentavalent vaccines, for their primary immunisations.

In 2022, the UK Health Security Agency (UKHSA) started supplying the vaccine, Vaxelis® in addition to Infanrix hexa® for use in the primary immunisation schedule. Vaxelis® is also a hexavalent vaccine and it protects against the same diseases (diphtheria, tetanus, pertussis, polio, Hib and hepatitis B) as Infanrix hexa®. Both vaccines are abbreviated to DTaP/IPV/Hib/HepB.

The purpose of this document is to provide information about the 2 hexavalent vaccines to healthcare practitioners who are involved in delivering or advising on the infant primary vaccination programme. Although originally published as 2 separate documents in 2017, (routine programme guidance and selective programme guidance), this updated version combines these 2 documents to ensure the information is easily accessible to all who need it and that important information about the selective HepB vaccination programme for high risk infants is highlighted.

The selective neonatal hepatitis B immunisation programme

All pregnant women should be offered screening for hepatitis B infection in every pregnancy.

Babies born to mothers who, following screening, are found to be chronically infected with hepatitis B virus (HBV) or who have had acute hepatitis B during pregnancy are at risk of becoming infected with HBV.

The objective of the selective neonatal hepatitis B immunisation programme is to provide post exposure immunisation to prevent mother to child transmission at or around the time of birth. To fulfil this objective, infected mothers need to be identified through antenatal screening and immunisation of the infant needs to start with a dose of monovalent hepatitis B vaccine at birth followed by a second dose at 4 weeks of age. They then need to receive further doses of hepatitis B vaccine, contained in the hexavalent vaccine given as part of the routine infant immunisation schedule at 8, 12 and 16 weeks. These infants should receive a further dose of monovalent hepatitis B vaccine at 12 months of age and at the same time, they should have a blood test to check for HepB infection. It is important that these high-risk infants are not overlooked now that HepB vaccine is part of the routine infant programme.

Infanrix hexa® and Vaxelis® vaccines

Infanrix hexa® and Vaxelis® are combination vaccines used for primary vaccination of infants at 8, 12 and 16 weeks of age to protect against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and disease caused by *Haemophilus influenzae* type b.

Multiple studies have shown that Infanrix hexa® and Vaxelis® are safe and highly immunogenic for all their component toxoids/antigens.

Further details can be found in the Summary of Product Characteristics (SPC) for Infanrix hexa and Vaxelis.

Both hexavalent vaccines are available to order online through the ImmForm website and are distributed by Movianto UK for use in the routine childhood primary immunisation schedule.

It is important to note that Infanrix hexa® requires reconstitution before being administered whilst Vaxelis® is presented in a pre-filled syringe

Interchangeability of Infanrix hexa and Vaxelis

Vaxelis® and Infanrix hexa® vaccines are considered interchangeable, but where possible and if local stock allows, it is preferable that the same DTaP/IPV/Hib/HepB vaccine be used for all 3 doses of the primary course. However, vaccination should never be delayed because the vaccine used for previous doses is not known or unavailable.

Children who are behind with the schedule

When the hexavalent vaccine was introduced into the schedule, it was recommended that children born before 1 August 2017 should complete the course with pentavalent vaccine (Pediacel® or Infanrix-IPV+Hib®). As there is now no pentavalent vaccine available to order, both Infanrix hexa® and Vaxelis® should be used for catch-up immunisation for children up to 10 years of age where these children have missed out on doses of primary immunisations.

Why a hexavalent vaccine was introduced into the infant schedule

Hepatitis B is an infection of the liver caused by the hepatitis B virus (HBV). Most new infections with HBV are sub-clinical or may only cause a flu-like illness. However, acute infection occasionally leads to sudden and severe liver damage which can be fatal. Chronic HBV infection can result in progressive liver disease, leading to cirrhosis (development of scar tissue) in some patients and an increased risk of developing liver cancer. In 1992, the World Health Assembly recommended that every country should have a universal hepatitis B immunisation programme by 1997.

As the UK is a low prevalence and low incidence country for hepatitis B however, introducing a universal hepatitis B programme using a monovalent hepatitis B vaccine would not have been cost-effective. In more recent years however, infant combination hepatitis B vaccines

(which also protect against diphtheria, tetanus, polio, pertussis and Hib) have become available in the UK.

In 2014, therefore, 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 and subsequently recommended the use of the hexavalent DTaP/IPV/Hib/HepB combination vaccine for all infants subject to securing the vaccine at a cost-effective price.

By providing hepatitis B vaccine as part of the combined infant vaccine, as well as being protected against diphtheria, tetanus, pertussis, polio and Hib, infants now have the benefit of protection against hepatitis B virus.

Other countries where the hexavalent vaccine is used

Neither of the hexavalent vaccines are new vaccines. Both vaccines have been widely used in other countries across the world for several years.

Safety and efficacy of the hexavalent vaccines

The safety profile of both hexavalent vaccines is excellent and any adverse events experienced are generally mild to moderate in severity. These may include redness, swelling and tenderness at the injection site, fever, sleepiness, irritability, loss of appetite, diarrhoea and vomiting.

Results from clinical trials show that nearly all infants given the 3 dose primary vaccination course of Infanrix hexa® at 2, 3 and 4 months of age develop protective levels of antibodies against diphtheria (100%), tetanus (100%), pertussis (100%), hepatitis B (99.5%), polio (99% to 100%) and Hib (96.4%).Similar levels of protection are seen with Vaxelis where protective levels of antibodies against diphtheria (100%), tetanus (100%), pertussis (varies by component), hepatitis B (98%), polio (100%) and Hib (98%) were seen one month after completing the 3 dose primary vaccination schedule.

Vaccine dosage and schedule

The routine schedule for the hexavalent vaccines

The infant immunisation schedule remains unchanged at 8, 12 and 16 weeks of age. The minimum age for a first dose is 6 weeks of age.

The first dose of the hexavalent vaccine can be given from 6 weeks if required in certain circumstances, for example travel to an endemic country. Rotavirus and MenB vaccines should also be given at the same time. The schedule should then be completed with a minimum of 4 weeks between subsequent doses of the hexavalent vaccine and 8 weeks between subsequent doses of MenB. As the pneumococcal conjugate vaccine (PCV13) should be given from 12 weeks of age, vaccine providers may decide to return a child who received the first set of primary immunisation early back to the routine schedule and give the second set at 12 weeks. An individual decision should be made depending on the circumstances and doses of HepB-containing vaccine should not be delayed if the infant is at high risk.

Note: MenB administration before 8 weeks of age is off-label. Patient Group Directions (PGDs) should be checked as to whether they cover administration of routine vaccinations before 8 weeks of age. A Patient Specific Direction (PSD) may be required.

The neonatal selective schedule for the hexavalent vaccine

Which vaccine schedule to use for high risk infants

High risk infants should receive monovalent hepatitis B vaccine at birth and 4 weeks of age and then 3 doses of the hexavalent vaccine at 8, 12 and 16 weeks of age. They should receive a booster dose of monovalent hepatitis B vaccine at 12 months of age, at which time they should also have a blood test to check for infection.

Table 1: Hepatitis B doses in immunisation schedule for the routine childhood and selective neonatal hepatitis B programmes

Age	Routine childhood programme. Yes or No	Routine childhood programme	Babies born to hepatitis B infected mothers. Yes or No	Babies born to hepatitis B infected mothers
Birth	No[1]		Yes	Monovalent HepB (Engerix B® or HBVaxPRO Paediatric®) (with HBIG if indicated)
4 weeks	No		Yes	Monovalent HepB (Engerix B® or HBVaxPRO Paediatric®)
8 weeks	Yes	DTaP/IPV/Hib/HepB (Infanrix hexa® or Vaxelis®)	Yes	DTaP/IPV/Hib/HepB (Infanrix hexa® or Vaxelis®)
12 weeks	Yes	DTaP/IPV/Hib/HepB (Infanrix hexa® or Vaxelis®)	Yes	DTaP/IPV/Hib/HepB (Infanrix hexa® or Vaxelis®)
16 weeks	Yes	DTaP/IPV/Hib/HepB (Infanrix hexa® or Vaxelis®)	Yes	DTaP/IPV/Hib/HepB (Infanrix hexa® or Vaxelis®)
1 year	No		Yes	Monovalent HepB (Engerix B® or HBVaxPRO Paediatric®) Test for HBsAg

[1]Newborn infants born to a hepatitis B negative woman but known to be going home to a household with another hepatitis B infected person may be at immediate risk of hepatitis B infection. In these situations, a monovalent dose of hepatitis B vaccine should be offered before discharge from hospital. They should then continue on the routine childhood schedule commencing at 8 weeks.

This schedule was agreed by the Joint Committee on Vaccination and Immunisation (JCVI) in October 2016. The Committee considered various schedule options and agreed that there

was no evidence of increased reactogenicity or adverse events associated with multiple doses of hepatitis B-containing vaccine and the schedule option chosen for babies born to hepatitis B infected mothers (shown in Table 1) reduced the risk of missing doses.

Vaccine dose

Infanrix Hexa should be administered as a 0.5mL dose after reconstitution.

Vaxelis is supplied as a pre-filled 0.5mL dose.

Administration of the hexavalent vaccine with other infant vaccines

The hexavalent vaccines can be administered at the same time as, or at any time before or after any other vaccine. Other countries routinely offer Infanrix hexa® and Vaxelis® with the other infant vaccines, including rotavirus and pneumococcal conjugate vaccine.

Giving the hexavalent vaccine to premature infants

Clinical data indicate that Infanrix hexa® and Vaxelis® can be given to premature infants and it is important that premature infants receive their immunisations at the appropriate chronological age (that is age since birth, not corrected), according to the schedule. As the benefit of vaccination is high in this group of infants, vaccination should not be withheld or delayed. The immune responses seen in premature infants to these vaccines in clinical trials were generally similar to that of those of the overall study population.

In comparative clinical studies, similar rates of adverse reactions were observed in pre-term and full-term infants. However, the occurrence of apnoea following vaccination is increased in infants who were born very prematurely. Very premature infants (born less than or equal to 28 weeks of gestation) who are in hospital should have respiratory monitoring for 48 to 72 hours when given their first immunisation, particularly those with a previous history of respiratory immaturity. If the child has apnoea, bradycardia or desaturations after the first immunisation, the second immunisation should also be given in hospital, with respiratory monitoring for 48 to 72 hours.

What you should do if the vaccine course is interrupted or an infant misses a scheduled dose

If the primary course of the DTaP/IPV/Hib/HepB-containing vaccine is interrupted, it should be resumed but not repeated, allowing an interval of 4 weeks between the remaining doses.

What you should give children with incomplete, uncertain or non-UK primary immunisations

Infants and children under 10 years of age who have not completed a primary course of 3 doses of diphtheria, tetanus, pertussis and polio-containing vaccine should complete their primary course with a DTaP/IPV/Hib/HepB-containing vaccine as this is now the only suitable vaccine containing high dose tetanus, diphtheria and pertussis antigen for priming children of this age. Children born from 1 August 2017 who received primary vaccines without HepB (for example if given a quadrivalent or pentavalent priming vaccine), should be opportunistically offered a 3 dose course of monovalent HepB vaccine. If they are in a high-risk group or are exposed to hepatitis B, they should be proactively offered a hepatitis B vaccine course.

Immunisers should ensure that all high risk children have received at least 4 doses of a hepatitis B-containing vaccine (either monovalent or as part of a combined DTaP/IPV/Hib/HepB vaccine) at 0, 1, 2 and 12 months (or similar if they have fallen behind with the schedule or received additional doses). They should also have had a blood test at 12 months of age to check whether they acquired infection. If any high risk children have not been tested at 12 months of age, the test can be carried out as soon as it is realised it has not been done previously.

Contraindications for receiving Infanrix hexa® or Vaxelis®

There are very few individuals who cannot receive the hexavalent vaccines. Where there is doubt, instead of withholding immunisation, appropriate advice should be sought from a consultant with immunisation expertise, a member of the screening and immunisation team or from the local health protection team.

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

- a confirmed anaphylactic reaction to a previous dose of the vaccine or
- a confirmed anaphylactic reaction to any component of the vaccine (this includes formaldehyde, neomycin and polymyxin)

Precautions to Infanrix hexa® or Vaxelis®

If an infant has a minor illness without fever or systemic upset, immunisations can still be given. If the infant is acutely unwell (for example with a fever above 38.5^{0}C), immunisation may be postponed until they have fully recovered. This is to avoid wrongly attributing any new symptom or the progression of symptoms to the vaccine.

The presence of a neurological condition is not a contraindication to immunisation but if there is evidence of current neurological deterioration, deferral of the DTaP/IPV/Hib/HepB vaccine may be considered to avoid incorrect attribution of any change in the underlying condition. The risk of such deferral should be balanced against the risk of the preventable infection and vaccination should be promptly given once the diagnosis and/or the expected course of the condition becomes clear.

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-hyporesponsive episodes (HHE)
- persistent crying or screaming for more than 3 hours, or
- severe local reaction, irrespective of extent

can continue to receive subsequent doses of DTaP/IPV/Hib/HepB vaccine. Seek further advice if required.

Very premature infants (born less than or equal to 28 weeks of gestation) who are in hospital should have respiratory monitoring for 48 to 72 hrs when given their first immunisation (see section on premature infants above).

Vaccine composition

Composition of Infanrix hexa® vaccine

As well as the diphtheria, tetanus, pertussis, polio, Hib and Hepatitis B antigens, Infanrix hexa® vaccine also contains the following.

The vial containing Hib powder also contains:

- lactose anhydrous

The pre-filled syringe containing the DTaP/IPV/HepB suspension also contains:

- sodium chloride
- medium 199 containing principally amino acids, mineral salts, vitamins
- water for injections

The vaccine contains the following adjuvants (substances added to enhance the immune response to the antigens):

- aluminium hydroxide, hydrated
- aluminium phosphate

The hepatitis B surface antigen component of the vaccine is produced in yeast cells (Saccharomyces cerevisiae) by recombinant DNA technology.

The vaccine may also contain traces of formaldehyde, neomycin and polymyxin which are used during the manufacturing process for inactivation and prevention of bacterial growth.

Infanrix hexa® does not contain any thiomersal or porcine gelatine.

A full list of vaccine excipients can be found in the Infanrix hexa vaccine SPC.

Composition of Vaxelis® vaccine

The prefilled syringe contains diphtheria, tetanus, pertussis, polio, Hib and Hepatitis B antigens, the vaccine also contains the following.

The Vaxelis® vaccine contains the following adjuvants (substances added to enhance the immune response to the antigens):

- amorphous aluminium hydroxyphosphate sulfate
- aluminium phosphate

The hepatitis B surface antigen component of the vaccine is produced in yeast cells (Saccharomyces cerevisiae) by recombinant DNA technology.

The vaccine may contain traces of glutaraldehyde, formaldehyde, neomycin, streptomycin, polymyxin B, and bovine serum albumin which are used during the manufacturing process Vaxelis® does not contain any thiomersal or porcine gelatine

A full list of vaccine excipients can be found in the Vaxelis® SPC.

Vaccine ordering

Infanrix hexa® and Vaxelis® should be ordered via the Immform website. Healthcare practitioners should refer to this website and Vaccine update (the vaccination newsletter for healthcare practitioners) for up to date information on vaccine availability. As the programme is a year-round programme and not a seasonal programme, vaccines should be ordered regularly throughout the year.

Healthcare practitioners are reminded to only order what they need for a 2 to 4 week period rather than over-ordering or stockpiling vaccines. Vaccines should be ordered, stored and monitored as described in the Green Book, chapter 3 (storage, distribution and disposal of vaccines).

Vaccine storage and administration

Storage of Infanrix hexa® and Vaxelis®

Infanrix hexa® and Vaxelis® should be stored in a vaccine refrigerator between +2°C and +8°C. The vaccines should be stored in the original packaging to protect them from light to ensure that the component parts are kept together and in order to retain the batch number and expiry date for the entire product which is printed on the outer vaccine carton. The vaccines should not be frozen.

Further information on vaccine storage is available in the Vaxelis® SPC and Infanrix hexa® SPC, the Patient Group Direction (PGD) and from the manufacturer.

Effectiveness cannot be guaranteed for vaccines unless they have been stored at the correct temperature. Those responsible for the ordering, storage and use of vaccines should be familiar with the recommendations in the Green Book, chapter 3. Vaccines should not be over-ordered or stockpiled.

Stability of Infanrix hexa®

In the event of an inadvertent or temporary temperature excursion outside of the recommended +2°C to +8°C range, stability data detailed in the Summary of Product Characteristics indicate that the vaccine components are stable at temperatures up to 25°C for 72 hours. At the end of this period Infanrix hexa® should be used or discarded.

Stability of Vaxelis®

In the event of an inadvertent or temporary temperature excursion outside of the recommended +2°C to +8°C range, stability data detailed in the Summary of Product Characteristics indicate that the vaccine is stable at temperatures up to 25°C for 228 hours. At the end of this period Vaxelis® should be used or discarded.

For both vaccines, breaches in the cold chain should be reported to the Screening and Immunisation Team in line with local arrangements. This data is intended to guide healthcare professionals in case of a temporary temperature excursion only.

Infanrix hexa® presentation

The vaccine is presented in 2 parts: a vial containing the freeze dried Hib component and a pre-filled syringe containing the DTaP/IPV/HepB components in a suspension.

It is very important that the freeze-dried Hib component is reconstituted correctly before administration or the child will not receive protection against this disease.

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

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

The Infanrix hexa® vaccine is supplied in single dose packs containing the syringe and vial.

When required for use, the pre-filled syringe should be shaken well in order to obtain a homogeneous turbid white suspension.

The vaccine is reconstituted by adding the entire contents of the pre-filled syringe to the vial containing the powder. The mixture should be well shaken until the powder is completely dissolved prior to administration.

The reconstituted vaccine appears as a slightly cloudier suspension than the liquid component alone. This is a normal observation.

After reconstitution, it is recommended that the vaccine is used immediately.

Full instructions for vaccine preparation are available in the SPC.

Vaxelis® presentation

The DTaP/IPV/HepB/Hib component is presented as a uniform, cloudy, white to off-white suspension in a pre-filled glass syringe.

Prior to administration, the pre-filled syringe should be shaken gently in order to obtain a homogeneous, whitish, cloudy suspension.

The suspension should be visually inspected, prior to administration, for foreign particulate matter and/or variation of physical appearance. If either is observed, discard the pre-filled syringe.

Administration

Infanrix hexa® and Vaxelis® should be administered intramuscularly.

The preferred site of injection for infants under one year of age is the anterolateral aspect of the thigh. With the change to the infant PCV schedule meaning that only 2 injections need to be given at each primary vaccine appointment, one injection can be given into each thigh. Should it be necessary to give more than one vaccine into the same limb, they should be given at least 2.5cm apart and the site at which each vaccine was given should be noted in the infant's records.

Post-immunisation care recommendations

Immunisers should recommend that prophylactic paracetamol is given when MenB vaccine is given at the same appointment as the DTaP/IPV/Hib/HepB vaccine.

For further information about administration of paracetamol, please see MenB vaccine and paracetamol webpage and the 'What to expect after vaccinations' leaflet.

Selective neonatal immunisation programme for babies at risk of hepatitis B

Why the selective neonatal immunisation programme is continuing now all infants receive hepatitis B vaccine as part of the routine childhood programme

Hepatitis B infection can be transmitted from infected mothers to their babies at or around the time of birth (perinatal transmission). This occurs mainly because infected blood from the mother passes through the placenta to the baby during delivery. Babies acquiring infection at this time have a high risk of becoming chronically infected with the virus. The development of chronic infection in infants born to infected mothers after perinatal transmission can be prevented in over 90% of cases by appropriate post-exposure prophylactic vaccination starting at birth. Timely vaccination at birth and at 4 weeks of age is critical to preventing infection in the infant.

The universal infant programme provides pre-exposure protection against hepatitis B virus which will benefit those who may have future risk of exposure to it. The dose that is given to all babies at 8 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.

Why Hepatitis B immunoglobulin (HBIG) is still required

Babies born to highly infectious mothers should continue to receive HBIG as well as vaccine at birth (see Green Book Hepatitis B chapter). HBIG provides ready-made hepatitis B-specific antibodies and gives some immediate protection until the hepatitis B vaccine, which should be given at the same time, becomes effective. Giving HBIG concurrently with hepatitis B vaccine does not affect the development of active immunity to the vaccine. HBIG should be given in a different site to the vaccine.

HBIG should be given as soon as possible, preferably within 48 hours of delivery (and within 24 hours of birth dose of vaccine), although it should still be considered up to a week after exposure.

What the newborn infant should receive if the mother is hepatitis B negative, but there is another person living in the household who is infected with hepatitis B

Newborn infants born to a hepatitis B negative woman but known to be going home to a household with another hepatitis B infected person may be at immediate risk of hepatitis B infection. In these situations, a monovalent dose of hepatitis B vaccine should be offered

before discharge from hospital. They should then continue on the routine childhood schedule commencing at 8 weeks.

How to explain the reason for giving 6 doses of hepatitis B vaccine to high risk infants

The JCVI considered the various different options for vaccinating high risk infants following the introduction of the hexavalent hepatitis B-containing vaccine into the routine immunisation schedule for all infants. It was agreed that having 2 different vaccines being used in the infant programme (a pentavalent without HepB for high risk infants and a hexavalent vaccine for all other infants) would be confusing and securing a continuous supply of the small amount of pentavalent vaccine would be difficult. Therefore, JCVI concluded that it is better to recommend that all high risk infants receive additional doses of hepatitis B vaccine in the hexavalent vaccine. Hepatitis B vaccine is well tolerated and additional doses should not be harmful.

How to manage a high risk infant who misses their 4 week dose of hepatitis B vaccine and then receives hexavalent vaccine at 8, 12 and 16 weeks

The key to giving optimal protection is the timing of the early doses. The doses given at birth, 4 and 8 weeks old should stimulate immunity in time to prevent the hepatitis B virus replicating to high levels. The doses normally given at 12 and 16 weeks, and the booster at one year of age, will help to provide longer term protection and boosting. Where an early dose (for example at 4 weeks) is missed or delayed, this may increase the risk of the child becoming infected but cannot be reversed by adding additional doses later. In the situation described above, it is very important that the child is tested at 12 months of age to check whether they were infected early in life as they missed an early dose of vaccine. The best approach to preventing these infants becoming hepatitis B positive is to ensure all scheduled doses of a hepatitis B-containing vaccine are given on time.

What to do if a high risk infant attends late for their first or second dose of monovalent hepatitis B vaccine but before 6 weeks of age

The infant should receive a dose of monovalent hepatitis B vaccine as early doses of vaccine are of critical importance in preventing maternally-acquired hepatitis B infection. The first primary dose of hexavalent DTaP/IPV/Hib/HepB vaccine, rotavirus vaccine and MenB vaccine should then be scheduled routinely at 8 weeks of age, irrespective of the timing of the late monovalent hepatitis B vaccine dose, in order not to delay protection against the other infections. A shorter interval between doses of hepatitis B vaccine in this situation is unlikely to be detrimental to the infant's overall protection against HBV. In the situation described above, it is very important that the child is tested at 12 months of age to check whether they were infected early in life as an early dose of vaccine was given late.

What to do if a high risk infant attends late for their first or second dose of monovalent hepatitis B vaccine after 6 weeks of age

Infanrix hexa® and Vaxelis® are approved for use from 6 weeks of age and studies have shown that infants respond effectively to DTP-containing vaccines at this age. The hexavalent vaccines should therefore be given to infants in this situation to provide rapid protection against hepatitis B. Rotavirus and MenB vaccines should also be given at the same time. The second and third doses of the hexavalent vaccines should then be given at 4 week intervals and the booster dose of hepatitis B at one year of age. In the situation described above, it is very important that the child is tested (at 12 months of age) to check whether they were infected early in life as they missed an early dose of vaccine. The second dose of rotavirus vaccine should be given 4 weeks after the first (with the second dose of hexavalent vaccine). The second dose of MenB vaccine should be given 8 weeks after the first dose (with the third dose of hexavalent vaccine). A single priming dose of PCV should be given from 12 weeks of age.

All booster doses should be given as per the schedule at one year of age.

NB MenB administration before 8 weeks of age is off label. Patient Group Directions (PGDs) should be checked as to whether they cover administration of routine vaccinations before 8 weeks of age – a Patient Specific Direction (PSD) may be required.

Routine infant immunisation programme – booster and catch-up doses

No HepB catch up programme for babies born before 1 August 2017

When any new vaccine programme is introduced, there always has to be a cut-off for eligibility. The incidence of hepatitis B is currently low in children and by vaccinating all infants born on or after 1 August 2017, this will ultimately help to keep the incidence of HBV low in the population as a whole. Any individuals born before 1 August 2017, will, as always, be eligible for hepatitis B vaccine if they are identified as being at increased risk of HBV.

Infants following the routine programme, receiving the hexavalent hepatitis B-containing vaccine do not need a booster dose of hepatitis B vaccine

For infants who have completed a primary course of vaccination, a routine booster dose of HepB vaccine is not required (except for high risk infants who should receive an additional dose of monovalent Hepatitis B vaccine at 12 months of age).

The full duration of protection afforded by hepatitis B vaccine is expected to be greater than 20 years. Even though levels of vaccine-induced antibody to hepatitis B decline over time, there is evidence that immune memory persists in those successfully immunised. If they are exposed later in life, this immune memory will help to protect them against serious disease and chronic infection. If there is a significant exposure to an unknown or known hepatitis B surface antigen (HBsAg) positive source however, a booster dose of vaccine may be indicated. See Green Book Hepatitis B chapter 18.

For those who may become at risk of infection later in life, for example if they become health care workers, additional doses of vaccine and/or antibody testing may be required. Check the Green Book Hepatitis B chapter.

Immunisation programme for neonatal selective babies at risk of hepatitis B – booster doses and blood tests

Why high risk children require a blood test at 12 months

Although the hepatitis B vaccine is highly effective at preventing infection if given at birth, a few infants may still acquire infection despite vaccination and HBIG.

Infants with hepatitis B infection are usually asymptomatic and do not display any signs of infection so testing infants at 12 months of age (when they attend for their booster dose) is important to enable a timely assessment of their infection status. Finding out if the infant is infected at this point allows for prompt referral to specialist care to reduce the risk of long term complications in later life. Additionally, if the infant's blood test is negative, parents can be reassured that transmission has been avoided and no further action is required.

The purpose of the 12 month blood test is to check for infection, not to check or measure response to the vaccine in the way that a healthcare worker's response is checked. Numerous studies have already demonstrated that the vast majority of infants who do not become infected make a protective response to a course of hepatitis B vaccine given in the first year of life. See the document 'Rationale for not requiring high anti-HBs levels in infants born to HBsAg positive mothers' for further information.

Why some babies acquire hepatitis B infection despite vaccination and HBIG

If infection has already become established before the full response to immunisation is made, virus replication may not be inhibited completely by HBIG or vaccine. This is why it is important that the child is tested at one year of age.

However, severe illness and, most importantly, development of the chronic, persistently infected state which can lead to serious liver disease and liver cancer, may still be prevented by immunisation.

Why immunocompetent, fully vaccinated, high risk children no longer require a pre-school booster dose of hepatitis B vaccine

Increasing evidence has now shown that protection from hepatitis B vaccine is long-lasting and studies demonstrate that, among successfully vaccinated immunocompetent individuals, protection against chronic infection persists for 20 to 30 years or more. The World Health Organization (WHO) has concluded from this that there is no compelling evidence for recommending a booster dose of hepatitis B vaccine in routine immunisation programmes.

A further dose of hepatitis B-containing vaccine at 3 years and 4 months is no longer recommended for high risk children who have either completed their routine primary immunisations with the hexavalent hepatitis B-containing vaccine or who received pentavalent DTaP/IPV/Hib vaccine, but who have completed a monovalent hepatitis B post exposure course and been tested for infection.

Immunisation providers are reminded however, to use the opportunity of the pre-school booster appointment (for MMR and dTaP/IPV vaccinations), to check that high risk children have received all of the required doses and been tested for Hepatitis B surface antigen (HBsAg) to exclude infection. A high risk child who has missed a dose of hepatitis B in infancy could be offered a dose of the hexavalent vaccine instead of the routine pre-school booster vaccine.

Potential vaccine errors

What you should do if a dose of the hexavalent vaccine is given at an interval of less than 4 weeks in error

A minimum 4 week interval is recommended between each of the 3 doses of hexavalent vaccine in the primary schedule. If one of these doses is given up to a week early, either inadvertently or deliberately, for example for travel reasons, then this can be counted as a valid dose and does not need to be repeated. However, no more than one dose should be given early in the 3 dose schedule and any doses given at less than a 3 week interval should be repeated 4 weeks after the final dose.

Actions to take if the immuniser forgets to reconstitute the Hib component of the Infanrix hexa® vaccine and only administers the DTaP/IPV/HepB component

A dose of the combined Hib/MenC vaccine (Menitorix) should be given either at the same visit or as soon as possible after the error is realised in order to provide protection against Hib.

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.

What to do if the hexavalent vaccine is inadvertently given as a pre-school booster vaccine

If either of the hexavalent vaccines are inadvertently given to children as a pre-school booster instead of the recommended dTaP/IPV vaccine, they will not require a dose of the correct vaccine to be given afterwards as the hexavalent vaccine will still boost their

antibodies against diphtheria, tetanus, pertussis and polio as the recommended pre-school booster vaccine would have done. They may be at increased risk from an adverse reaction since the antigen dose is higher in the hexavalent vaccines than in the quadrivalent pre-school vaccine.

Addressing parental concerns

What to say to a parent or carer who is concerned about receiving a vaccine containing 6 components

It is acknowledged that some parents or carers may be concerned that their child is receiving a 6 component combination vaccine. Whilst these concerns are understandable, parents or carers should be reassured that there is no evidence to support arguments of 'overloading' the immune system. From the moment a child is born, they are continually being exposed to a huge number of bacteria and viruses on a daily basis. From birth, their immune system is able to respond to both the many antigens in the environment and the relatively small number of selected antigens in vaccines.

Additionally, before a combined vaccine is licensed for use, it must have demonstrated in pre-licensure studies that a satisfactory immune response is made to each of the combined antigens and that the rates of adverse reactions are lower or the same as they would be if the vaccines were administered separately.

What to do if a parent or carer does not want to receive a vaccine containing hepatitis B

Healthcare professionals should ascertain what the parent or carer's specific concerns about the hepatitis B vaccine are and address these. They should also provide them with information as to the benefits of receiving it.

There is now no alternative vaccine with which to adequately protect infants and young children against diphtheria, tetanus, polio, pertussis and Hib disease. The vaccines that are licensed for pre-school boosters contain lower levels of antigens and are therefore only suitable for boosting children who have already received infant priming vaccinations.

Other issues

Protection against whooping cough from 3 component acellular pertussis (3aP) vaccines compared to 5 component (5aP) vaccines

Between 2004 and 2008, the UK only used infant acellular pertussis vaccines that contained 5 components to ensure optimal protection against whooping cough. UK follow up of children who had received a 3aP vaccine suggested, however, that protection was equivalent to 5aP vaccines to pre-school age.

In 2008, JCVI advised that a 3aP combination vaccine could be used for primary immunisation. In 2010, the WHO also reviewed all the global data on pertussis control in countries using acellular vaccines. They concluded that acellular pertussis vaccines with 3 or more components have higher protective efficacy than vaccines with fewer components and did not find consistent evidence of a difference between 3 and 5 components. A 3aP component vaccine (Infanrix®-IPV+Hib), similar to Infanrix hexa®, has now been used widely in the UK since 2014.

About the UK Health Security Agency

UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation's health secure.

UKHSA is an executive agency, sponsored by the Department of Health and Social Care.

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