INFORMATION FOR HEALTHCARE PRACTITIONERS

about the **neonatal selective immunisation programme** for babies at risk of hepatitis B

ISLE OF MAN VACCINATION PROGRAMME - AUTUMN 2017

HEALTH PROTECTION

The hexavalent DTaP/IPV/Hib/HepB combination vaccine

Isle of Man Government

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HEALTH PROTECTION

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BACKGROUND

From **Autumn 2017**, all babies born on or after **1 August 2017** will become eligible for a hexavalent vaccine which includes hepatitis B (HepB) for their primary immunisations. This vaccine, called Infanrix hexa®, will replace the pentavalent infant vaccines Infanrix®-IPV+Hib and Pediacel®. Whilst this should benefit infants at increased risk of hepatitis B (e.g. those born to an infected mother) as they are more likely to complete the full course of hepatitis B, these babies still require the critical early doses at birth and one month of age. Healthcare professionals administering the programme may mistakenly assume that these doses are no longer needed or find the schedule for high risk infants confusing or complicated.

The following questions and answers are intended to provide healthcare professionals with more information about vaccinating high risk infants in light of the new universal hepatitis B infant programme. Answers to more general questions about the hexavalent vaccine may be found in ***'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'*** document Ref: IMM48 0817.

What is the selective neonatal hepatitis B immunisation programme?

All pregnant women should be offered screening for infection with hepatitis B 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 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 four weeks of age. Up until now, they received further doses at eight weeks of age and twelve months of age and a dose with their pre-school booster vaccines.

Why is the selective neonatal immunisation programme continuing if all infants are going to 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 four 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 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.

Will Hepatitis B immunoglobulin (HBIG) still be required?

Yes. 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.

Does the Infanrix hexa® vaccine provide the same protection as giving the pentavalent DTaP/IPV/Hib vaccine with a monovalent hepatitis B vaccine?

Large clinical studies have shown that Infanrix hexa® produces a strong immune response against all the antigens contained in it in infants who have received a dose of hepatitis B vaccine at birth[1] (Dhillon, 2010).

These studies have also shown that infants who received monovalent hepatitis B vaccines at birth followed by a three dose course of the Infanrix hexa® vaccine achieve the same protection against hepatitis B as those who received the pentavalent DTaP/IPV/Hib vaccine with a monovalent HepB vaccine.

VACCINE SCHEDULING

What is the vaccine schedule for high risk infants?

High risk infants should receive monovalent hepatitis B vaccine at birth and 4 weeks of age and then three doses of Infanrix hexa® 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 one: Hepatitis B doses in the immunisation schedule for routine childhood and selective neonatal hepatitis B programme

Age		Routine childhood programme		Babies born to hepatitis B infected mothers
Birth	✗ *		✓	Monovalent HepB (Engerix B® or HBvaxPRO Paediatric®) (with HBIG if indicated)
4 weeks	✗		✓	Monovalent HepB (Engerix B® or HBvaxPRO Paediatric®)
8 weeks	✓	DTaP/IPV/Hib/HepB (Infanrix hexa®)	✓	DTaP/IPV/Hib/HepB (Infanrix hexa®)
12 weeks	✓	DTaP/IPV/Hib/HepB (Infanrix hexa®)	✓	DTaP/IPV/Hib/HepB (Infanrix hexa®)
16 weeks	✓	DTaP/IPV/Hib/HepB (Infanrix hexa®)	✓	DTaP/IPV/Hib/HepB (Infanrix hexa®)
1 year	✗		✓	Monovalent HepB (Engerix B® or HBvaxPRO Paediatric®) Test for HBsAg

* *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 eight 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 the table above) reduced the risk of missing doses.

Is it safe for high risk infants to receive a total of six doses when they previously only received four doses in infancy?

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 two different vaccines being used in the infant programme (pentavalent and hexavalent) 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.

If a high risk infant misses their 4 week dose of hepatitis B vaccine and then receives hexavalent vaccine at 8, 12 and 16 weeks, is a further dose of hepatitis B vaccine indicated?

No. 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 (e.g. 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 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 do you do if a high risk infant attends late for their first or second dose of monovalent hepatitis B vaccine but before six 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 Infanrix hexa® dose, rotavirus, PCV and MenB vaccines 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 to check whether they were infected early in life as they missed an early dose of vaccine.

What do you do if a high risk infant attends late for their first or second dose of monovalent hepatitis B vaccine after 6 weeks of age? Do you give monovalent vaccine or a dose of Infanrix hexa® early?

Infanrix hexa® is approved for use from six weeks of age and studies have shown that infants respond effectively to DTP-containing vaccines at this age. Infanrix hexa® should therefore be given to infants in this situation to provide rapid protection against hepatitis B. Rotavirus, MenB and PCV vaccines should also be given at the same time. The second and third doses of Infanrix

hexa® should then be given at four week intervals and the booster of hepatitis B at one year of age. In the situation described above, it is very important that the child is tested 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 Infanrix hexa®). The second doses of PCV and MenB vaccine should be given 8 weeks after the first doses (with the third dose of Infanrix hexa®).

Note: MenB administration before 8 weeks of age is off-label. Patient Group Directions (PGDs) if used 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.

What should be done if the pentavalent DTaP/IPV/Hib vaccine is given in error to a high risk infant who should have received hepatitis B-containing hexavalent DTaP/IPV/Hib/HepB vaccine?

If a child at high risk of hepatitis B inadvertently receives the pentavalent vaccine at 8 weeks of age, they should be urgently offered a monovalent hepatitis B vaccine. No additional vaccination is required if the same error occurs at the 12 or 16 week dose appointment.

Should high risk infants born before August 2017 transfer onto the new schedule?

No. Infants born before August 2017 should continue to receive the monovalent hepatitis B vaccine as per the previous 0, 1, 2, 12 month schedule with a blood test at 12 months to check whether they acquired infection. If any babies have not yet received their 2 month/8 week dose of hepatitis B however, this can be offered as Infanrix hexa®.

What should be given to other infants at risk of exposure to hepatitis B, for example those born into a family where there is a household contact (other than the mother) who is hepatitis B positive?

Infants born to a hepatitis B negative mother but known to be going home to a household with another hepatitis B infected person may be at risk of hepatitis B infection. Whilst the risk of transmission to these infants is lower than for infants born to infected mothers who have already been exposed at birth, these infants should be given pre-exposure immunisation. Where there is an immediate risk of exposure, a monovalent dose of hepatitis B should be offered as soon as possible after birth. They can then continue to receive the routine doses of hexavalent vaccine at 8, 12 and 16 weeks old so that they receive a total of four doses of a hepatitis B containing vaccine. They do not require a dose at 4 weeks of age or a booster at 12 months of age. Other infants, who are not at immediate risk, can be vaccinated routinely at 8, 12 and 16 weeks of age.

Infants who do not receive this dose at birth should receive it as soon as the need for it is realised. A risk assessment should be carried out as to the potential that the infant has been infected prior to this dose being given and therefore the need to test for infection at 12 months of age. If the infant is less than six weeks of age when the need for protection against hepatitis B in this situation is realised, they should be given a dose of monovalent hepatitis B vaccine. Doses of Infanrix hexa® should then be given as per the infant schedule at 8, 12 and 16 weeks, irrespective

of the timing of the late monovalent hepatitis B vaccine dose, in order not to delay protection against the other infections. If it is only realised that the infant needs protection against hepatitis B after they are six weeks of age, instead of giving monovalent hepatitis B vaccine, they should start their infant immunisation schedule early and receive their first dose of Infanrix hexa® along with their first dose of rotavirus, MenB and PCV vaccines.

BOOSTER DOSES AND BLOOD TESTS

Why do high risk children still require a blood test a 12 months if they are receiving six doses of hepatitis B vaccine?

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 given in the first year of life. See Public Health England's document 'Rationale for not requiring high anti- HBs levels in infants born to HBsAg positive mothers' - for further information.

Why do 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 do high risk children who receive Infanrix hexa® 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 20-30 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[2] (WHO, 2017).

Booster doses are only recommended for:

- healthcare workers, including students and trainees, who should be offered a single booster dose of vaccine, once only, around five years after primary immunisation
- patients with renal failure
- at the time of a subsequent significant exposure

When is the pre-school hepatitis B booster dose for high risk children going to be dropped from the schedule?

A further dose of hepatitis B-containing vaccine at 3 years and 4 months will no longer be recommended for those children who have completed their routine primary immunisations with the hexavalent hepatitis B-containing vaccine.

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

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2 World Health Organization (2017) Global Hepatitis Report 2017, Global Hepatitis Programme.
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OTHER USEFUL LINKS

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Further information

To find out more visit our website at

www.gov.im/vaccinations

The information in this leaflet can be provided in large format or in audio format on request

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