

Understanding hepatitis B vaccine for travel health

In the UK we have two brands of hepatitis B vaccine (Engerix B and HBvaxPRO) and each have an adult and paediatric formulation. Each also have an extra strength vaccine (Fendrix and HBvaxPRO40), which we don't use in travel health. Engerix B and Fendrix are GlaxoSmithKline vaccines and the HBvaxPRO range are Sanofi Pasteur MSD vaccines. These vaccines are all inactivated, do not contain live organisms and cannot cause hepatitis B disease.

The values of the content of the two hepatitis B vaccine is to do with the manufacturing process and as long as you use the right age-specific vaccine this is what is important. It is always ideal to complete a course of vaccine with the brand you started, but if this isn't feasible then the hepatitis B vaccines are interchangeable.

The table below indicates the dose and volume of the four hepatitis B vaccine presentations

Name of vaccine	Age group used in	Dose	Volume
Engerix B®	0 – 15 years	10 µg	0.5 ml
Engerix B®	16 years and over	20 µg	1.0 ml
HBvaxPRO Paediatric®	0-15 years	5 µg	0.5 ml
HBvaxPRO®	16 years and over	10 µg	1.0 ml

Schedules of courses of hepatitis B vaccine - there are a number of different courses

Paediatric vaccines: both vaccines have a choice of the same two courses and Engerix B has a third option:

Engerix B® 10 µg		HBvaxPRO Paediatric 5 µg	
1.	0, 1, 2 and 12 months (This schedule is given to babies born to hepatitis B positive mothers. The mother is screened ante-natally and when the baby is born, the course begins - the first dose is given within 24 hours of birth. Full details of this are found on page 173 of the Green Book). If giving for travel, then a 0,1 and 2 month schedule is indicated with only those at continued risk being given a 4 th dose at 12 months	1.	0, 1, 2 and 12 months (This schedule is given to babies born to hepatitis B positive mothers. The mother is screened ante-natally and when the baby is born, the course begins - the first dose is given within 24 hours of birth. Full details of this are found on page 173 of the Green Book). If giving for travel, then a 0, 1 and 2 month schedule is indicated with only those at continued risk being given a 4 th dose at 12 months
2.	0, 1 and 6 months	2.	0, 1 and 6 months
3.	Engerix B (20µg dose) can also be given to children aged 11-15 years in a two dose schedule at 0 and 6-12 months schedule		

Adult schedules: both vaccines have a choice of two courses and Engerix B has a third option:

Engerix B® 20 µg		HBvaxPRO 10 µg	
1.	0, 1, 2 months	1.	0, 1, 2 months
2.	0, 1 and 6 months	2.	0, 1 and 6 months
3.	0, 7 and 21 days with a 4th reinforcing dose at 12 months – licenced for 18 years and over. However , the Green Book states that where it is important to provide rapid protection and to maximise compliance, although not licenced, this schedule can also be used in the 16-18 year old age group. (see page 177 of the Green Book).		

Which schedule should you follow?

This is dependent on how high the risk may be and what the likelihood of compliance is. Some of the regimens described in the Green Book are addressing those patients who may be at higher risk as detailed in the 'Recommendations for the use of vaccine' categories. There are few circumstances related to a 'travel' situation.

*The Green Book states that for pre-exposure prophylaxis in most adults and childhood risk groups, an accelerated schedule should be used, with vaccine given at zero, one and two months. For those who are at continued risk, a fourth dose is recommended at 12 months. An alternative schedule of zero, one and six months should only be used where rapid protection is not required and there is a high likelihood of compliance. Higher completion rates are achieved with the accelerated schedule (at 0, 1, 2 months) in groups where compliance is difficult (e.g. IDUs and GUM clinic attenders). This improved compliance is likely to offset the slightly reduced immunogenicity when compared to the 0, 1 and 6 month schedule and similar response rates can be achieved by use of a fourth dose after 12 months.

The Green Book also address use of Engerix B using the rapid schedule with three doses given at zero, seven and 21 days and recommends a fourth dose being given 12 months after the first dose. It describes using it in a situation where adults over 18 years of age are at immediate risk and a more rapid induction of protection is required. This also includes travellers to areas of high endemicity.

The following table of seroprotection rates was taken from the Summary of Product Characteristics for Engerix B – see the EMC at

http://www.medicines.org.uk/emc/medicine/9283#PHARMACODYNAMIC_PROPS

The table below summarizes seroprotection rates (i.e. percentages of subjects with anti-HBs antibody concentrations ≥ 10 IU/l) obtained in clinical studies with Engerix B 20 μ g, given according to the different schedules mentioned in Section 4.2:

Population	Schedule	Seroprotection rate
Healthy subjects 16 years of age and above	0, 1, 6 months	at month 7: ≥ 96 %
	0, 1, 2 – 12 months	at month 1: 15 % at month 3: 89 % at month 13: 95.8 %
Healthy subjects 18 years of age and above	0, 7, 21 days – 12 months	at day 28: 65.2 % at month 2: 76 % at month 13: 98.6 %
Patients with renal insufficiency including patients undergoing haemodialysis 16 years of age and above	0, 1, 2, 6 months (2 x 20 μ g)	at month 3: 55.4 % at month 7: 87.1 %

The data in the above table were generated with thiomersal containing vaccines. Two additional clinical studies conducted with the current formulation of Engerix B, which contains no thiomersal, among healthy infants and adults, elicit similar seroprotection rates as compared to former thiomersal containing formulations of Engerix B.

The table above indicates that with a 0, 1 and 2 month schedule for Engerix B there would also be a fourth dose at 12 months. However, note the paragraph stated above at * where this fourth dose would only be given to those at continued risk. In this situation, one would follow the advice from the Green Book – see chapter 4 page 25, first paragraph where it indicates recommendations in the Green book would override the SPC. <https://www.gov.uk/government/publications/immunisation-procedures-the-green-book-chapter-4>

Hepatitis B protection is also available in the combination hepatitis A+B vaccines

The table below indicates the dose and volume of the four hepatitis B vaccine presentations

Name of vaccine	Age group used in	Dose HAV	Dose HBV	Volume
Twinrix Adult®	16 years and over	720 ELISA units	20 µg	1.0 ml
Twinrix Paediatric®	1 – 15 years	360 ELISA units	10 µg	0.5 ml
Ambirix®	1 – 15 years	720 ELISA un	20 µg	1.0 ml

Note:

HAV = hepatitis A virus

HBV = hepatitis B virus

Havrix monodose contains 1440 ELISA units

Havrix Junior monodose contains 720 ELISA units

The combination A+B vaccines have the following schedules

Twinrix Adult®		Twinrix Paediatric®		Ambirix®	
1.	0, 1 and 6 months (16 years and over)	1.	0, 1 and 6 months (1 – 15 years)	1.	0 and 6-12 months (1 – 15 years)
2.	0, 7, 21 days and 4th dose at 12 months (18 years and over)				

The Green Book states that Twinrix Adult® given at zero, seven and 21 days will provide more rapid protection against hepatitis B than other schedules but full protections against hepatitis A will be provided later that with vaccines containing a higher dose of hepatitis A. When using this schedule, a fourth dose is recommended 12 months after the first dose.

PLEASE NOTE: Twinrix Adult® and Twinrix Paediatric® vaccines contain half the amount of hepatitis A protection and therefore **before travel it is essential to give two doses** to ensure full hepatitis A protection is given. If there is insufficient time to get the two doses in, then monovalent hepatitis A and Hepatitis B vaccines need to be administered instead.

Many errors occur in regard to the combined hepatitis A and B vaccines. Once the content and schedules are understood, there is nothing particularly difficult about their use. Follow these additional guidelines as well to ensure mistakes aren't made:

1. **If you start a course of hep A and hep B protection using either Twinrix Adult® or Twinrix Paediatric® vaccines then COMPLETE the course using these vaccines.**
2. **If you start a course of hep A and B protection using monovalent hep A and hep B vaccines, then you cannot use a combined hep A and hep B vaccine to complete the course.** (this is all because of the content value of hepatitis A).

Length of protection for travellers

For hepatitis B - at the current time, according to the Green Book, it is recommended that travellers who have completed the primary course of vaccination, a booster at 5 years is no longer recommended unless they are considered to be at continuing risk of infection. Measurement of anti-HBs levels is not required either before or after this dose.

For hepatitis A – in the combination hep A + B vaccines, protection on the hepatitis A would be expected for 25 years from the completing dose of the initial course.

Who should be offered pre exposure hepatitis B?

The following list is from the Green Book, chapter 18, pages 168 – 175

- Injecting drug users
- Individuals who change sexual partners frequently
- Close family contacts of a case or individual with chronic hepatitis B infection
- Foster carers
- Individuals receiving regular blood or blood products and their carers
- Patients with chronic renal failure
- Patients with chronic liver disease
- Inmates of custodial institutions
- Individuals in residential accommodation for those with learning difficulties
- People travelling to or going to reside in areas of high or intermediate prevalence
- Individuals at occupational risk
- Healthcare workers in the UK and overseas (including students and trainees)
- Laboratory staff
- Staff of residential and other accommodation for those with learning difficulties
- Other occupational risk groups such as morticians and embalmers

Occupational Health Hepatitis B

This is not part of travel health but the question is often raised.

Information about occupational health and the provision or not within an NHS setting is found at

<https://www.bma.org.uk/advice/employment/gp-practices/hepatitis-b-immunisations>

make sure you scroll right down to the bottom of the page.

For details from the 'Green Book' regarding 'response to vaccine and use of additional doses, see page 178 at

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/263311/Green_Book_Chapter_18_v2_0.pdf

Please note this is an abbreviated summary of information from the Green Book to help you understand the issues of hepatitis B vaccine administration in relation to travel. You will need to review further information in the future to check whether or not guidelines have changed. This information was correct at the time of writing.

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