



UPDATED ATAGI CLINICAL ADVICE REGARDING ALTERNATIVES DURING SUPPLY SHORTAGE OF THE ADULT FORMULATIONS OF HEPATITIS B VACCINES

It is important to read this statement in conjunction with the current online version of The Australian Immunisation Handbook available on the [Immunise Australia](http://www.immunise.health.gov.au) website (www.immunise.health.gov.au).

The substitute options that the Australian Technical Advisory Group on Immunisation (ATAGI) recommends for adult hepatitis B vaccination in the event of unavailability of either of the two brands of the adult formulation of hepatitis B vaccines (1mL per dose) are either:

- Concurrent* administration of two doses of the paediatric formulation of a hepatitis B vaccine (0.5 mL per dose), *OR*
- Administration of an adult dose of the combined hepatitis A and hepatitis B vaccine (Twinrix[®]) – there may be further dose requirements of hepatitis A-containing vaccine if protection against hepatitis A is also desired. If the adult Twinrix[®] formulation is not available, each of the required adult Twinrix[®] dose can be substituted by 2 concurrently* administered doses of Twinrix[®] Junior.

* The doses can be concurrently administered at adjacent sites (≥ 2.5 cm apart) on the same arm *or* separately with one dose in each arm

The original vaccination schedule should be maintained. While using the same brand product is preferable, use of the alternative brand product to complete the vaccination course is acceptable.

For immunocompetent individuals with documented serology results demonstrating an adequate immune response to hepatitis B vaccination at any time at least 4 weeks after completion of the primary course (hepatitis B surface antibody [anti-HBs antibody] levels ≥ 10 mIU/mL tested at least 4 weeks after the final dose), further booster dose of hepatitis B vaccination **are not necessary and are therefore not recommended**.

Background: supply shortage of the adult formulation of hepatitis B vaccines

Due to a manufacturing halt of Engerix-B[®] from November 2016, there is currently a shortage of the adult formulation of Engerix-B[®] available to Australia,¹ which is expected to continue until at least February 2018.² Subsequent to this, there have also been periods of shortage of both the adult and the paediatric formulation of the alternative brand, H-B-Vax II[®], as well as Twinrix[®], the combination hepatitis A and hepatitis B vaccine.²

Supply for the National Immunisation Program has not been affected at this time, so vaccination using the adult formulation of hepatitis B vaccines should continue as scheduled for eligible individuals. However, the shortage has impacted on private market supply for others who require hepatitis B vaccination, including healthcare workers. As of early February 2018, the paediatric formulation of Engerix-B[®] as well as both the adult and the paediatric formulation of Twinrix[®] are available.²

Unnecessary vaccinations should be avoided

- For immunocompetent individuals in whom there is documented serology results demonstrating an adequate immune response to hepatitis B vaccination after completion of the primary course (hepatitis B surface antibody [anti-HBs antibody] levels ≥ 10 mIU/mL tested at least 4 weeks after the final dose), any further booster dose of hepatitis B vaccination is not necessary and not recommended, even if subsequent serology test shows an anti-HBs antibody level to be < 10 mIU/mL.
- With the inclusion of hepatitis B vaccination for infants in the National Immunisation Program since 2000 as well as the nation-wide catchup program for adolescents until 2013, most Australian-born persons aged < 18 years would have completed a hepatitis B vaccination course. Their vaccination records should be checked on the Australian Immunisation Register before considering the need of any further doses of hepatitis B vaccination.

Recommended alternative vaccination strategies

Adults requiring completion of hepatitis B vaccination (aged ≥ 20 years, requiring 1.0 mL per dose)

The original vaccination schedule should not be altered – the standard 3-dose schedule consists of 1.0 mL of the adult formulation to be administered at 0, 1 and 6 months. (The 4-dose accelerated schedules should only be used for those persons with an imminent risk of exposure, such as those intending to travel to hepatitis B endemic areas with a very limited time before departure).³

In the event that neither of the brands of the adult formulation (1.0 mL per dose) is available, each of the doses can be substituted with either of these two alternatives:

A) Substitute a dose with concurrent administration of two doses of a paediatric formulation

The paediatric and adult formulations of Engerix-B[®] are identical in composition and concentration. They differ only in volume.⁴ This is also true of H-B-VAX II[®] paediatric and adult formulations.⁵ Although Engerix-B[®] and H-B-Vax II[®] are formulated differently¹, the adult formulation volume for both brands is 1.0 mL per dose, and the paediatric formulation volume is 0.5 mL per dose. Hence the options are either:

- i) Two concurrent doses of Engerix-B[®] paediatric formulation 0.5 mL (10 µg/0.5 mL) per dose; *OR*
- ii) Two concurrent doses of H-B-Vax II[®] paediatric formulation 0.5 mL (5 µg/0.5 mL) per dose.

Although this practice may not be ideal, ATAGI considers it acceptable in terms of safety and effectiveness in the event of supply shortage of the adult formulations.

Both paediatric formulations are only available as pre-filled syringes in Australia. Pre-filled syringes should be administered as separate injections. Doses **should not** be transferred into a single syringe for administration, due to the risk of contamination and dosing errors.

Although there is no preference for site of additional doses, injections at adjacent sites on the same arm should be at least 2.5 cm apart.³ Concurrent mixed use of one paediatric dose each of Engerix-B[®] and H-B-Vax II[®] is not recommended, as efficacy is unclear.

Where possible the same brand of hepatitis B vaccine should be used over the entire course. Where circumstances prevent this, ATAGI considers it acceptable to complete a course with the other brand.³

B) Substitute a dose with an adult dose of Twinrix[®]

A single dose of the adult formulation of Twinrix[®] contains 720 ELISA units of hepatitis A virus antigen and 20 µg of hepatitis B surface antigen per 1.0 mL; the hepatitis B surface antigen content in an adult dose of Twinrix[®] is equivalent to that in a 1.0 mL dose of Engerix-B[®]. Each single dose of the paediatric formulation of Twinrix[®] (Twinrix[®] Junior) consist of half of the volume of the adult formulation of Twinrix[®] (i.e. 0.5 mL per dose of Twinrix[®] Junior), but the concentration of hepatitis A virus antigen and hepatitis B surface antigen is equivalent to that as in the adult formulation.³

For adults who have not previously been vaccinated against either hepatitis A or hepatitis B, completing a course of Twinrix[®], according to the standard 3-dose schedule at 0, 1 and 6 months, would provide adequate protection against both hepatitis A and hepatitis B infection.

Where a course of Engerix-B[®] or H-B-Vax II[®] vaccination has commenced, completing the course according to the original schedule with adult formulation Twinrix[®] would provide adequate protection against hepatitis B. However, further dose(s) of a hepatitis A-containing vaccine will be required if long-term protection against hepatitis A is also desired or indicated. For completing the hepatitis A vaccination requirements:

- If only one dose of Twinrix[®] was received as a substitute for completing a hepatitis B vaccination course, the options are to give either:
 - A complete course of a hepatitis A vaccine (any brand), i.e. two doses 6–12 months apart; *OR*
 - Two more doses of Twinrix[®], at 1 and 6 months after the first (i.e. a 3-dose Twinrix[®] course).
Note: If the first dose of Twinrix[®] was used as the substitute for the second dose of the hepatitis B vaccination course and this Twinrix[®] schedule is followed, the hepatitis B vaccination course is regarded as complete only after the third Twinrix[®] dose is completed, due to minimum interval requirements of hepatitis B vaccination between dose 2 and dose 3.
- If a total of two doses of Twinrix[®] were received as a substitute for completing a hepatitis B vaccination course (as doses 2 and 3, respectively), one more dose of Twinrix[®] or a hepatitis A vaccine, to be given 5–12 months after the latest dose of Twinrix[®], is required to complete the hepatitis A vaccination course.

In the event that the adult Twinrix[®] formulation is not available, each of the required adult Twinrix[®] dose can be substituted by 2 concurrently administered doses of Twinrix[®] Junior.

Adolescents aged 11–15 years requiring catch-up of hepatitis B vaccination

The use of two doses of the **adult** formulation of a hepatitis B vaccine given 6 months apart (a 0-, 6-month schedule) is an alternative schedule for adolescents aged 11–15 years, and has been the schedule used in previous school-based hepatitis B vaccination programs for 11–15 year olds in most states and territories.

For adolescents **aged 11–15 years** who require catch-up hepatitis B vaccination, in the event of unavailability of the adult formulation of the hepatitis B vaccine:

- For those who have previously received an adult formulation (1.0 mL per dose) as their first dose and are due for the second dose, two doses of the paediatric formulation can be administered concurrently as the substitute dose if at least 4 months have elapsed since the previous dose of adult formulation.
- For those in this age group who have never received any hepatitis B vaccines, the options are:
 - To administer concurrently two doses of the paediatric formulation (0.5mL per dose) of the hepatitis B vaccine as a substitute for each of the adult formulation dose, according to a 2-dose schedule, to be given 6 months apart (a 0-, 6-month schedule); *OR*

¹Concentration of the hepatitis B surface antigen in Engerix-B[®] is 20 µg/mL, compared to 10 µg/mL in H-B-Vax II[®]. Given that these two products are formulated differently, comparison of vaccine efficacy on a per-weight basis is not appropriate.

- To use the paediatric formulation (0.5mL per dose), administered according to the standard 3-dose schedule at 0, 1 and 6 months; *OR*
- To give two doses of the **adult** formulation of Twinrix[®] (1.0mL per dose), 6 months apart – completion of these two doses would provide protection against both hepatitis A and hepatitis B.

References

1. GlaxoSmithKline. GSK hepatitis B vaccine availability, 18 August 2017. Melbourne: GlaxoSmithKline; 2017 [accessed 8 August 2017]: <http://au.gsk.com/en-au/media/press-releases/2017/gsk-hepatitis-b-vaccine-availability/>.
2. Therapeutic Goods Administration (TGA). Hepatitis B surface antigen recombinant – medicine shortage information. Canberra: Therapeutic Goods Administration; 2017 [accessed 05 February 2018]: <http://apps.tga.gov.au/Prod/msi/Search/Details/hepatitis-b-surface-antigen-recombinant>.
3. Australian Technical Advisory Group on Immunisation (ATAGI). The Australian immunisation handbook. 10th ed (updated July 2016). Canberra: Australian Government Department of Health; 2016. <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home~handbook10part4~handbook10-4-5>
4. GlaxoSmithKline. ENGERIX[®]-B Product information. Canberra: Therapeutic Goods Administration; 2013.
5. Merck Sharp & Dohme. H-B-VAX[®] II Product information. Canberra: Therapeutic Goods Administration; 2014.